सी डी एफ डी
CDFD

वार्षिक प्रतिवेदन

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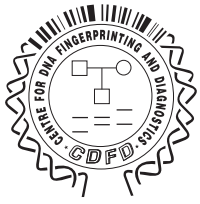

डी एन ए फिंगरप्रिंटिंग एवं निदान केन्द्र

नामपल्ली, हैदराबाद - 500 001

Centre for DNA Fingerprinting and Diagnostics

Nampally, Hyderabad - 500 001

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अधिदेश

सीडीएफडी सोसाइटी के संगम ज्ञापन तथा नियम एवं विनियमों में बताए गए के अनुसार डीएनए फिंगरप्रिंटिंग एवं निदान केन्द्र की स्थापना जिन उद्देश्यों के लिए हुई वे निम्न प्रकार हैं :

i. पितृत्व विवाद, आप्रवास, और अस्पतालों में नवजात शिशुओं की अदला-बदली जैसे मामलों में निजी पक्षों सहित विविध अभिकरणों के लिए पर्याप्त अदायगी पर डीएनए प्रोफाइलिंग और उससे संबंधित विश्लेषण का वैज्ञानिक अनुसंधान करना।

ii. अपराध अन्वेषण अभिकरणों को डीएनए फिंगरप्रिंटिंग और उससे संबंधित विश्लेषण तथा सुविधाएँ प्रदान करना।

iii. अपराध अन्वेषण और परिवार मामलों में डीएनए प्रोफाइल विश्लेषण और उससे संबंधित तकनीकों के साक्ष्य संबंधी मूल्य को समझने में पुलिस कर्मियों, न्यायिक वैज्ञानिकों, वकीलों तथा न्यायपालिका की सहायता करना।

iv. आनुवंशिक अव्यवस्थाओं को संसूचित करने हेतु डीएनए नैदानिक विधियाँ सिद्ध करना और इस प्रकार के संसूचन के लिए संपरीक्षाएँ विकसित करना।

v. पादप और जंतु कोशिका माल, कोशिका लाइनों के प्रामाणीकरण के लिए डीएनए फिंगरप्रिंटिंग तकनीकों का उपयोग करना और ऐसे प्रयोजनों के लिए आवश्यकतानुसार नई संपरीक्षाएँ विकसित करना।

vi. डीएनए फिंगरप्रिंटिंग तकनीकों पर प्रशिक्षण प्रदान करना।

vii. मूलभूत, अनुप्रयुक्त अनुसंधान एवं विकास कार्य करना।

viii. देश में चिकित्सा संस्थाओं, जन-स्वास्थ्य अभिकरणों और उद्योग को परामर्शी सेवाएँ प्रदान करना।

ix. केंद्र के उद्देश्यों से संगत क्षेत्रों में विदेशी अनुसंधान संस्थाओं एवं प्रयोगशालाओं और अन्य अंतर्राष्ट्रीय संगठनों के साथ सहयोग करना।

x. अनुसंधान छात्रों को स्नातकोत्तर उपाधियों के लिए पंजीकृत कर सकने के प्रयोजन हेतु उच्चतर अधिगम के मान्यता प्राप्त विश्वविद्यालयों एवं संस्थाओं के साथ संबंधन स्थापित करना।

xi. भारत सरकार, राज्य सरकारों, देश में स्थित पूर्त संस्थाओं/न्यासों, व्यक्तियों और उद्योग से नकद के रूप में या अन्य रूपों में अनुदान, दान एवं अंशदान प्राप्त करना।

xii. केंद्र सरकार के पूर्व अनुमोदन से प्रशिक्षण कार्यक्रमों, वैज्ञानिक अनुसंधान और अन्य गतिविधियों के लिए अंतर्राष्ट्रीय संगठनों सहित विदेशी स्रोतों से आर्थिक सहायता प्राप्त करना।

xiii. केंद्र की गतिविधियों को चलाने के लिए जैसा आवश्यक या सुविधाजनक हो, कोई भी संपत्ति चल या अचल या भवनों एवं निर्माणों को निर्मित करने, सुधार करने, परिवर्तित करने, गिरा देने या मरम्मत करने हेतु उपहार, क्रय, विनिमय, पट्टा, भाड़े पर लेने द्वारा या अन्यथा किसी भी तरह अर्जित करना।

xiv. केंद्र के प्रयोजन हेतु, भारत सरकार और अन्य प्रोनोटों, विनिमय पत्रों, चैक या अन्य परक्राम्य लिखतों को आहरित करना और स्वीकार करना, तैयार करना और पृष्ठांकित करना, बट्टा करना और परक्रामण करना।

xv. केंद्र को सौंपी गई निधियों या धन को निवेश करने के लिए, ऐसी प्रतिभूतियों को खोलने या ऐसे तरीके से, जो कि समय-समय पर शासी परिषद् द्वारा निर्धारित किए जाते हैं, इस प्रकार के निवेश को विक्रय या पक्षांतरण करना।

xvi. उक्त सभी उद्देश्यों या उनमें से किसी उद्देश्य की प्राप्ति के लिए सभी ऐसे अन्य विधिसम्मत कार्य, जैसा आवश्यक, प्रासंगिक या सहायक हो, करना।

xvii. केंद्र के उद्देश्यों को वास्तविक बनाने के लिए प्रोफेसरियों, अन्य संकाय पदों, अभ्यागत अध्येतावृत्तियों सहित अध्येतावृत्तियों, अनुसंधान एवं संवर्ग पदों, छात्रवृत्तियों आदि को संस्थापित करना।

xviii. केंद्र के वैज्ञानिक एवं प्रौद्योगिकीय कार्य के लिए प्रयोगशालाओं, कर्मशालाओं, भंडार, पुस्तकालय, कार्यालय और अन्य सुविधाओं को स्थापित करना।

xix. तकनीकी जानकारी को उद्यमकर्ताओं और उद्योगों से प्राप्त या उनको अंतरण करना; और

xx. पेटेंटों, डिज़ाइनों एवं तकनीकी जानकारी जो कि केंद्र द्वारा विकसित की गई हो, को पंजीकृत करना और केंद्र के हित में ऐसे पेटेंटों/डिज़ाइनों/तकनीकी जानकारी के किसी भाग को अंतरण करना।

MANDATE

The objectives for which the Centre for DNA Fingerprinting and Diagnostics (CDFD) was established, as enumerated in Memorandum of Association and Rules and Regulations of CDFD Society, are as follows:

i. To carry out scientific research pertaining to DNA profiling and related analysis in civil cases like paternity disputes, immigration, and exchange of newborns in hospitals, for various agencies including private parties, on appropriate payment;

ii. To provide DNA fingerprinting and related analysis and facilities to crime investigation agencies;

iii. To assist police personnel, forensic scientists, lawyers and the judiciary in understanding the evidential value of the DNA profile analysis and related techniques in crime investigation and family matters;

iv. To establish DNA diagnostic methods for detecting genetic disorders and to develop probes for such detection;

v. To use DNA fingerprinting techniques for the authentication of plant and animal cell material, cell lines and to develop new probes where necessary for such purposes;

vi. To provide training in DNA fingerprinting techniques;

vii. To undertake basic, applied and developmental R & D work;

viii. To provide consultancy services to medical institutions, public health agencies and industry in the country;

ix. To collaborate with foreign research institutions and laboratories and other international organizations in fields relevant to the objectives of the Centre;

x. To establish affiliation with recognized universities and institutions of higher learning for the purpose of enabling research scholars to register for post-graduate degrees;

xi. To receive grants, donations and contributions in cash or in other forms from the Government of India, State Governments, Charitable Institutions/Trusts, individuals and industry within the country;

xii. To receive, with the prior approval of the Central Government, monetary assistance from foreign sources including international organizations for training programmes, scientific research and other activities;

xiii. To acquire by gift, purchase, exchange, lease, hire or otherwise howsoever, any property movable or immovable or to construct, improve, alter, demolish or repair buildings and structures as may be necessary or convenient for carrying on the activities of the Centre;

xiv. For the purpose of the Centre, to draw and accept, make and endorse, discount and negotiate Government of India and other Promissory Notes, Bills of Exchange, Cheques or other Negotiable Instruments;

xv. For investing the funds of or money entrusted to the Centre, to open such securities or in such manner as may from time to time be determined by the Governing Council and to sell or transpose such investment;

xvi. To do all such other lawful acts as may be necessary, incidental or conducive to the attainment of all or any of the above objectives;

xvii. To institute Professorships, other faculty positions, fellowships including visiting fellowships, research and cadre positions, scholarships, etc. for realizing the objectives of the Centre;

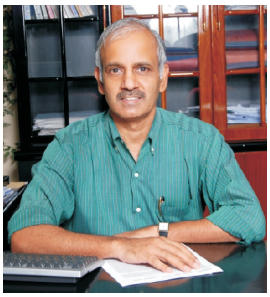
xviii. To establish, maintain and manage laboratories, workshops, stores, library, office and other facilities for scientific and technological work of the Centre;

xix. To acquire or transfer technical know-how from/to entrepreneurs and industries; and

xx. To register patents, designs & technical know-how that may be developed by the Centre and transfer any portion of such patents/designs/technical know-how in the interest of the Centre.

निदेशक का संदेश
From the Director’s Desk

निदेशक का संदेश



अपने सहयोगियों और स्वयं की ओर से वर्ष 2010-2011 के लिए सीडीएफडी की वार्षिक रिपोर्ट पेश करते हुए मुझे हार्दिक खुशी हो रही है । यह केंद्र विशिष्ट रुप से दो प्रकार की गतिविधियों का संचालन करता है, पहली गतिविधि कानून प्रवर्तन एजेंसियों का संचालन करता है, पहली गतिविधि कानून प्रवर्तन एजेंसियों के लिए डीएनए प्रोफाइलिंग और आनुवंशिक विकारों के लिए नैदानिक परीक्षणों के दो क्षेत्रों में सेवाएं प्रदान करना है, और दूसरी गतिविधि आधुनिक जीव विज्ञान के विभिन्न विषयों में अत्याधुनिक बुनियादी अनुसंधान है जिसे इस प्रकार अंजाम दिया जाता है कि प्रत्येक एक दूसरे का सहयोग करते हैं और बदले में एक दूसरे से लाभान्वित भी होते हैं । मुझे यकिन है कि यह सहजीविता हमारे वार्षिक रिपोर्ट में वर्णित अधिकांश कार्यों में प्रमाणित होगी ।

अपनी अपेक्षाकृत छोटी प्राध्यापक क्षमता (एक मामूली-आकार के विश्वविद्यालय विभाग के समान) के साथ इस केंद्र ने समीक्षाधीन अवधि में अंतराराष्ट्रीय सहकर्मी समीक्षा संबंधी पत्रिकाओं में प्रकाशनों का एक प्रभावशाली रिकॉर्ड हासिल किया है । अपनी कामयाबी के रास्ते में इसे कई पुरस्कार और सम्मान प्राप्त हुए हैं जिनमें आंध्र प्रदेश विज्ञान अकादमी के प्रो. ई. ए. सिद्धिक को पद्म श्री पुरस्कार, फैलोशिप (शेखर सी मांडे) और एसोसिएट फैलोशिप (एचए नागाराजाराम, आकाश रंजन और अभिजीत ए सरदेसाई), नेशनल एकेडमी ऑफ साइंसेज की फैलोशिप (संगीता मुखोपाध्याय) और रामलिंगास्वामी फैलोशिप (श्वेता त्यागी) शामिल हैं; रोहित जोशी रामानुजन फैलोशिप, वेलकम ट्रस्ट डीबीटी इंडिया एलायंस के इंटरमीडिएट फैलोशिप और आविष्कारी युवा बायोटेक्नोलॉजिस्ट पुरस्कार के प्राप्तकर्ता रहे हैं । समीक्षाधीन अवधि के दौरान केंद्र कार्यरत नौ अनुसंधान विद्वानों को मणिपाल विश्वविद्यालय द्वारा पीएचडी की उपाधि से सम्मानित किया गया ।

केंद्र द्वारा किये गए कार्यों के विवरण से, जिन्हें इस रिपोर्ट में किसी स्थान पर वर्णित किया गया है, मैं नीचे कुछ विशेष बातों पर प्रकाश डाल रहा हूँ जो अनिवार्य रुप से विस्तृत नहीं हैं । डीएनए फिंगरप्रिंटिंग सेवाओं की प्रयोगशाला द्वारा निपटाया गया एक प्रमुख मामला मई 2010 में मंगलौर में एक एयर इंडिया एक्सप्रेस यात्री विमान की हवाई दुर्घटना के शिकार लोगों की पहचान का था । हमारी जानकारी में यह इस देश की पहली ऐसी कार्यवाही थी जिसमें एक बड़े पैमाने की आपदा के पीड़ितों की डीएनए आधारित पहचान सामायिक तरीके से की गई थी । हमारा विश्लेषण जो उन 22 पीड़ितों के अवशेषों पर किया गया था जिनके लिए उनके रिश्तेदारों ने पहले दावा नहीं किया था, इस विश्लेषण ने निर्णायक रुप से यह बताया कि पहले के कुछ दावे वास्तव में गलत थे जिससे यह सुझाव निकल कर सामने आया कि भविष्य में आपदा प्रबंधन प्रोटोकॉल को एक ऐसी नीति का पालन करना चाहिए जिसके अनुसार रिश्तेदारों को मृतक के अवशेष केवल उपयुक्त और प्रामाणिक पहचान (जैसे कि डीएनए परीक्षण) का काम पूरा होने के बाद ही सौंपा जाना चाहिए ।

नैदानिक प्रभाग ने इस वर्ष लगभग 1650 रोगियों कोआनुवंशिक मूल्यांकन और परामर्श प्रदान किया है । हैदराबाद के निज़ाम आयुर्विज्ञान संस्थान में स्थापित चिकित्सा आनुवंशिकी इकाई (मेडिकल जेनेटिक्स यूनिट) बाह्यरोगी रेफरल सेवाओं की पेशकश का सफलतापूर्वक संचालन कर रही है और एक चिकित्सा आनुवंशिकी (मेडिकल जेनेटिक्स डिपार्टमेंट) प्रभाग बनाने की प्रक्रिया शुरु कर दी गई है ।

जीनोमिक्स और प्रोफाइलिंग एप्लिकेशनों की प्रयोगशाला फोरेंसिक कंकाल के अवशेषों की पहचान के लिए मानव और गैर मानव डीएनए युक्त मिश्रण से मानव डीएनए के संवर्धन के लिए उत्कृष्ट रणनीतियों के विकास की दिशा में काम कर रही है । यह प्रयोगशाला आणविक मार्करों के विकास कार्य में भी संलग्न है जो केला, काली मिर्च, आलू, गन्ना और वनीला जैसे टिशु कल्चर से उत्पन्न महत्वपूर्ण फसली पौधों के ट्रू टू टाइप परीक्षण के लिए उपयोगी होगा ।

इस वर्ष बासमती डीएनए विश्लेषण के एपीडा सीडीएफडी केंद्र ने बासमती चावल की शुद्धता के लिए इसके 200 सेअधिक नमूनों का परीक्षण किया है ।

आण्विक आनुवंशिकी की प्रयोगशाला ने लिंग निर्धारण जीनों बॉम्बिक्स मोरी के साथ साथ सिल्कमोथ्स, एन्थरिया एसामा और ए. माइलिट्टा में डबलसेक्स (डीएसएक्स) और इंटरसेक्स (आईएक्स) के होमोलॉगों की पहचान और विशेषता बताई है । इस समूह ने इन सिलिकोऔर प्रायोगिक विधियों का संयुक्त रुप से उपयोग करते हुए चार बी. मोरी न्यूक्लियोपोलीहेड्रोसिस वायरस एनकोडेड miRNAs की भी पहचान की है ।

संरचनात्मक जीव विज्ञान (स्टक्चरल बायोलॉजी) की प्रयोगशाला ने GroEL1 के विरुद्ध उत्पन्न मोनोक्लोनल एंटीबॉडी का उपयोग कर माइकोबैक्टीरियम ट्युबरकुलोसिस में चिप चिप (ChIP-chip) प्रयोगों को निष्पादित किया है । माइक्रोआरेडेटा से पता चलता है कि GroEL1 मुख्य रुप से जीनोम के कोडिंग क्षेत्रों और जीसी समृद्ध क्षेत्रों से जुड़ता है ।

स्तनधारी आनुवंशिकी की प्रयोगशाला में किए गए कार्यों के माध्यम से यह दिखाया गया है कि इपिजेनेटिक रीप्रोग्रामिंग और कार्सिनोजेनेसिस में शामिल डीएनए मिथाइलट्रांसफरेज़ *DNMT3L* के बीच एक मजबूत समसंबंध मौजूद है । यह भी दिखाया गया है कि अन्य डीएनए मिथाइलट्रांसफरेज़ के विपरीत *Dnmt2* कोशिकीय तनाव के दौरान आरएनए प्रसंस्करण में शामिल रहता है ।

इस केंद्र के आण्विक कैंसर विज्ञान समूह से प्राप्त परिणामों ने प्रारंभिक अवस्था के मलाशय के कैंसर के विशिष्ट नैदानिक व्यवहार में अंतर्दृष्टि प्रदान की है । इनके कार्यों ने दिखाया है कि *ARID1B* जो SWI/SNF क्रोमैटिन रीमॉडलिंग कॉप्लेक्स का एक घटक है, संभवतः अग्नाशय के कैंसर के लिए एक उत्कृष्ट ट्युमर अवरोधक जीन है ।

इम्युनोलॉजी की प्रयोगशाला डॉक्सोरुबिसिन की मध्यस्थता वालेएपोप्टोसिस पर Ras और p53 की भूमिकाओं का पता लगाने में गहनता से जुटी हुई है । सीडीएफडी के सेल सिग्नलिंग समूह द्वारा युकेरियोटिक सेल फिज़ियोलॉजी के विनियमन का अध्ययन किया जा रहा है जिसमें विशेष रुप सेआइनोसाइटोल पाइरोफॉस्फेटों द्वारा एक्टिन साइटोस्केलेटन डायनोमिक्स और सेल माइग्रेशन का संदर्भ लिया गया है ।

एम. ट्यूबरकुलोसिस में प्रोमोटरों और ट्रान्सक्रिप्शन फैक्टर बाइंडिंग साइटों की पहचान और लाक्षणिक विशेषता से संबंधित प्रोजेक्टों, ई. कोलाई के एक जीनोम आधारित प्रोटीन प्रोटीन कार्यात्मक लिंकेज नक्शेके पुनर्निमाण और प्रोटियोम पर एटी प्रचुरता के प्रभाव को समझने के लिए पी. फैल्सीपेरम के जीनोम विश्लेषण का कार्य कम्प्यूटेशनल और कार्यात्मक जीनोमिक्स प्रायोगशाला द्वारा पूरा किया जा रहा है । कम्प्यूटेशनल बायोलॉजी समूह ने बीमारियों और तटस्थ nsSNPs का पूर्वानुमान करनेके लिए एक उत्कृष्ट, उच्च क्षमता वाली एसवीएम आधारित विधि विकसित की है ।

जीवाणु आनुवंशिकी की प्रयोगशाला में एस्केरीकिया कोलाई में रोडिपेंडेंट टान्सक्रिप्शन टर्मिनेशन में NusA के लिए एक भूमिका का प्रदर्शन किया गया है और न्युक्लियोइड प्रोटीनों के एच एनएस परिवार द्वारा टर्मिनेशन प्रक्रिया के मॉड्यूलेशन के लिए एक मॉडल प्रस्तावित किया गया है । रो डिपेंडेंट टर्मिनेशन के लिए दोषपूर्ण स्टेंस में निर्मित आर लूप्स RNase E के दोमार्गों की अनुपस्थिति के लिए एक बाईपास प्रणाली प्रदान करती हुई दिखाई दे रही है । अंत में, ArgP ट्रान्सक्रिप्शनल रेगुलेटर के कई नए लक्ष्यों की पहचान की गई है जिनमें *lysP*, *dapD*, *asd*, *lysA* और *lysC* शामिल हैं ।

हैदराबाद के मेसर्स सैंडोर प्रोटिओमिक्स कोअपनेउपकरणों के संचालन कोआउटसोर्स करने का केंद्र का उद्यम काफी अच्छा प्रदर्शन कर रहा है और यह व्यवस्था केन्द्र के लिए आप तटस्त रही है । केंद्र ने अपने स्वामित्व वाली और पेटेंटशुदा उच्च क्षमता की तकनीकों के व्यवसायीकरण के अपने प्रयासों के तहत हैदराबाद के लाइफ साइंस इन्क्युबेटर, आईकेपी नॉलेज पार्क के साथ एक समझौता ज्ञापन में प्रवेश किया है; इस व्यवस्था के तहत इन तकनीकों के अनुसंधान और विकास के लिए तीन सीडीएफडी आईकेपी फेलोनियुक्त किये गए हैं ।

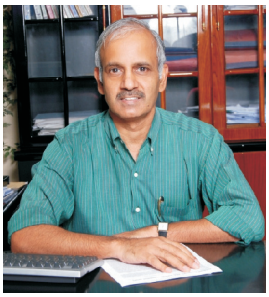
मैं इस साल केंद्र के परिसर के मुद्दों से संबंधित दो नई बातों पर भी रिपोर्ट करना चाहता हुँ । भारत सरकार के विज्ञान और प्रौद्योगिकी मंत्रालय के विज्ञान और प्रौद्योगिकी विभाग की पहल पर सीडीएफडी और सर्वे ऑफ इंडिया (SoI) के बीच एक समझौता ज्ञापन पर हस्ताक्षर किया जाना है जिसके द्वारा केंद्र हैदराबाद के उप्पल में सर्वे ऑफ इंडिया (SoI) की 20 एकड़ जमीन पर अपना नया परिसर बनाएगा और बदले में सर्वे ऑफ इंडिया (SoI) गंडिपेट में सीडीएफडी की जमीन और भवनों का उपयोग अपनी विशिष्ट गतिविधियों के लिए करेगी । इसके अलावा, चूंकि नामपल्ली में सीडीएफडी के वर्तमान परिसर में जानवर संबंधी सुविधा नहीं है, इसलिए शमीरपेट (नामपल्ली से~45 किमी. दूर) में स्थित मेसर्स विम्टा लैब्स की पहचान केंद्र की प्रयोगशाला संबंधी जानवर प्रयोग सेवाओं के लिए स्थान और बुनियादी सुविधाएं प्रदान करनेके लिए की गई है ।

इस रिपोर्ट में वर्णित सभी कार्यों के लिए मैं वैज्ञानिक, तकनीकी और प्रशासनिक कैडरों में अपने सहयोगियों के साथ साथ केंद्र में विभिन्न परियोजनाओं में कार्यरत कर्मचारियों और छात्रों के योगदान और उनके सहयोग को पूरी ईमानदारी से स्वीकार करता हूँ । इस वर्ष के दौरान हम जैव प्रौद्योगिकी विभाग के अधिकारियों और समाज, प्रशासकीय परिषद, अनुसंधान क्षेत्र के पैनलों की वैज्ञानिक सलाहकार समिति (आरएपी-एसएसी), वित्तीय समिति, भवन समिति और सीडीएफडी की अन्य अनौपचारिक विशेषज्ञ समितियों के प्रतिष्ठित सदस्यों के महत्वपूर्ण सलाह, समर्थन और प्रोत्साहन से लाभान्वित हुए हैं । आने वाले वर्षों में हम अपनी गतिविधियों के सभी क्षेत्रों में अधिक से अधिक ऊंचे मुकामों कोहासिल करने का निरंतर प्रयास करते रहेंगे ।

ज गौरीशंकर

31 मार्च 2011

Director's Message



On behalf of my colleagues and myself, I am delighted to present the Annual Report of CDFD for the year 2010-11. The Centre uniquely combines two kinds of activities, the first being those of services in the twin areas of DNA profiling for law-enforcement agencies and diagnostic tests for genetic disorders, and the second that of cutting-edge basic research in various disciplines of modern biology, in such a way that each supports and in turn is enriched by the other. I am sure that this symbiosis will be evident in much of the work that is described in the Annual Report.

With its relatively small faculty strength (similar to that of a modest-sized University department), the Centre has achieved an impressive record of publications in international peer-reviewed journals in the reporting period. Several awards and honours have come its way, including the award of Padma Shree to Prof EA Siddiq, Fellowship (Shekhar C Mande) and Associate Fellowships (HA Nagarajaram, Akash Ranjan and Abhijit A Sardesai) of the Andhra Pradesh Akademi of Sciences, Fellowship of the National Academy of Sciences (Sangita Mukhopadhyay), and Ramalingaswamy Fellowship (Shweta Tyagi); Rohit Joshi has been recipient of the Ramanujan Fellowship, Intermediate Fellowship of the Wellcome Trust-DBT India Alliance and Innovative Young Biotechnologist Award. During the reporting period, nine research scholars working at the Centre were awarded PhD by the University of Manipal.

From the details of the work undertaken by the Centre that are given elsewhere in the Report, I give below a few highlights, not necessarily exhaustive. A major case undertaken by the Laboratory of DNA Fingerprinting Services was the identification of victims of the air crash involving an Air India Express passenger flight at Mangalore in May 2010. This exercise represents, to our knowledge, the first in this country wherein DNA based identification of victims from a mass disaster was undertaken in a time-sensitive manner. Our analysis, which was done on the remains of 22 victims who had not earlier been claimed by relatives, showed conclusively that some of the earlier claims had indeed been erroneous, thereby suggesting that disaster management protocols in future must follow a policy of release of mortal remains to relatives only after suitable and authentic identification (such as by DNA testing) is completed.

The Diagnostics Division provided genetic evaluation and counselling to about 1650 patients this year. The Medical Genetics Unit established at Nizam's Institute of Medical Sciences, Hyderabad has been operating successfully to offer outpatient referral services, and the process of creating a Department of Medical Genetics has been initiated.

The Laboratory of Genomics and Profiling Applications is working towards the development of novel strategies for enrichment of human DNA from mixtures containing human and non-human DNA for identification of forensic skeletal remains. This laboratory is also involved in developing molecular markers which would be useful for true-to-type testing of important tissue-culture raised crop plants like banana, black pepper, potato, sugarcane and vanilla. During this year, the APEDA-CDFD Centre for Basmati DNA Analysis tested more than 200 basmati rice samples for their purity.

The Laboratory of Molecular Genetics has identified and characterised sex determining genes – the homologs of *doublesex (dsx)* and *intersex (ix)* genes in *Bombyx mori* as well as in wild silkmoths, *Antheraea assama* and *A. mylitta*. The group has also identified four *B. mori* nucleopolyhedrosis virus encoded miRNAs using a combination of *in silico* and experimental methods.

The Laboratory of Structural Biology has carried out ChIP-chip experiments in *Mycobacterium tuberculosis* using monoclonal antibody raised against GroEL1. The mircoarray data reveal that GroEL1 binds predominantly to the coding regions and to GC-rich regions of the genome.

Through the work carried out in the Laboratory of Mammalian Genetics, it has been shown that a strong correlation exists between the DNA methyltransferase *DNMT3L* involved in epigenetic reprogramming and carcinogenesis. It has also been shown that, unlike other DNA methyltransferases, *Dnmt2* is involved in RNA processing during cellular stress.

Result from the Molecular Oncology group of the Centre have provided insights into the distinct clinical behaviour of early-onset rectal cancer. Their work has shown that *ARID1B*, a component of the SWI/SNF chromatin remodelling complex, is likely a novel tumor suppressor gene for pancreatic cancer.

The Laboratory of Immunology has been intensively involved in detecting the roles of Ras and p53 on doxorubicin-mediated apoptosis. The Cell Signalling Group of CDFD has been studying the regulation of eukaryotic cell physiology, with particular reference to actin cytoskeleton dynamics and cell migration, by inositol pyrophosphates.

Projects related to identification and characterization of promoters and transcription factor binding sites in *M. tuberculosis*, reconstruction of a genome-wide protein-protein functional linkage map of *Escherichia coli,* and genome analysis of *P. falciparum* to understand the effect of AT-richness on the proteome, have been carried out by the Laboratory of Computational and Functional Genomics. The Computational Biology Group has developed a novel, high performing SVM-based method to predict disease and neutral nsSNPs.

In the Laboratory of Bacterial Genetics, a role for NusA in Rho-dependent transcription termination in *E. coli* has been demonstrated, and a model has been proposed for modulation of the termination mechanism by the H-NS family of nucleoid proteins. R-loops formed in strains defective for Rho-dependent termination appear to provide a bypass mechanism for the absence of two pathways of RNase E. Finally, several new targets of the ArgP transcriptional regulator have been identified, including *lysP, dapD, asd, lysA,* and *lysC*.

The Centre's venture to outsource its equipment operations to M/s Sandor Proteomics, Hyderabad has been performing reasonably well, and this arrangement has been revenue-neutral for the Centre. The Centre has also entered into a Memorandum of Understanding with Life Science Incubator, IKP Knowledge Park, Hyderabad to further its attempts towards commercialization of high potential technologies owned and patented by it; under this arrangement, three CDFD-IKP Fellows have been recruited for research and development on these technologies.

I also wish to report on two developments this year related to the campus issues of the Centre. At the initiative of the Department of Science and Technology, Ministry of Science and Technology, Govt. of India, a Memorandum of Understanding is to be signed between CDFD and the Survey of India (SoI) by which the Centre would construct its new campus in 20 acres of SoI's land at Uppal, Hyderabad, and in turn, the latter would utilize the land and buildings of CDFD at Gandipet for their specific activities. Further, since the current campus of CDFD at Nampally does not have an animal facility, M/s Vimta Labs located at Shamirpet (~45 km from Nampally) have been identified to provide space and infrastructure support for the Centre's laboratory animal experimentation services.

For all the work described in this Report, I must sincerely acknowledge the contributions of and co-operation from my colleagues in scientific, technical and administrative cadres as well as from students and staff working in various projects at the Centre. We have also benefitted immensely during the year from the advice, support, and encouragement from the officers of the Department of Biotechnology, and the distinguished members of the Society, Governing Council, Research Area Panels-Scientific Advisory Committee (RAP-SAC), Finance Committee, Building Committee, and other *ad hoc* expert committees of CDFD. We shall continue to strive to greater heights in all spheres of our activities in the years ahead.

J Gowrishankar

March 31, 2011

सेवाएं
Services

Laboratory of DNA Fingerprinting Services

Scientist In-charge	Madhusudan R Nandineni	Staff Scientist
Other Members	SPR Prasad	Technical Officer II
	Ch V Goud	Technical Officer I
	DS Negi	Technical Officer I
	Ch Annapurna	Technical Officer I (Since Jun. 2010)
Coordinator	J Nagaraju	Staff Scientist

Objectives

1. To provide DNA fingerprinting services in cases forwarded by law-enforcing agencies and judiciary of State and Federal Governments, relating to murder, rape, paternity, maternity, child swapping, body identification, kidney transplantation, etc.

2. To develop human resources skilled in DNA fingerprinting, to cater to the needs of State and Federal Government agencies

3. To impart periodical training to manpower involved in DNA fingerprinting sponsored by State and Federal Government agencies

4. To provide advisory services to State and Federal Government agencies in establishing DNA fingerprinting facility

5. To create DNA marker databases of different caste populations of India.

Summary of services provided until the beginning of the reporting year (April 1, 2009 to March 31, 2010)

A total number of 107 cases were received for DNA fingerprinting examination during the period under report. Out of these, 49 cases are related to paternity / maternity, 47 cases are related to identification of deceased, 7 cases are pertaining to sexual assault (rape), 3 cases are related to murder and 2 cases are pertaining to biological relationship (kidney transplantation). Fifteen States of India availed DNA fingerprinting services of CDFD during this period. Rajasthan forwarded the highest number of cases (36) followed by Andhra Pradesh (20), Chhattisgarh (9), Uttar Pradesh (9), Karnataka (9), Himachal Pradesh (6), Maharashtra (5), Kerala (3), Madhya Pradesh (3), Bihar (1), Jammu & Kashmir (1), Orissa (1), Uttarakhand (1) and West Bengal (1).

Details of services provided in the current reporting year (April 1, 2010 - March 31, 2011)

Breakup of the cases during this reporting period is given below under following heads:

Identity of Deceased	57
Maternity / Paternity	40
Rape and Murder	04
Sexual Assault (Rape)	08
Kidney Transplantation	03
Total No. of Cases	**112**

Prominent cases during April 1, 2010 to March 31, 2011

Air India Express air crash case, Mangalore, Karnataka.

Deposition of evidence in Hon'ble Courts

During this reporting year, the DNA experts defended their reports in 11 cases in various Hon'ble Courts throughout the country.

Training/Lectures/Workshops on DNA fingerprinting examination

Training

1. Training on DNA fingerprinting techniques to personnel from Andhra Medical College, Department of Forensic Medicine, Visakhapatnam, Andhra Pradesh in December 2010.

2. Training on DNA fingerprinting examination has been provided to the scientists from the State Forensic Science Laboratory, Lucknow, Uttar Pradesh.

Lectures/ Workshops

1. Delivered lecture for the benefit of the students from Jankidevi Bajaj College of Science, Wardha, Maharashtra on 19.11.2010 on their visit to CDFD as part of their study tour.

2. Lecture has been delivered for the benefit of the Air Force Officers from Air Force Intelligence School, Lohegaon, Pune.

3. Lecture for the benefit of the foreign police officers from 22 different countries; coordinated by the National Crime Records Bureau (NCRB), New Delhi.

4. Delivered lecture for the benefit of the Judicial Officials from Andhra Pradesh Judicial Academy, Hyderabad.

State or Union Territory	Biological Relationship	Identity of Deceased	Maternity/ Paternity	Rape & Murder	Sexual Assault (Rape)	No. of Cases
Andaman and Nicobar Islands	0	0	1	0	0	1
Andhra Pradesh	1	3	12	0	0	16
Bihar	0	0	1	0	0	1
Chhattisgarh	0	5	4	0	0	9
Daman and Diu	0	1	0	0	0	1
Karnataka	1	3	5	1	0	10
Madhya Pradesh	0	0	2	0	0	2
Maharashtra	0	1	3	0	0	4
Puducherry	0	0	1	0	0	1
Punjab	0	4	3	0	3	10
Rajasthan	1	24	5	3	4	37
Tamil Nadu	0	0	1	0	0	1
Uttar Pradesh	0	16	1	0	1	18
Uttarakhand	0	0	1	0	0	1
Total No. of Cases	**3**	**57**	**40**	**4**	**8**	**112**

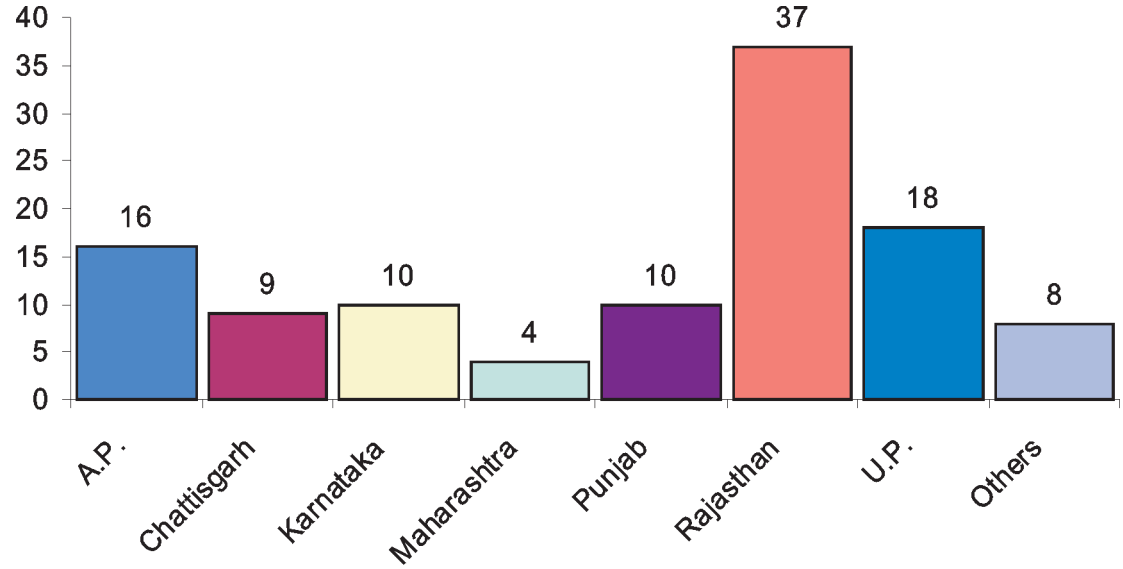


Fig. 1: Details of state-wise cases received

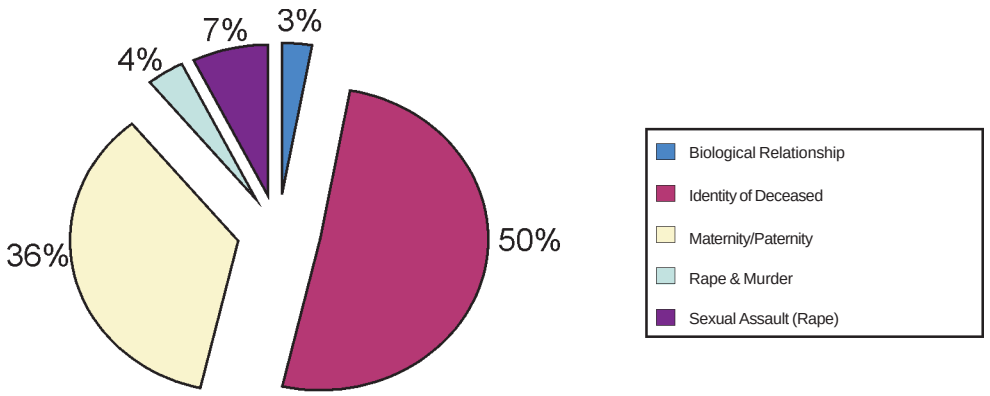


Fig. 2 : Details of types of cases received

Diagnostics Division

Principal Investigator	Ashwin Dalal	Staff Scientist
PhD Students	Anusha Uttarilli	Junior Research Fellow
	Hiranmay Joag	Junior Research Fellow
	Fahad Ahmed Khan	Junior Research Fellow
Other Members	Prajnya Ranganath	Clinical Research Associate
	P Rajitha	Technical Officer III
	KP Pooja	Technical Officer II
	GR Savithri	Technical Officer II
	Angalena Ramachandran	Technical Officer II
	Usha Rani Dutta	Technical Officer I
	Jamal Md Nurul Jain	Technical Officer I
	G Sri Lakshmi Bhavani	Research Assistant
	C Sai Shruthi	Research Assistant
	Vijay Kumar Pidugu	Project Assistant
	SN Rajashree	Project Assistant
	C Krishna Prasad	Technician II
	R Sudheer Kumar	Technician II

Objectives

1. To conduct genetic evaluation for patients / families with genetic disorders
2. To develop new methods and assays for genetic analysis and engage in research on chromosomal and single gene disorders
3. To act as national referral center for analysis and quality control of genetic tests for few genetic diseases
4. To impart training in genetic evaluation of patients with genetic disorders.

I. Services provided during the year 2010-2011

Clinical Genetics

A total of 1646 patients attended the genetic clinic for genetic evaluation and counseling, during the year 2010-11. These consisted of patients with chromosomal disorders, monogenic disorders, mental retardation, congenital malformations, inborn errors of metabolism, and familial disorders.

The Medical Genetics Unit established at Nizam's Institute of Medical Sciences, Hyderabad is running successfully and creation of Department of Medical Genetics has been initiated. A total of 365 patients were examined and counseled in the unit during 2010-11.

Genetic investigations done during 2010-11

Investigation	Total cases	Positives
Cytogenetics	774	77 (9.9%)
Proband	695	72 (10.3%)
Prenatal	79	5 (6.3%)
Molecular Genetics	593	254 (42.8%)
Proband	565	247 (43.7%)
Prenatal	28	7 (25%)
Biochemical Genetics	655	167 (25.5%)
Proband	640	162 (25.3%)
Prenatal	15	5 (33.3%)

Cytogenetics

Disease	Abnormality	No of cases
Down Syndrome	Trisomy 21	26
	46,XY,rob(21;21) +21	2
	46,XX,t(14;21)+21	1
Edward Syndrome	47,XX+18	1
Turner Syndrome	Monosomy X (45,X)	8
	iso X,(46,X,i(X))	3
	Mosaic 45,X/46,X,i(X)	1
	46,X,del(X)(q21.2;qter)	1
	45,X/46,X,dup(X)(q12q21)	1
	Mosaic 46,XX/45X	1
	Mosaic 45X/46XY	1
Klinefelter Syndrome	47,XXY	2
Sex reversal	Phenotypic female with 46,XY	5
Triple X syndrome	Mosaic 46XX/47,XXX	1
Structural chromosomal abnormalities		**9**
Inversions		
46,XY,inv(9)		1
Translocations		
46,XX,t(8;10)(q24.2;q25.2)		1
45,XY,rob(13;14)		1
46,XX,t(13;15)		1
46,XX,t(X;2)(q22;q13)		1
46,XX,t(2;18)(q31;p11.2)		1
45,XX,t(14;21)(q10;q10)		1
46,SC,t(13;14)+13		1
46,SC,t(16;20)(p13.1;p13)		1
Chromosomal breakage study for Fanconi Anemia		2

Quantitative Fluorescent Polymerase Chain Reaction (QF-PCR)

QF-PCR	No of cases	No of Positives
Prenatal	16	2 (Trisomy 21)

Biochemical Genetics

Disease/Test	Positives
Urine Metabolic Screening (207)	**57**
Amino acid disorders (N=104)	14
Maple syrup urine disease	4
Non Ketotic Hyperglycinemia	3
Hyperornithinemia	1
Tyrosinemia	1
Hyperhomocysteinemia	2
Phenylketonuria	3
Lysosomal storage disorders (N=329)	**91**
Hurler syndrome (18)	11
Hunter syndrome (15)	7
Sanfilippo B disease (13)	0
Morquio A syndrome (13)	8
Maroteaux Lamy syndrome (7)	5
Sly syndrome (2)	0
GM1-Gangliosidosis (47)	10
Chitotriosidase (26)	11
Gaucher disease (24)	1
Krabbe disease (12)	1
Pompe disease (10)	3
Pseudo Hurler polydystrophy (2)	2
Niemann Pick disease (25)	11
Mucolipidosis (4)	4

Disease/Test	Positives
Metachromatic Leukodystrophy (59)	9
Hexosaminidase A & B (48)	
Tay Sach's disease	4
Sandhoff 's disease	4
Fabry disease (2)	0
Alpha mannosidase (2)	0
Prenatal diagnosis (15)	**5**
Hexosaminidase A & B (4)	
Tay Sach's disease	2
Sandhoff disease	1
Hurler disease (3)	0
Gaucher disease (1)	1
GM1 – Gangliosidosis (2)	0
Krabbe disease (1)	0
Morquio A syndrome (1)	0
Maroteaux Lamy syndrome (3)	1

Fluorescence *in situ* Hybridization (FISH)

Disease/translocation	Probe	No. of cases	No. of positives
Prader-willi Syndrome	SNRPN(15q11)/PML(15q24)	10	2
Angelmann Syndrome	E3A(15q11)/PML(15q24)	1	1
Di-George Syndrome	TUPLE(22q11.2)/ARSA(22q13)	6	0
Williams-Beuren	ELN(7q11)/Control(7q22)	3	1
45,X,t(Y;22)	WCP-22/Y	1	1
47,XX+14(q11.1?q22)	WCP-14	1	1
46,XXt(X;20)(q13;p13)	WCP-X/20	1	1
46,XX,t(2;18)(q31;p11.2)	WCP-2	1	1
Mosaic Turner	SE(X)/(Y)	2	1

Molecular Genetics

Name of Disorder	No. of Cases	Positive	Negative		
DMD/BMD	140	87	53		
DMD Carrier Analysis	15	08	07		
Spinal Muscular Atrophy	63	33	30		
SMA Carrier Analysis	22	09	13		
		Normal	Homozygous	Heterozygous	Compound Heterozygous
Thalassemia and Sickle cell Anemia	65	07	25	25	08
Factor V Leiden	16	16	-	-	-
Factor II mutation	06	06	-	-	-
Cystic Fibrosis	75	73	02	-	-
Triplet Repeat Disorders		**Positive**	**Negative**		
Friedreichs Ataxia	35	08	27		
Myotonic Dystrophy	24	20	04		
Huntington Disease	33	19	14		
SCA Panel (1,2,3,6 &7)	71	28	43		
DRPLA	01	-	01		
Prenatal Diagnosis					
DMD	02	01	01		
Spinal Muscular Atrophy	07	-	07		
		Normal	Homozygous	Heterozygous	Compound Heterozygous
Thalassemia	19	07	03	06	03

II. Diagnostics Research

Project 1: Cloning, Characterization and analysis of chromosomal rearrangements in human genetic disorders

Summary of work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

Structural chromosomal rearrangements alter the genome architecture and may result in human disease phenotypes. The patients with trans-locations and inversions often have breakpoints located within the disease gene, or very close to it. In order to identify the disease gene, breakpoints can be characterized and if any gene is disrupted by rearrangement then it is considered as a candidate gene for that disease. Cloning their

breakpoint can provide the quickest route to identifying the disease gene. This project deals with the molecular characterization of chromosomal breakpoints associated with specific clinical phenotypes. We have identified two cases of novel balanced translocations associated with disease and we are presently working with the first case i.e. a girl with delayed milestones and seizures with a karyotype of 46,XX,t(X;20)(q13;p13) (Figure 1).

the two clones RP11-804E20 and RP11-770E18 (Figure 2).

b) Delineation of the breakpoint region on 20p13 region

Among the 2 clones on the 20p13 region; RP11-706G18 showed signals on normal 20 and on derived 20 whereas RP11-666H23 showed signals on normal 20 and derived X, thus anchoring the

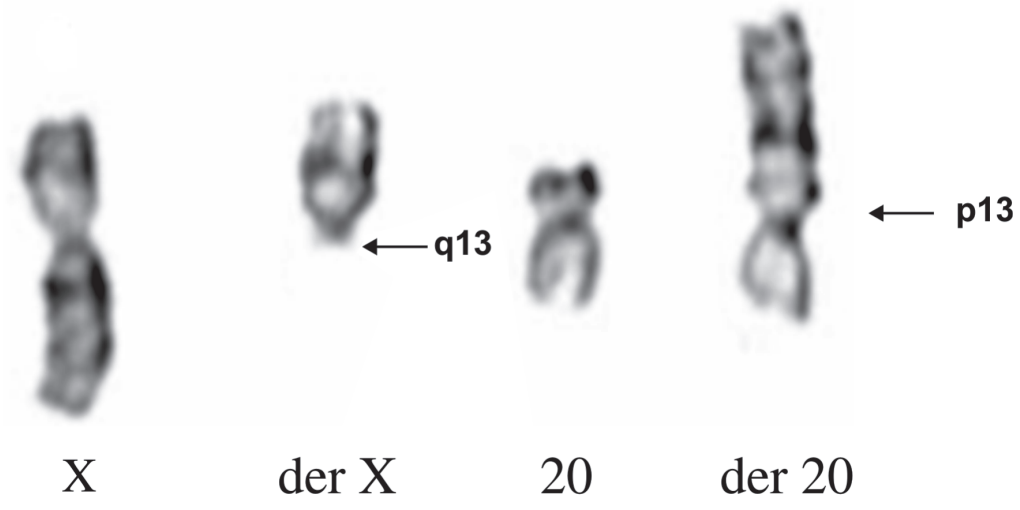


Figure 1. GTG banded partial karyotype showing the translocation t(X; 20)(q13; p13)

Details of progress made in the current reporting year (April 1, 2010 – March 31, 2011)

In order to confirm the breakpoint regions, FISH (Fluorescence-*in situ*-hybridization) experiments were performed. Initially FISH was performed with Whole Chromosome Paint probes to confirm the translocation as well to rule out the involvement of any other chromosomes. Further characterization was achieved by BACs (Bacterial Artificial Chromosome) which were selected by *in silico* analysis using the human genome databases. BAC clones were first labelled by nick translation and the probes thus made were used for further FISH experiments.

a) Delineation of the breakpoint region on Xq13 region

Initially 8 BAC clones were selected from Xq13 region (Figure 2), out of which 6 showed signals on normal X and derived 20 whereas 2 showed signals on normal X and derived X. Hence the breakpoint region was narrowed down to 4Mb region between

breakpoint region between these two clones to a distance of 2.3Mb (Figure 2).

A contig of 14 clones on Xq and 6 clones on 20p region were identified covering the breakpoint spanning region. The identification of breakpoint spanning BAC clone from the contig is still underway.

Project II: Clinical, biochemical and molecular analysis of common lysosomal storage disorders

Summary of work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

Lysosomal storage disorders are a heterogenous group of disorders associated with specific lysosomal enzyme deficiency. The diagnosis and prenatal diagnosis in most of these disorders is based on enzyme assay. There is a large amount of overlap in enzyme levels among carriers and normal people; hence it is very difficult to detect

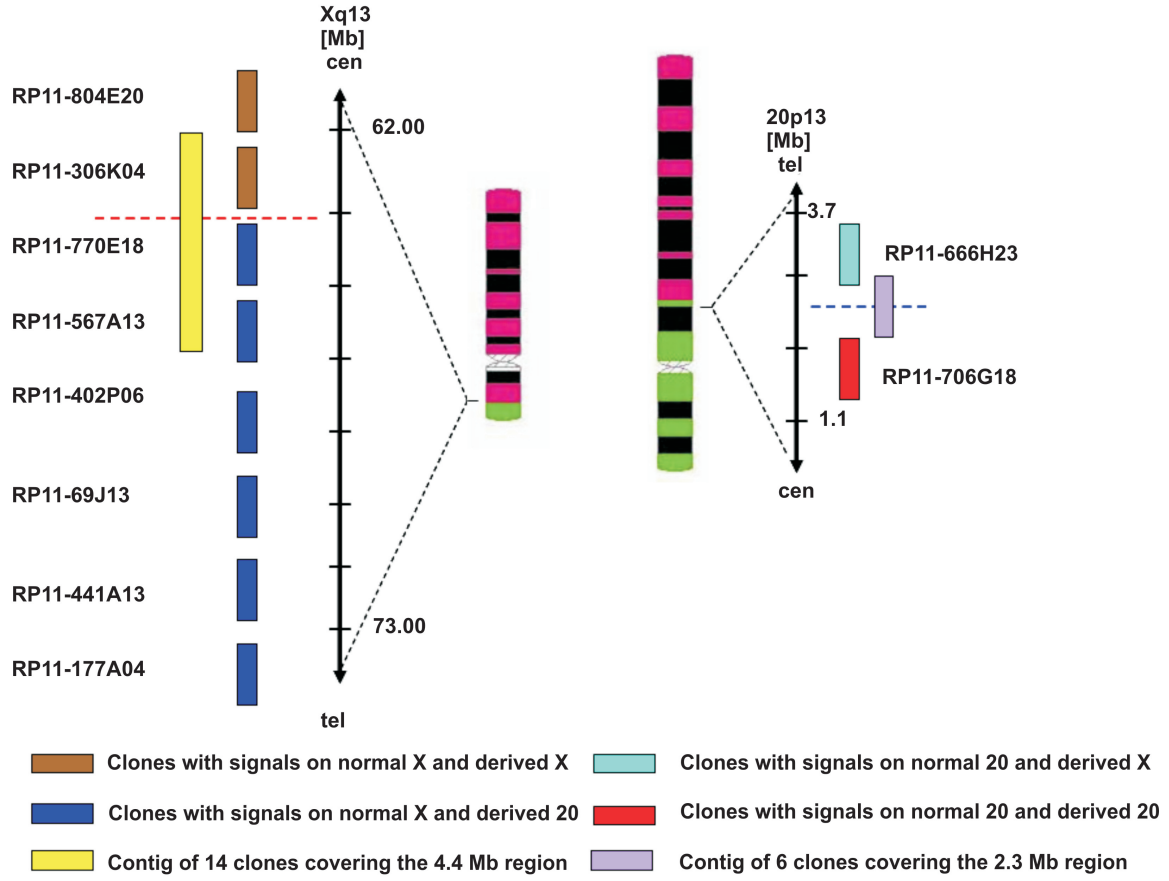


Figure 2. A detailed physical map of the translocation breakpoint region. The red and blue dotted lines show the breakpoint regions

carriers by enzyme assay. Mutation detection is helpful for carrier detection and accurate prenatal diagnosis. Our study aims to characterize the clinical features, biochemical parameters and molecular defects in common lysosomal storage disorders.

Details of progress made in the current reporting year (April 1, 2010 – March 31, 2011)

We focused mainly on 3 lysosomal storage disorders viz. Niemann-Pick Disease, Meta-chromatic Leukodystrophy and Sialidosis.

For mutation analysis, we extracted genomic DNA by salting out procedure from patients who were referred to the Diagnostics Division of CDFD. Primers were designed using PRIMER 3 Software and PCR was carried out with primers encompassing the entire exons and the flanking intronic regions of the corresponding gene in all the patients. Bidirectional sequencing was carried out on all the purified PCR products by capillary electrophoresis on ABI 3130 automated genetic analyzer (Applied Biosystems, Foster City, CA).

Niemann-Pick Disease

Acid sphingomyelinase activity was measured in the leucocytes collected from all the twelve patients using the substrate 2-N-(hexadecanoyl)-amino-4-nitrophenyl-phosphoryl-choline in the presence of sodium taurocholate. Protein concentration was determined by the Lowry method. The homogenates were incubated in the presence of the substrate for 18 hours and the residual enzymatic activity was expressed as percentage of normal values.

A total of eleven mutations were observed in the patients (Table 1). The enzyme levels were severely decreased in all the patients with the observed mutations. None of the aforementioned mutations were observed in the 50 healthy individuals.

No. of the Patient	Exon	Mutation
Patient 1	Exon 1/ Exon 1	L35fs/ L35fs
Patient 2	Exon 2/ Exon 2	R230C/ R230C
Patient 3	Exon 2/ Exon 2	L263X/ L263X
Patient 4	Exon 2/ Exon 2	L363R/ L363R
Patient 5	Exon 3/ Exon 3	Y369V/ Y369V
Patient 6	Exon 4/ Exon 4	W393R/ W393R
Patient 7	Exon 6/ Exon 6	W535R/ W535R
Patient 8	Exon 6/ Exon 6	R542X/ R542X
Patient 9	Exon 6/ Exon 6	R542X/ R542X
Patient 10	Exon 4/Exon 4	R494I/W393R
Patient 11	Exon 2/Exon 6	L216R/R542X
Patient 12	Exon 4/Exon 6	R443X/R542X

Table 1. Mutations in SMPD1 gene

Metachromatic Leukodystrophy

The Arylsulfatase A enzyme activity in patients was measured in the leucocytes obtained from the blood sample. The substrate used was P-Nitrocatechol in the presence of sodium acetate-acetic acid containing sodium pyrophosphate. Protein concentration was determined by the Lowry method. The homogenates were incubated in the presence of the substrate for 1 hour and the residual enzymatic activity was expressed as percentage of normal values.

A total of seven mutations were observed in the patients (Table 2) (Figure 3). The enzyme levels were severely decreased in all the patients with the observed mutations. None of the aforementioned mutations were observed in the 50 healthy individuals.

No. of the Patient	No. of the Exon	Mutation
Patient 1	Exon 1	Y63X/ Y63X
Patient 2	Exon 3	C156R/ C156R
Patient 3	Exon 5	R311Q/ R311Q
Patient 4	Exon 5	R311X/ R311X
Patient 5	Exon 6	N350S/ N350S
Patient 6	Exon 6	N350S/ N350S
Patient 7	Exon 7	R390W/ R390W

Table 2. Mutations in ARSA gene

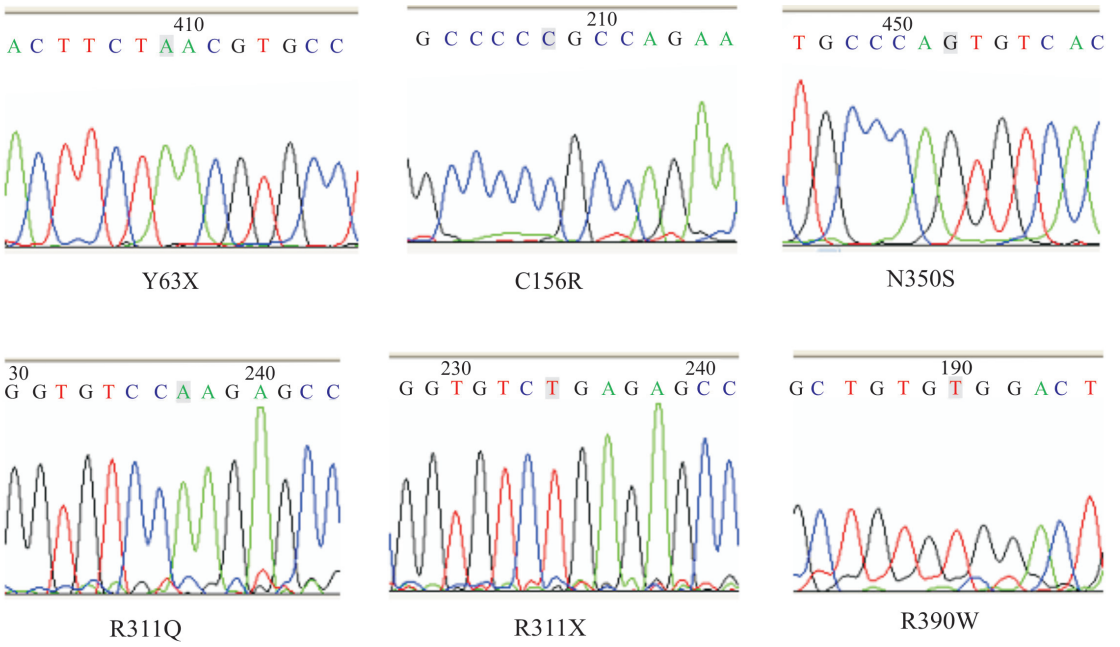


Figure 3. Mutations observed in ARSA gene

No. of Patient	Exon	Mutation
Patient 1	Exon 1	G25fs (Homozygous)
Patient 2	Exon 5	R294C (Heterozygous)
	Exon 6	R397fs (Heterozygous)

Table 3. Mutations in Sialidosis

Sialidosis

A total of three novel mutations were found in two patients. The G25fs mutation was found in a child in homozygous condition and the mutation analysis of the parents showed heterozygous condition for the same. The enzyme levels were severely decreased in all the patients with the observed mutations (Table 3).

Publications

1. Agarwal S, Tamhankar PM, Kumar R and Dalal A (2010). Clinical and haematological features in a compound heterozygote (HBB:c.92+ 5G>C/HBB:c.93-2A>C) case of thalassaemia major. ***International Journal of Laboratory Hematology*** 32: 369-372.
2. Angalena R, Prabitha KN, Chaudhary AK, Bashyam MD, Jain S and Dalal A (2010). A novel homozygous point mutation at codon 82 (HBB:c.247A>T) in the beta-globin gene leads to thalassemia major. ***International Journal of Laboratory Hematology*** 32: 548-549.
3. Dalal A, Sarkar A, Priya TP and Nandineni MR (2010). Giuffrè-Tsukahara syndrome: Evidence for X-linked dominant inheritance and review. ***American Journal of Medical Genetics*** 152: 2057-2060.
4. Girisha KM, Vahab SA, Dalal A, Gopinath PM and Satyamoorthy K (2010). Compound heterozygosity for HbD Punjab and polyadenylation signal mutation causes clinically asymptomatic mild hypochromia and microcytosis. ***Annals of Hematology*** 89: 625-626.
5. Priya TP, Philip N, Molho-Pessach V, Busa T, Dalal A and Zlotogorski A (2010). H syndrome: Novel and recurrent mutations in SLC29A3. ***British Journal of Dermatology*** 162: 1132-1134.

6. Dutta UR, Rajitha P, Kumar PV and Dalal A (2011). Cytogenetic abnormalities in 1162 couples with recurrent miscarriages in southern region of India: Report and review. ***Journal of Assisted Reproduction and Genetics*** 28: 145-149.

7. Ponnala R and Dalal A (2011). Partial monosomy 7q. ***Indian Pediatrics*** (In press).

8. Priya TP and Dalal A (2011). Tuberous sclerosis: Diagnosis and prenatal diagnosis by MLPA. ***Indian Journal of Pediatrics*** (In press).

Other Publications

1. Priya TP and Dalal A (2010). Triplet Primed PCR (TP-PCR) – A versatile method for molecular diagnosis of triplet repeat disorders. ***Newsletter of Genetics Chapter of Indian Academy of Pediatrics*** Vol 3, Issue 3 (July-Sept 2010).

2. Dalal A (2011). Annual review of genomics and human genetics, 2010. (Book Review) ***Current Science*** 100: 933-934.

3. Dalal A (2011). Genetic tests. ***API Textbook of Medicine***, 9th Edition 21-25.

4. Dutta UR, Pidugu VK and Dalal A (2011). Molecular cytogenetics illustrated: SKY and FISH. ***Newsletter of Genetics Chapter of Indian Academy of Pediatrics*** Vol 4, Issue 1 (Jan-Mar 2011).

शोध
Research

LABORATORY OF MOLECULAR GENETICS

Centre of Excellence (CoE) for Genetics and Genomics of Silkmoths

Principal Investigators	J Nagaraju	Staff Scientist
	KP Arun Kumar	Staff Scientist (Since Jan. 2011)
PhD Students	Jyoti Singh	Senior Research Fellow (Till Feb. 2011)
	Asha Minz	Senior Research Fellow
	Chandrapal Singh	Senior Research Fellow
	S Suresh Kumar	Senior Research Fellow
	Deepa Badrinarayan	Senior Research Fellow
	G Gopinath	Junior Research Fellow
	TR Sitalakshmi	Junior Research Fellow
	Vandana	Junior Research Fellow
	K Akanksha	Junior Research Fellow
Other Members	Varsha	Staff Scientist
	VV Satyavathi	Technical Officer IV (CoE)
	A Sobhan Babu	Technical Officer II
	M Muthulakshmi	Technical Officer I
	S Annapurna	Technical Officer I (CoE)
	Archana Tomar	Bioinformatician (CoE)
	R Lakshmi Vaishna	Technical Assistant (CoE)
	MJ Reddy	Technical Assistant (CoE)
	P Nagamanju	Research Associate (Till Aug. 2010)
	K Adarsh Gupta	Project Assistant
	M Nagamuralidhar	Project Assistant (Till Sep. 2010)
	Deepa Narra	Project Assistant

Objectives

1. Functional characterization of silk genes and sex-determination genes
2. Generation of transgenic silkworms resistant to *Bombyx mori* nucleopolyhedrosis virus (BmNPV) using RNAi strategy and introduction of anti-baculoviral property to commercial silkworm strains
3. Target validation of microRNAs involved in host-pathogen interaction of silkmoths
4. Identification and functional characterization of novel genes involved in immune response pathways of silkmoths.

The progress made in the projects related to sex determination and microRNAs is reported here.

Summary of the work done until the beginning of this reporting year (April 1, 2009 - March 31, 2010)

Our lab is pursuing modelling of sex determination mechanism in *Bombyx mori* and its wild relatives. Earlier, we examined the testis transcriptome in the female-heterogametic system of *B. mori*. We assigned chromosomal positions of testis-specific genes validated by microarray on the *B. mori* genome to examine their distribution on different chromosomes.

Using *B. mori*, we have discovered many host-encoded miRNAs that have targets in the baculovirus essential transcripts and many baculoviral-encoded microRNAs that have targets in the host genes involved in immune function.

Details of progress made in the current reporting year (April 1, 2010 - March 31, 2011)

Project 1: Analysis of orthologs of sex determining genes in silkmoths

The sex-determining system differs considerably among organisms. Even among insect species, the sex determination mechanism is highly diverse. Wilkin's hypothesis suggests that evolution of the sex-determination cascade has taken place in reverse order, the bottom most gene being most conserved and the upstream genes having been recruited at different time points during evolution. As a part of the lab's main theme to study the mechanism of sex determination in silkworms, we initiated work on downstream regulators of sex determination in the silkworm *B. mori* and wild silkmoths. As a result, we identified and characterized homologs of *doublesex* (*dsx*) and *intersex* (*ix*) genes in *B. mori* and in two species of wild silkmoths, *Antheraea assama* and *A. mylitta.*

The *B. mori doublesex* (*Bmdsx*) plays a very crucial role in somatic sexual development. Its pre-mRNA sex-specifically splices to generate two splice variants; one encodes female-specific and the other encodes male-specific polypeptides which differ only at their C-termini. The open reading frame (ORF) of *Bmdsx* consists of 5 exons, of which exons 3 and 4 are female-specific and are skipped in males. In the present study, we have identified a third splice form of the *Bmdsx* which is specific only to females and differs from the previously reported *Bmdsxf* isoform by the presence of 15 bp sequence. This new female splice form is generated as a result of alternative splice site selection in the third exon adding additional 15 bp sequence in exon 3 which results in alteration of the reading frame leading to incorporation of an early stop codon. Thus the protein encoded by this splice form is 20 aa shorter than the known *BmDsxF*. We propose a model (Figure 1) to explain the pathway of female sexual differentiation governed by the two female specific DSX proteins. BmDsxF2 might be acting as an additional factor in co-ordination with BMIX, in addition to BmDsxF1, to execute female sexual differentiation.

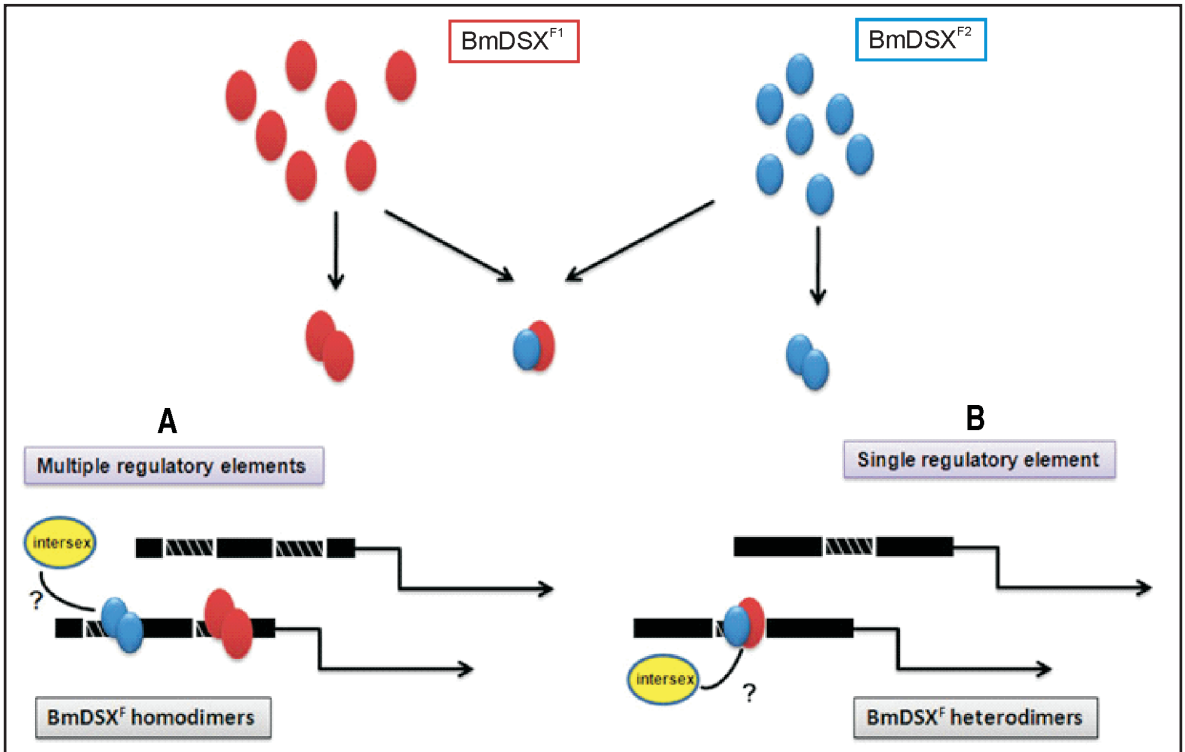


Figure 1. Model explaining the mode of action of two BmDsx proteins in females. A) Two different regulatory elements (RE) are present in the promoters of downstream target genes (*vitellogenin*, *SP1-Storage Protein* and *PBP-Pheromone Binding Protein*). Homodimers of BmDsx bind separately to these regulatory elements to independently regulate them. B) alternatively, heterodimers of BmDsx bind to the single regulatory element present in the promoters of downstream target genes to regulate their expression. Products of *intersex* gene may also possibly interact with BmDsx.

We cloned and characterized the *dsx* homologues from two saturniid silkmoths, *A. assama* and *A. mylitta* (Figure 2). Interestingly, the *dsx* pre-mRNA of these wild silkmoths sex-specifically splices to generate multiple splice variants. On the basis of their ORFs and conceptual translation, two female-specific (DSX^{F1} and DSX^{F2}) and one male-specific (DSX^{M}) proteins could be inferred, in both the moths. Presence or absence of a 15 bp stretch within the ORF of the two groups of female-specific transcripts resulted in the production of two distinct female-specific DSX proteins. The sex-specific DSX proteins have common amino-terminal sequence but sex-specific carboxy termini. The two female-specific DSX proteins (DSX^{F1} and DSX^{F2}) share common DNA binding domain (DM domain) and oligomerization domain (OD domain) and differ only at their extreme C-termini by 21aa. Functional analysis of *dsx* transcripts in *A. assama* by dsRNA mediated knockdown resulted in complete abolition of expression of *vitellogenin* and *hexamerin* genes, the direct targets of the DSX proteins, irregular differentiation of gonads, and drastic reduction in fecundity and hatchability. Together, these results suggest the involvement of both the female-specific DSX proteins in the process of female sexual differentiation. Further, conservation of the 4th exon sequence, especially the PESS sequence essential for the sex-specific splicing of *Bmdsx* in the female specific transcripts of *Aadsx* and *Amydsx*, indicated the existence of a common mechanism of sex-specific splicing of *dsx* homologues in silkmoths.

Intersex, a gene required for female sexual development in *Drosophila*, acts in concert with *dsx* at the end of the sex determination pathway. We identified a homologue of *ix* in *B. mori*. Expression analysis of this gene by RT–PCR and RNase protection assay revealed a diagnostic alternative splice form present only in testis, whereas the most common splice form was found to express in all other tissues from early embryonic developmental stages (Figure 3). The present study provides evidence for the presence of an alternative splice form of *ix* in three species of silkmoths examined. Taken together with the results of an earlier study on *ix* in piralid moth, *Maruca vitrata*, the present study suggests that the testis-specific splice form may be a characteristic feature of lepidopterans.

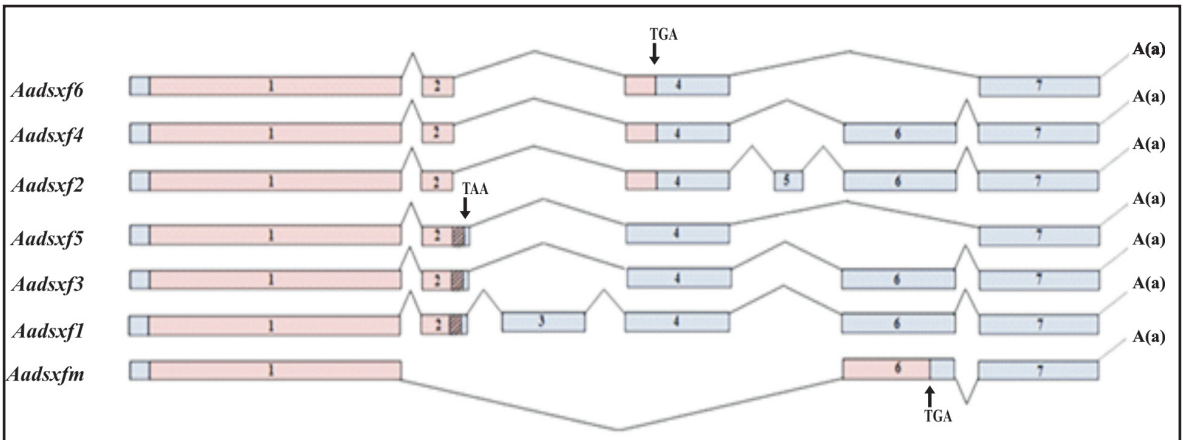


Figure 2. Schematic representation of different splice forms of *Aadsx* pre-mRNA. Boxes are exons and lines are introns. Pink coloured portion is the ORF whereas blue coloured regions are UTRs. Seven different splice products of *Aadsx* pre-mRNA, six female-specific (*Aadsxf1, Aadsxf2, Aadsxf3*, *Aadsxf4, Aadsxf5* and *Aadsxf6*) and one male-specific (*Aadsxm*), are produced. A(*n*) represents the polyadenylation site. Vertical arrows represent stop codon sites. Hatched boxes indicate 15 bp additional sequences in the exon 2 present only in *Aadsxf1*, *Aadsxf3* and *Aadsxf5*.

Though *ix* lacks a conserved splicing pattern it appears to have retained its functional conservation in terminal sexual differentiation. We speculate that the presence of an additional splice form, perhaps encoding non-functional protein only in testis, may prevent the feminizing effects exerted by the functional IX protein.

Project 2: Understanding the role of miRNAs in insect-pathogen interaction using silkworm as a model

MicroRNAs (miRNAs), a family of endogenous small non-coding RNAs of ~ 22 nucleotides, have emerged as key post-transcriptional regulators of gene expression, and have revolutionized our understanding of the post-transcriptional regulation

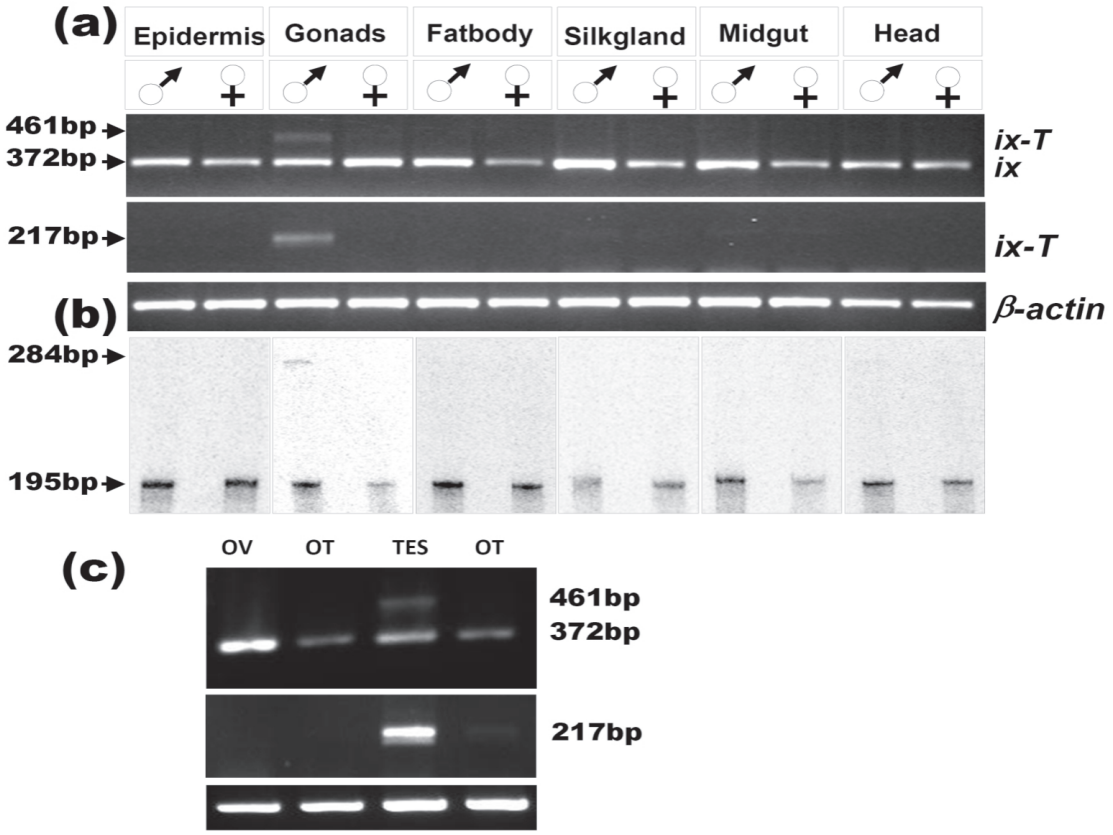


Figure 3. Expression of *Bmix* mRNA during different developmental stages of *B. mori* as revealed by RT-PCR. (a) Upper panel shows RT-PCR profile of different tissues from 5th instar larvae amplified using primers (ix and ix-T), which will amplify both common (*Bmix*) and testis specific (*Bmix-T*) splice forms. Middle panel is the RT-PCR profile, obtained by using primers binding to first and second exons which will specifically amplify *Bmix-T*. Lower panel shows α-actin levels as control. (b) Shows the RNase protection assay for six tissues of both sexes separately, of fifth instar larvae, wherein only testis is showing the second splice form. (c) Shows the expression pattern of *ix* in gonads and other tissues of moths (OV: Ovary, TES: Testis, OT: Other tissues).

of gene expression. MicroRNAs are derived from ~80 nucleotides long precursors (pre-miRNAs), which can fold back into typical stem-loop structure. Although the mechanism of miRNA regulation is still unclear and is a subject of intense investigation, the miRNAs are known to play important role in almost every cellular and developmental process investigated so far including cell division, cell death, hormone secretion, neural development, cancer, and recent evidences suggest that miRNAs have been implicated in the cross talk between host and pathogen during various viral infections. The overview of the role of miRNAs in host-virus interaction is schematically represented in Figure 4.

Recently, many virus-encoded miRNAs have been identified from different mammalian species. However, the large family of invertebrate viruses of Baculoviridae, which include many devastating pathogens infectious to several economically important arthropods, particularly insects of the order Lepidoptera infects diverse species of beneficial insects and agriculture pests, has hardly been investigated for elucidating the role of miRNAs in host-pathogen interaction. *B. mori* is a Lepidopteran model system for genetics and molecular studies. BmNPV is a natural pathogen of *B. mori*, which inflicts a very high mortality on *B. mori* resulting in heavy silk cocoon loss, thus

causing a major economic damage to the silk industry.

We chose to examine the expression of viral miRNAs in midgut (infection initiation site) and fat body tissues (viral replication site) and generated more than 50,000 small RNA reads per sample. These sequences were then sorted for potential viral miRNAs taking many important key features into consideration based on published works. Final scanning of the hits based on the free energy change for the characteristic secondary structure of the precursor RNA resulted in the discovery of 4 potential viral miRNAs. The expression of predicted miRNAs were then validated by a variety of techniques including Northern blotting, stem-loop RT-PCR and poly(A)-tailed RT-PCR, followed by cloning and sequencing. The expression profile of these four miRNAs by Northern blot is shown in Figure 5.

Interestingly, all the four miRNAs that we have characterized are evolutionarily conserved among many closely related viral genomes unlike most of the other reported viral miRNAs that show a very little evidence of conservation. Two of the four viral miRNAs were found to be transcribed from the antisense strand of their respective cis viral targets as reported previously for a few of the mammalian viruses. In addition, we have also predicted 8 viral as well as 64 host targets of these viral encoded miRNAs by employing, a) miRanda program, which utilizes thermodynamics and dynamic-programming alignments and b) stringent filters based on several statistical parameters to ensure least false positives. Putative functions of these targets clearly suggest a possible involvement of viral miRNAs in insect-pathogen interactions by modulating the viral replication genes as well as those involved in host immune defense system, a strategy devised by the virus to conquer the host for its successful proliferation.

Presently, we are validating the potential targets of these four viral encoded miRNAs.

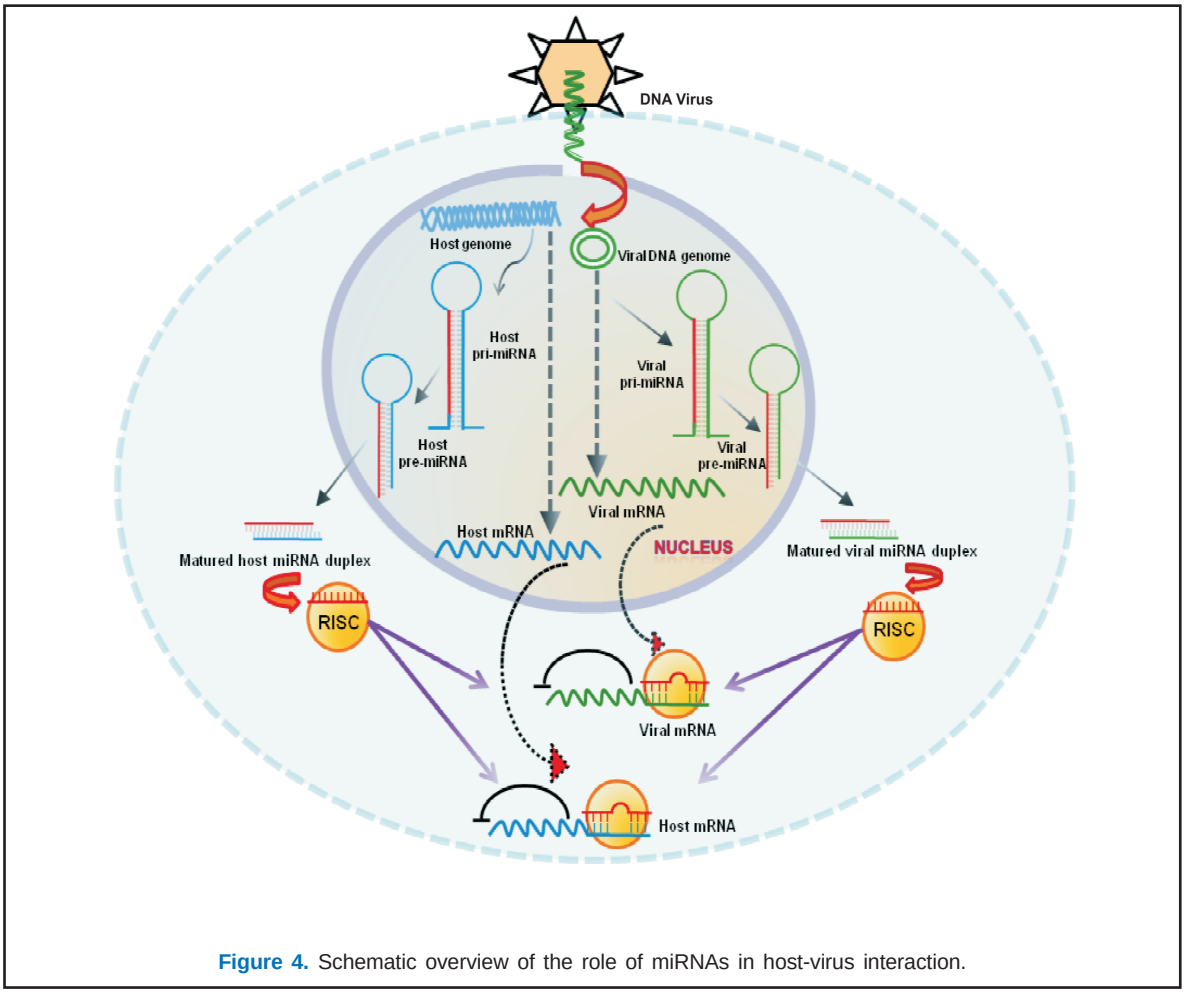


Figure 4. Schematic overview of the role of miRNAs in host-virus interaction.

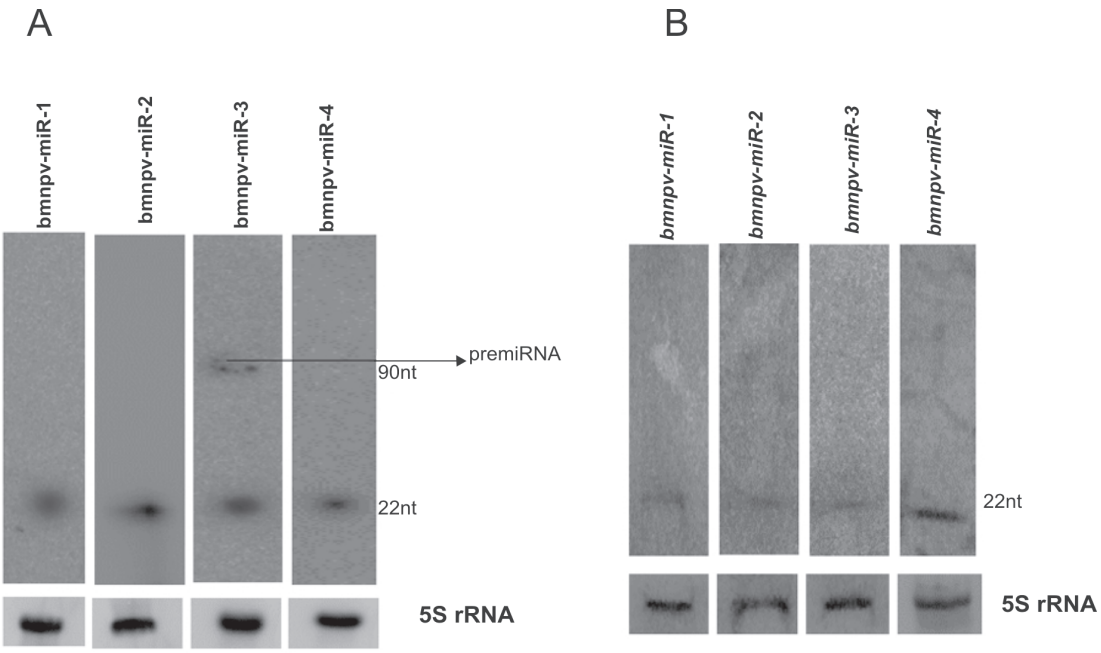


Figure 5. Northern blot confirmation of predicted BmNPV-encoded miRNAs expression (A) Northern blot analysis of small RNA samples derived from infected fat body tissue. Lane 1: *bmnpv-miR-1;* lane 2: *bmnpv-miR-2*; lane 3: *bmnpv-miR-3*; lane 4: *bmnpv-miR-4*. (B) Northern blot analysis of small RNA sample derived from infected midgut. Lane 1: *bmnpv-miR-1*; lane 2: *bmnpv-miR-2*; lane 3: *bmnpv-miR-3*; lane 4: *bmnpv-miR-4*. 5S rRNA was used as a loading control.

APEDA-CDFD Centre for Basmati DNA Analysis

Principal Investigator and Consultant	J Nagaraju	Staff Scientist
Other Members	A Srividya	Research Associate
	Revathi Nagaraja	Project Assistant (Till Aug. 2010)
	Manju Shukla	Project Assistant

Objectives

1. Testing of purity of Basmati samples received from Export Inspection Council (EIC), Ministry of Commerce, Govt. of India, Basmati rice exporters from India and other countries
2. Fine mapping and characterization of the candidate genes of grain appearance traits of Basmati rice.

Basmati rice genetics and genomics

Project 1: Fine mapping and association study of candidate genes in a promising region on chromosome 5 controlling grain appearance traits of Basmati rice

Objective

1. Association analysis of candidate genes of promising QTL for grain appearance traits of Basmati rice on chromosome 5.

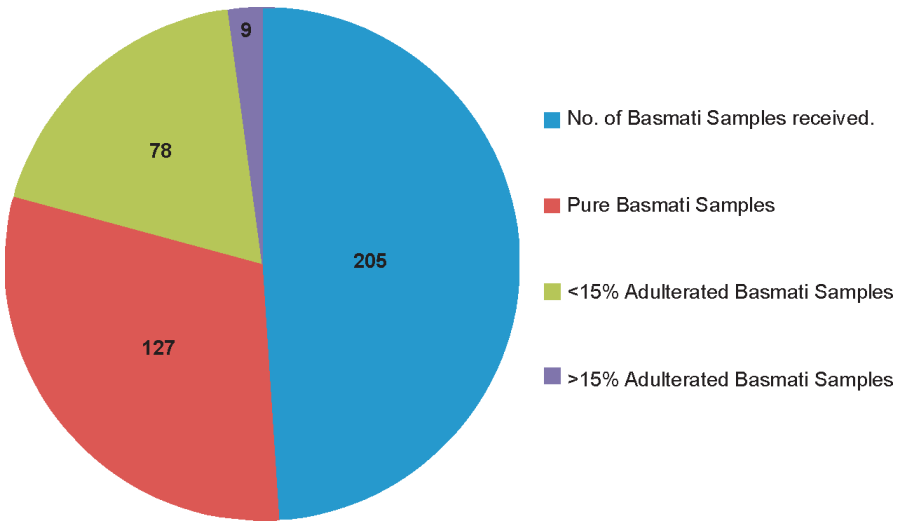


Figure 6. Basmati samples analyzed at APEDA-CDFD centre in the current reporting year.

Basmati samples analyzed at APEDA-CDFD Centre in the current reporting year April 2010 – March 2011

During the period under report, a total of 205 Basmati samples were analyzed and the number of samples indicating the percentage of adulteration with non-basmati rice is shown in Figure 6.

Summary of the work done until the beginning of this reporting year (April 1, 2009 - March 31, 2010)

A QTL mapping approach was employed in an F_2 mapping population of 181 plants, derived from a cross between a traditional Basmati variety, Basmati370 and a semi dwarf variety Jaya. With

this mapping, a total of 47 QTLs for 16 different agronomic and quality traits were identified. Interestingly, a single region on chromosome 5 was found to be controlling important grain appearance traits viz., grain length, grain breadth, length-breadth ratio and grain elongation ratio. Further fine mapping of this region, using additional SSRs, Indels and ESTs has been attempted. Based on rice genomic sequence information four candidate genes have been predicted in this region. Among these predicted genes two were sequenced at cDNA level with Basmati 370 and compared with indica and japonica reference sequences. One of these two genes showed five SNPs which includes three non synonymous SNPs at base positions 1379, 1840 and 1984.

Details of progress made in the current reporting year (April 1, 2010 – March 31, 2011)

Three non synonymous SNPs from a predicted candidate gene were sequenced in different accessions of basmati, non basmati, indica and wilds to analyze their association among accessions. Among three, two SNPs at base positions 1840 (sixth exon) and 1984 (seventh exon) possess interesting associations. Sequencing of these two SNPs with other short and long grain rice accessions is being performed. Further, we identified two intron/exon differences of Basmati 370 with indica reference sequence. Currently, sequencing of this region employing basmati and non aromatic long grain varieties is going on. Once we identify any Basmati specific sequence, confirmation studies will be carried out which includes expression analysis and transgenic studies.

Publications

1. Morrison NI, Koukidou M, Franz G, Miller TA, Saccone G, Simmons GS, Alphey LS, Polito LC and Nagaraju J (2010). Review: Genetic improvements to the sterile insect technique for agricultural pests. ***Asian Pacific Journal of Molecular Biology and Biotechnology*** 18: 275-295.
2. Mrinal N and Nagaraju J (2010). Dynamic repositioning of dorsal to two different *kB* motifs controls its autoregulation during immune response in *Drosophila*. ***Journal of Biological Chemistry*** 285: 24206-24216.
3. Nagaraju J and Saccone G (2010). Preface (to special issue: How is sex determined in insects?) ***Journal of Genetics*** 89: 269-270.
4. Nagaraju J and Saccone G (2010). How is sex determined in insects? An epilogue**.** ***Journal of Genetics*** 89: 389-390.
5. Shukla JN and Nagaraju J (2010). Doublesex: A conserved downstream gene controlled by diverse upstream regulators. ***Journal of Genetics*** 89: 341-356.
6. Shukla JN and Nagaraju J (2010). Two female-specific DSX proteins are encoded by the sex-specific transcripts of *dsx*, and are required for female sexual differentiation in two wild silkmoth species, *Antheraea assama* and *Antheraea mylitta* (Lepidoptera, Saturniidae). ***Insect Biochemistry and Molecular Biology*** 40: 672-682.
7. Singh J, Singh CP, Bhavani A and Nagaraju J (2010). Discovering microRNAs from *Bombyx mori* nucleopolyhedrosis virus. ***Virology*** 407: 120-128.
8. Arunkumar KP and Nagaraju J (2011). Drosophila intersex orthologue in the silkworm, *Bombyx mori* and related species. ***Genetica*** 139: 141-147.
9. Bentur JS, Sinha DK, Padmavathy C, Revathy C, Muthulakshmi M and Nagaraju J (2011). Isolation and characterization of microsatellite loci in the asian rice gall midge (*Orseolia oryzae*) (Diptera: Cecidomyiidae). ***International Journal of Molecular Science*** 12: 755-772.
10. Shukla JN, Jadhav S and Nagaraju J (2011). Novel female-specific splice form of *dsx* in the silkworm, *Bombyx mori*. ***Genetica*** 139: 23-31.
11. Terenius O, …(67 authors)…, Nagaraju J, Richard H, Herrero S, Gordon K, Swevers L and Smagghe G (2011). RNA interference in Lepidoptera: An overview of successful and unsuccessful studies and implications for experimental design. ***Journal of Insect Physiology*** 57: 231-245.

Patent filed

1. J Nagaraju *et al*. Virus resistant transgenic silkworms. *Indian Patent* No. 332/CHE/2011 (applied on 04.02.2011).

LABORATORY OF GENOMICS AND PROFILING APPLICATIONS

Principal Investigator	Madhusudan R Nandineni	Staff Scientist
PhD Students	Anujit Sarkar	Senior Research Fellow
Other Members	Vishakha Sharma	Project Assistant
	G Sreeja Reddy	Project Assistant
	S Seethalakshmi	Project Assistant
	Gadde Srinath	Project Assistant (Till Sep. 2010)
	Sibapriya Chaudhuri	Project Assistant (Till Mar. 2011)

Objectives

1. Development of DNA-based markers for genetic fidelity testing of tissue culture raised plants and for phylogenetic studies
2. Development of novel strategies/ methodologies for enrichment of human DNA from mixtures containing human and non-human DNAs for DNA profiling-based human identification
3. To study the human genetic diversity among various population groups of India.

Project 1: Development and validation of DNA-based markers for genetic fidelity testing of tissue culture-raised plants and for phylogenetic studies.

Summary of work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

As a referral centre for the genetic fidelity testing of tissue culture-raised plants employing DNA markers, one of our laboratory's focus has been to develop DNA-based molecular markers which could be used for true-to-type testing of important tissue culture raised crop plants like banana, black pepper, potato, sugarcane and vanilla. For this purpose, we had proposed to employ microsatellites or simple sequence repeats (SSRs) in genetic fidelity testing of the above mentioned crops. In the previous report, we had reported about the efforts to explore the suitability of some of the whole genome scanning molecular markers such as **i**nter-**s**imple **s**equence **r**epeats (ISSR) and retrotransposon-based markers for true-to-type testing in these crop plants.

Details of progress made in the current reporting year (April 1, 2010 – March 31, 2011)

(A) Varietal and clonal typing studies using the retrotransposon-based marker systems

- For the various experiments referred herein, forty varieties of potato were obtained from Central Potato Research Institute (CPRI), Shimla, Himachal Pradesh, while twenty four of the common cultivars of banana were procured from National Research Centre for Banana (NRCB), Trichy, Tamil Nadu.
- In the previous report we had mentioned that few of the ISSR markers screened were found to be useful for true-to-type testing, whereas few others had shown inconsistency in the pattern of amplified fragments among the tested plant varieties. Therefore, alternative multi-locus marker systems like **i**nter-**r**etrotransposon **a**mplified **p**olymorphism (IRAP) and **r**etrotransposon **m**icrosatellite **a**mplified **p**olymorphism (REMAP) were thought of for true-to-type testing, as they offer some advantages over ISSR assays.
- Retrotransposon-based molecular markers are dominant, multi-locus marker system that scans variation in retrotransposons' insertion sites in the plant genomes. Since the idea was to assess the genetic fidelity (true-to-typeness) of tissue culture raised micropropagules, we hypothesized that the retrotransposon-based markers could be well-suited for the purpose. After screening multiple IRAP and REMAP primer combinations, ten IRAP and seventeen REMAP combinations in banana and twenty two IRAP and nine REMAP combinations in potato were shortlisted for further studies.

The results showed that, these retrotransposon-based markers were able to distinguish different potato/banana varieties and were also amenable for clonal fidelity (true-to-type) testing of tissue cultured-raised micropropagules.

- Further work is in progress to finalize the IRAP and REMAP combinations for genetic fidelity testing and to standardize the conditions for testing in these crops.

(B) Phylogenetic studies and genetic fidelity testing employing SSR markers

- Various SSR loci reported in the literature for the above-mentioned crops were examined for their usefulness in true-to-type testing and diversity or phylogenetic studies. As mentioned in previous year's report, thirty three of the forty SSR loci tested in case of potato and thirty two of the forty two SSR loci in case of banana were shortlisted for further analysis based on polymorphism in polyacrylamide gel electrophoresis (PAGE) analysis.
- For those loci which were polymorphic, capillary-electrophoresis based genotyping employing fluorescently-labelled primers was carried to determine the allele sizes accurately. Tables 1 and 2 show summary statistics of SSR marker study in potato and banana respectively.
- Data analysis was carried out using standard softwares. In potato, the number of alleles detected per SSR at single locus across forty cultivated varieties ranged from 5 to 10 (Table 1) and for banana it was 4 to 8 (Table 2). Polymorphism information content (PIC) values were calculated for ten microsatellites for potato and banana from total number of genotypes; the values varied from 0.76 to 0.88 for forty potato cultivars (Table 1) and 0.70 to 0.86 for seventeen banana cultivars (Table 2) that were employed in this study.

Table 1. Summary statistics of 10 different SSR loci among 40 different common potato cultivars.

S. No.	SSR loci (type)	Na	H_o	H_e	F_{IS}	PIC
1	Locus 1(-Tri-)	7	0.978	0.854	-0.142	0.836
2	Locus 2 (complex -di-)	7	0.914	0.856	-0.067	0.838
3	Locus 3 (-Tri-)	7	0.914	0.856	-0.067	0.838
4	Locus 4 (-di-)	6	0.851	0.833	-0.021	0.8
5	Locus 5(-Tri-)	6	0.957	0.833	-0.148	0.81
6	Locus 6(-Tri-)	7	0.957	0.856	-0.117	0.839
7	Locus 7(-Tri-)	5	0.68	0.799	0.14	0.767
8	Locus 8(-Tri-)	10	0.936	0.897	-0.043	0.88
9	Locus 9(-Tri-)	8	0.234	0.855	0.726	0.837
10	Locus10 (-complex di-)	8	0.914	0.874	-0.045	0.864

Table 2. Summary statistics of 10 different SSR loci among 17 different common banana cultivars.

S. No.	SSR loci (type)	N_a	H_o	H_e	F_{IS}	PIC
1	Locus 1(-di-)	7	0.944	0.857	-0.101	0.839
2	Locus 2 (complex –di-)	7	0.388	0.857	0.547	0.839
3	Locus 3 (-di-)	4	0.5	0.749	0.332	0.703
4	Locus 4 (-di-)	7	0.166	0.857	1.193	0.839
5	Locus 5(-di-)	4	0.44	0.749	0.412	0.703
6	Locus 6(-di-)	4	0.722	0.749	0.036	0.703
7	Locus 7(-di-)	6	1.11	0.833	-0.332	0.809
8	Locus 8(-di-)	7	1	0.856	-0.168	0.839
9	Locus 9(-Tri-)	8	0.166	0.874	0.81	0.861
10	Locus 10 (-di-)	4	0.44	0.749	0.412	0.703

Type: Dinucleotide (di-), Trinucleotide (-Tri-), N_a: Number of alleles observed, H_o: Observed Heterozygosity, H_e: Expected Heterozygosity, F_{IS}: Fixation index, **PIC**: Polymorphic Information Content.

- The numbers of polymorphic loci were 71 and 58 for potato and banana respectively and the range of percentage of polymorphic loci were 76% to 88% and 70% to 86% for potato and banana, respectively. Based on **u**nweighted **p**air **g**rouping by **m**athematically **a**veraging (UPGMA) analysis, in potato all the forty cultivars were clustered into three major groups, while in banana the seventeen varieties were clustered in four major groups.
- Future experiments will focus on using these and other informative SSRs for phylogenetic studies of different crop plants.

(C) Multiplexing of SSR loci for accessing the clonal fidelity

- Multiplexing increases the information content of each PCR reaction, thereby lowering the cost for large scale use of SSRs as genetic markers. For accessing the true-

to-typeness of tissue culture raised plants, multiplex PCR protocols were standardized employing the SSR markers reported in literature or developed in our laboratory.

- In banana, ten multiplex (six triplex and four tetraplex) SSR sets were developed employing different combinations of twenty SSR primer pairs and the PCR conditions were optimized. In potato, twenty-eight of the thirty three SSR markers screened were selected for developing ten multiplex (seven triplex and three tetraplex) SSR sets. In sugarcane, ten primer pairs were selected for development of four triplex sets for true-to-type testing. The multiplex reactions have generated identical pattern in all the clones (as one would have expected if they are true-to-type). Further work is in progress to standardize these conditions for genetic fidelity testing in other crop plants.

Project 2: Developing novel strategies for enrichment of human DNA from mixtures containing human and non-human DNAs for DNA profiling-based human identification.

Summary of work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

- Three major reasons have been ascribed for the failure in obtaining good DNA profile for human identification (HID) purposes from degraded/decomposed forensic skeletal exhibits *viz.*, the DNA isolated from such sources are often highly fragmented/ degraded, contaminated with non-human DNAs and presence of PCR inhibitors. The approach of "selective enrichment" of short tandem repeats (STR)-containing regions of human DNA using biotinylated oligos was proposed to address two of these problems *i.e.*, contamination with non-human DNAs and presence of PCR inhibitors.

- As mentioned in our previous report, locus specific 3'-biotinylated oligos were used to 'capture' the regions of STRs currently used for HID purposes. Since the DNA recovered from challenging forensic human skeletal samples most often includes both human and non-human DNAs, in order to simulate such conditions, reconstitution experiments were performed by mixing human DNA with varied concentrations of bacterial DNA. The results of STR 'pull down' experiments showed that the amplification of target loci was successful at lower bacterial contamination but at higher ratios, the peak heights of targeted loci have decreased considerably along with allele or locus drop-outs. Hence in order to increase the efficiency and specificity of the enrichment method, we had modified and adopted the primer extension capture (PEC) method (*Briggs et al, Science 17, 2009, 325: 318-321*) for this purpose.

Details of progress made in the current reporting year (April 1, 2010 - March 31, 2011)

- As part of the modification of the PEC method, we had designed eighteen oligos specific to eighteen STR loci represented in both the commercially available STR multiplex PCR kits (Applied Biosystems Inc, USA and Promega Corp., USA) universally employed for HID purposes. These oligos were designed as close as possible to the STR repeat units in their respective loci so that one would be able to "pull down" the respective fragments even in cases of degraded DNA molecules.

- In brief, the protocol consisted of binding all the eighteen 5'-biotinylated oligos to the complementary regions (either upstream or downstream) of their corresponding STR loci, followed by a single cycle of extension (polymerization) wherein the 5'-biotinylated oligos act as primers and undergo an extension step in the presence of dNTPs and thermostable DNA polymerase to produce long, double stranded hybrid molecules which would be 'captured' subsequently by streptavidin-coated magnetic beads. The longer double stranded DNA molecule thus obtained during the single extension step was expected to withstand more stringent final wash conditions, while allowing the other non-specific DNA fragments and any PCR inhibitors present to be washed away.

- Standardization experiments were performed to optimize conditions such as biotinylated oligo concentration, amount of streptavidin-coated magnetic beads to be used, stringency conditions such as number of washes and temperature of final wash, etc. Reconstitution experiments were carried out by mixing human DNA and bacterial DNA in different proportions to simulate the mixed

DNA obtained from forensic human skeletal samples (1:10, 1:100, 1:500, 1:1000, 1:2000, 1:5000 and 1:10000 ratio of human to bacterial DNA by weight).

- The results showed that in samples without PEC enrichment, full profile was obtained only up to 1:500 ratio of human to bacterial DNA by weight, few allele and locus dropouts were observed above that ratio and there was no amplification beyond 1:2000 ratio of the mixture. Also the amplification efficiency has been decreased (as represented by decrease in the peak heights of the STR alleles in the electropherogram) with increasing bacterial contamination.
- In 'pull down' experiments with the modified PEC method, full profile was obtained even upto 1:10000 ratio of the mixture. A representative graph comparing the fluorescence peak intensities of STR loci, without and with PEC enrichment has been shown in Figure 1.
- Since only one 5'-biotinylated (either upstream or downstream) oligo was used for each STR locus; theoretically only 50% of enrichment is possible while the remaining template molecules are washed-off. Therefore, in order to retain all the precious template molecules, we had used 5'-biotinylated oligos complementary to both upstream and downstream sequences of the respective STR loci. By using both sets of oligos we could successfully increase the efficiency of amplification which is reflected in the increase of peak intensities of relative fluorescent units (RFU) up to 35% in few cases. The results comparing the enrichment of some of the representative STR loci using single or both 5'-biotinylated oligos has been depicted in Figure 2.
- In future experiments, we plan to test both forward and reverse sets of 5'-biotinylated oligos for reconstitution samples to increase the sensitivity of the method and adopt this methodology for improving the success rate of DNA profiling of challenging forensic skeletal samples.

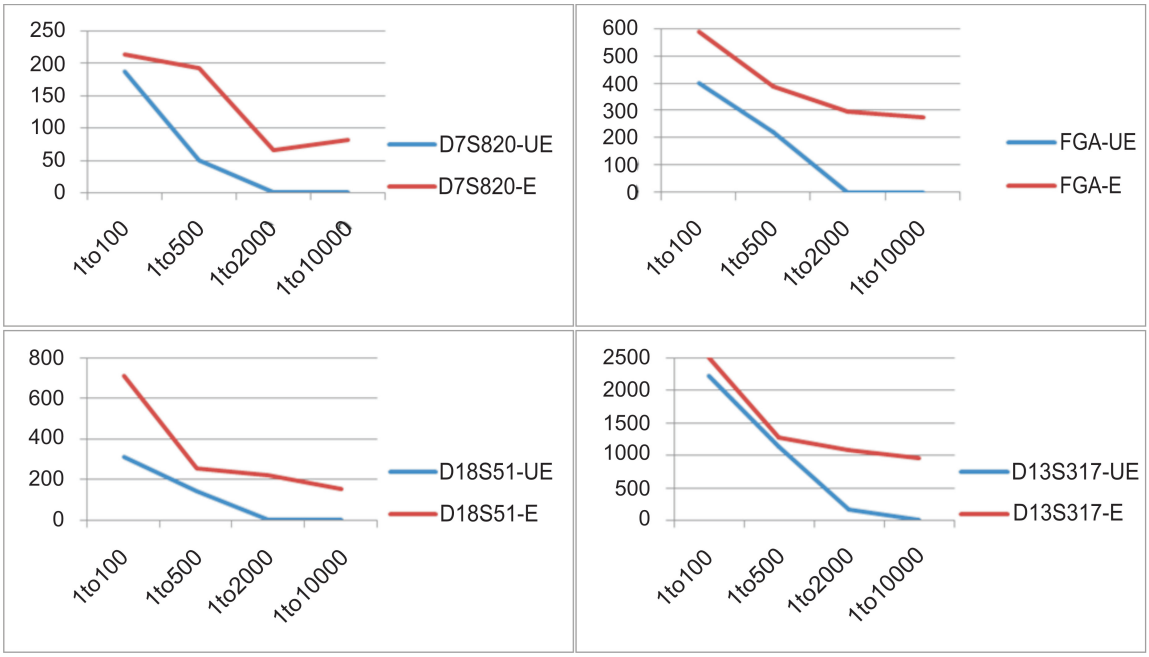


Figure 1. Enrichment of STR loci by modified PEC method. FGA, D7S820, D18S51, D13S317 are the representative STR loci. Graphs represent the peak intensities of the respective loci at different reconstitution ratios. ■ Without enrichment (UE), ■ After enrichment (E). X-axis represents different reconstitution ratios; Y-axis represents Relative Fluorescent Units (RFU).

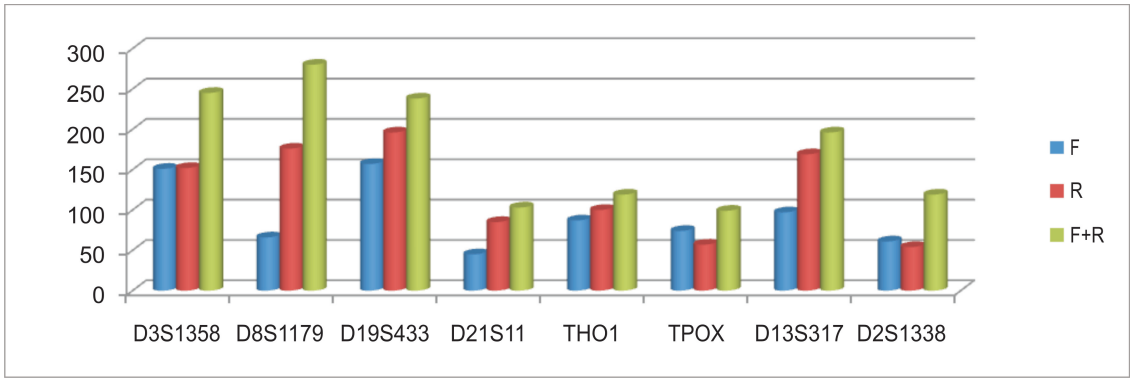


Figure 2. Graph showing the increased amplification after enrichment using both forward and reverse sets of oligos. Peak intensity with only forward set of oligos, Peak intensity with only reverse set of oligos, Peak intensity with both forward and reverse sets of oligos. X-axis represents different loci and Y-axis represents Relative Fluorescent Units (RFU).

Project 3: To study human genetic diversity in various populations groups in India.

Summary of work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

Another area of interest of our laboratory is to access the genetic diversity among different population groups in India and to address questions related to the phenotypic effects of genetic variation(s) within and between population groups. As part of the genotype-phenotype correlation study, we are trying to validate the putative genetic variants such as single nucleotide polymorphisms (SNPs), that play an important role in determining the common phenotypic traits such as skin pigmentation and body-mass index in different population groups in India. To address this question, human saliva samples were collected with informed consent from volunteers belonging to different geographical regions in the country along with melanin index (for skin pigmentation) for our studies. Previously, we had reported about the collection of samples and some preliminary genotyping experiments.

Details of progress made in the current reporting year (April 1, 2010- March 31, 2011)

- **Collection of human samples:** During the current year, additional human saliva samples and necessary phenotypic traits including melanin-index and body-mass index were collected from volunteers belonging to different geographical locations in India.
- **SNP typing experiments for HID purposes:** In the area of DNA forensics, currently, a panel of 16-18 short tandem repeats (STR) loci is employed for human identification (HID) throughout the world. However, a limitation of the STR-based panel has been its failure to generate a complete DNA profile in case of heavily degraded DNAs as encountered in forensic skeletal samples because some of the STR loci have large amplicon sizes (of up to 300-400 bp). Hence, as an alternative, SNP-based panel has been proposed. This can generate full DNA profile even with degraded DNA samples because of their shorter amplicon sizes (40-120 bp). Additionally, SNPs are less prone to mutation than STRs and are also more amenable to higher multiplexing than STRs.
- In view of these advantages, the SNPs have recently gained a lot of attention for its applicability in DNA forensics. In this regard, three panels (Kidd *et al.*, Sanchez *et al.*, and SNP*for*ID) comprising a total of about 140 SNPs have been reported in the literature to be forensically relevant. Though these panels have been formed after studying various worldwide populations, but the panels were not tested in Indian populations and hence, their applicability HID in Indian populations is yet to be ascertained.
- As part of our genetic variation studies and its application in DNA forensics, we had decided to validate the forensically relevant SNPs mentioned above in Indian populations. To ascertain the allelic frequencies of a set

of 90-100 SNPs, shortlisted mostly from Kidd *et. al.* and SNP*for*ID, SNP panel, we plan to use the Illumina BeadXpress platform for genotyping the samples collected as described above in future experiments.

- **Validation of Genplex SNP panel for HID purposes:** In order to validate the Sanchez *et al.* panel, Genplex panel (containing 48 SNPs manufactured by Applied Biosystems, USA) was employed in the lab to ascertain the allele frequencies of these SNPs in various Indian populations. The conditions for Genplex panel were standardized in the lab and are currently employed to determine the allele frequencies of all the 48 SNPs in different Indian populations.

- **Paternity testing with Genplex SNP panel:** Apart from determining the allele frequencies of the 48 SNPs in Indian populations, the applicability of the Genplex panel was tested in determining the paternity cases. In this study, 25 paternity trio cases (i.e. where DNA profiles of mother, disputed child and alleged father are available) were studied. The results obtained from these studies were in good agreement with the results deduced earlier from STR-typing of the same samples.

- During the initial SNP-typing experiments, differences in peak heights among the loci and non-amplification of few loci were observed. We are presently working on addressing these technical issues. Random match probability and power of exclusion values can be calculated only when the allele frequencies of the 48 SNP loci in Genplex panel have been gathered for different Indian population groups. Currently, work is in progress to determine the allele frequencies of all the 48 SNPs in Genplex panel in different Indian population groups. If needed, additional SNPs may be included based on other studies reported in literatures so as to design a SNP-based panel for HID in Indian populations.

Training / Workshops

Workshop conducted on “Genetic fidelity testing of tissue culture raised micropropagules employing DNA-based markers” in February 2011.

Publications

1. Dalal A, Sarkar A, Priya TP and Nandineni MR (2010). Giuffrè-Tsukahara syndrome: Evidence for X-linked dominant inheritance and review. ***American Journal of Medical Genetics*** 152: 2057-2060.

2. Gunnarsdóttir ED, Nandineni MR, Li M, Myles S, Gil D, Pakendorf B and Stoneking M (2011). Larger mtDNA than Y-chromosome differences between matrilocal and patrilocal groups from Sumatra. ***Nature Communications*** 2: 228.

3. Nandineni MR, Prasad SPR, Goud ChV, Negi DS, Nagaraju J and Gowrishankar J (2010). DNA-based identification of victims of the Mangalore air crash of May 2010. ***Current Science*** 99: 341-342.

LABORATORY OF FUNGAL PATHOGENESIS

Understanding the Pathobiology of an Opportunistic Human Fungal Pathogen *Candida glabrata*

Principal Investigator	Rupinder Kaur	Staff Scientist
PhD Students	Gaurav	Senior Research Fellow
	Maruti Nandan Rai	Senior Research Fellow
	Sapan Borah	Senior Research Fellow
	Vivek Kumar Srivastava	Junior Research Fellow
Other Members	DPSS Lakshmi	Technical Assistant
	G Neelima	Project Assistant (Till Sep. 2010)
	Sriram Balusu	Project Assistant
	Shivarathri Raju	Project Assistant
	Rosalin Sahoo	Project Assistant (Since Oct. 2010)

Candida glabrata is an opportunistic human fungal pathogen that resides as a commensal in the mucosal membranes of healthy individuals but can cause both superficial mucosal and life threatening, invasive systemic infections under conditions of immuno-compromise. *C. glabrata* accounts for ~12-20% of total *Candida* blood stream infections worldwide and is the second or third most common cause of Candidemia depending upon the geographical location. In addition, *C. glabrata* infections are usually associated with a high mortality rate, presumably in part, due to its low inherent susceptibility to antifungal drugs including fluconazole. Research in our laboratory is centered on elucidating the molecular basis of low intrinsic susceptibility of *C. glabrata* towards fluconazole and its interaction with host immune cells.

Project 1: Functional genomic analysis of *C. glabrata*-macrophage interaction

Objectives

1. Analysis of intra-cellular behavior
2. Screening of *C. glabrata* mutant library for altered survival profiles
3. Identification and analysis of the genes required for survival *in vitro*.

Summary of the work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

Using an *in vitro* system consisting of human monocytic cell line THP1, we showed that wild-type *C. glabrata* cells are not killed by activated macrophages, instead, they undergo a moderate 5-7 fold replication over a period of 24 h upon co-incubation with macrophages. Next, we screened a *C. glabrata* mutant library (18,432 mutants; generated by homologous recombination of *in vitro* generated Tn*7* insertions in *C. glabrata* genomic clones) for altered survival profiles in macrophages *via* a modified version of signature-tagged mutagenesis approach. Mutants with an output/input ratio of = 6.0 and = 0.1 were selected as 'up' (increased survival) and 'down' (reduced survival) mutants, respectively. Using this ratio as cut-off criteria, a total of 175 mutants were identified that displayed altered survival profiles in differentiated THP1 cells. Tn*7* insertion mapping and sequence analyses of the mutants identified a set of 102 genes in *C. glabrata* that are required for its survival/replication in cultured human macrophages. The survival defect of identified mutants was confirmed by conducting single infection assays. Additionally, phenotypic profiling of the mutants under several stress conditions including acidic pH, high temperature, oxidative stress, cell wall stress revealed overlapping sensitivities to different stresses for very few mutants, thereby, precluding the possibility of general sick mutants (slow-growers) coming through the screen.

Details of the progress made in the current reporting year (April 1, 2010 – March 31, 2011)

During the current reporting period, we classified identified genes into functional classes based upon the Gene Ontology (GO) annotations (for biological processes) of their *S. cerevisiae* homologs in the

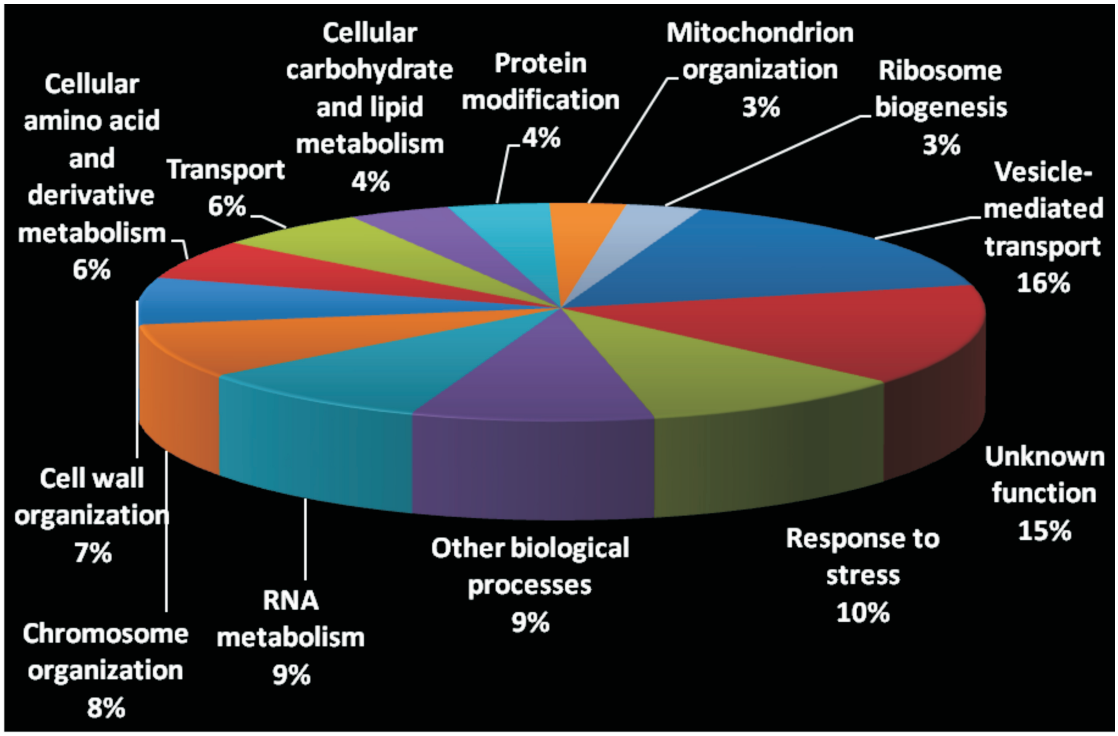


Figure 1. Pie chart showing putative gene functions of insertion loci in mutants identified by the screen

Saccharomyces Genome Database (SGD). 10% of the identified genes were involved in stress response while genes implicated in cell wall organization, chromatin remodeling and vesicular transport constituted 7%, 8% and 15%, respectively of total identified genes (Figure 1).

To assess the physiological functions of the identified genes in survival/replication in macrophages, we extracted chromatin from macrophage-internalized wild-type *C. glabrata* cells and examined both total levels of histone proteins as well as several post-translational modifications of histones H3 and H4. An altered epigenetic signature was observed for chromatin isolated from internalized yeasts compared to the wild-type cells grown in RPMI medium under tissue-culture conditions. In accord with this, chromatin isolated from internalized yeasts displayed resistance to micrococcal nuclease digestion post 6 and 12 h of co-incubation with macrophages (Figure 2).

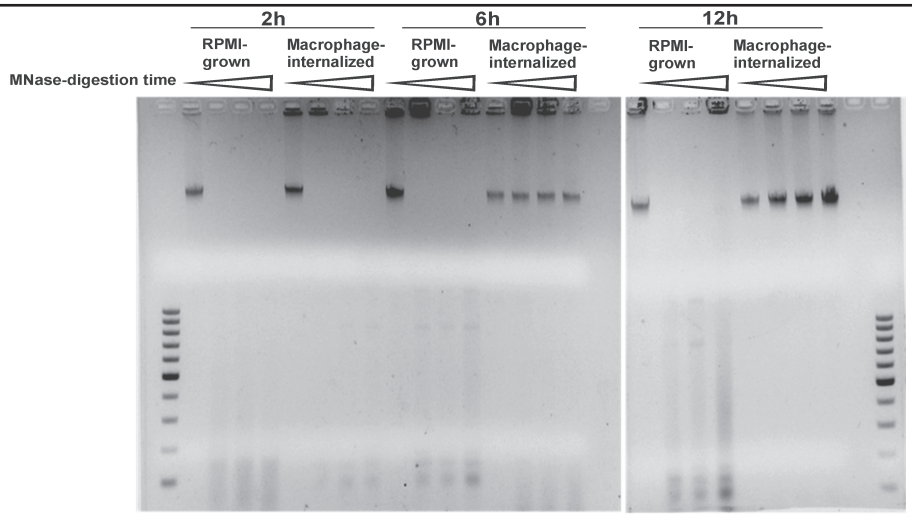


Figure 2. Chromatin of phagocytosed wild-type cells is resistant to Micrococcal nuclaease digestion

Together, these data indicate that upon internalization by macrophages, wild-type *C. glabrata* cells remodel their chromatin structure, probably, to adapt to the nutrient-poor environment and to survive/counteract oxidative and nitrosative stress exerted by human macrophages.

Next, we chose a total of 17 genes belonging to chromosome organization, stress response and vesicle-mediated transport for further analysis; we have successfully generated knock-out strains for nine of these genes and are currently trying to delete the remainder 8 genes. Phenotypic and molecular characterization of the strains deleted for genes, implicated in DNA damage response, revealed that inability to survive in macrophages is partially due to defective repair of ROS-induced DNA damage and incapacity to withstand the oxidative stress generated by host immune cells.

Future studies will be focused at transcriptional profiling of internalized wild-type and select knock-out strains to identify the genes differentially regulated in response to intracellular milieu of macrophage and at determining the virulence potential of knock-out strains in murine model of systemic infection.

Project 2: Innate resistance of *C. glabrata* to fluconazole

Objectives

1. Understanding the molecular basis of low inherent susceptibility of *C. glabrata* towards fluconazole
2. Identification of targets for combinatorial therapy with azole antifungals.

Summary of the work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

We have previously reported two mutants, carrying Tn7 insertions in genes *FLV1* and *FLV2* (fluconazole loss of viability), to display sensitivity to fluconazole as well as to lose viability during fluconazole stress. While our attempts to delete *FLV2* were unsuccessful indicating *FLV2* to be an essential gene, the *flv1*D*::hph* knock-out, surprisingly, exhibited high level of resistance to fluconazole. However, subsequent studies revealed that fluconazole resistance of *flv1*D*::hph* strain was due to the presence of *hph* gene (confers hygromycin resistance) rather than the disruption of the *FLV1* gene as removal of *hph* cassette led to fluconazole sensitivity in *flv1*D*::hph* strain. Thus, we generated another deletion strain where *FLV1* was replaced with dominant nourseothricin resistance marker (encoded by *nat1*) by fusion PCR-based disruption strategy and further studies are being carried out with *flv1*D*::nat1* strain which showed increased sensitivity to fluconazole.

Details of the progress made in the current reporting year (April 1, 2010 – March 31, 2011)

In a previous screen for altered fluconazole susceptibility profiles, we had identified catalytic and regulatory subunits of calcium channel, CgCch1 and CgMid1, whose disruption rendered fluconazole a fungicidal drug. During the current reporting period, expanding upon our earlier findings, we screened 9,134 additional *C. glabrata* Tn*7* insertional mutants for inability to survive fluconazole stress by plate growth assays. Methylene Blue (MB) was used to distinguish live cells from dead cells as MB is

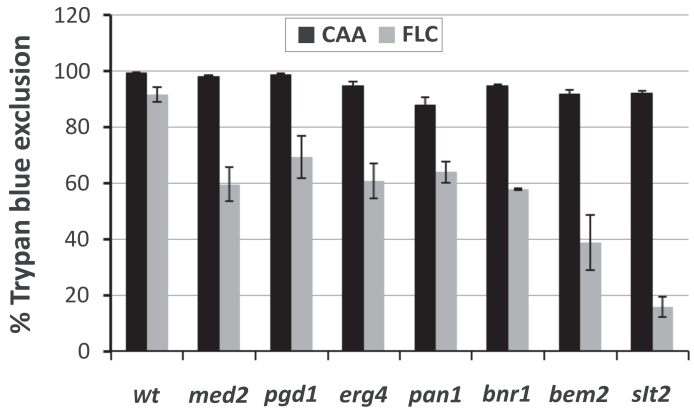


Figure 3. Trypan blue exclusion assay to assess the viability of fluconazole (FLC) sensitive mutants in the presence of fluconazole. Cells were grown in CAA medium with or without 128 mg/ml fluconazole for 24 h, harvested and were washed twice with PBS. Cells were stained with 0.4% trypan blue and a minimum of total 300 cells (stained (dead) and unstained (viable)) were counted microscopically for each strain. Cell viability data were plotted as the percentage of trypan blue exclusion and represent the mean of three to six independent analyses (± SEM)

enzymatically broken down to a colorless product by viable cells while non-viable cells accumulate un-degraded MB resulting in dark blue colored colonies. From a set of 9,134 mutants screened, a total of 200 mutants showed significant growth inhibition in the presence of 8 µg/ml fluconazole. Of these, 91 mutants displayed a distinct dark blue color on plates supplemented with 0.01% methylene blue and 16 µg/ml fluconazole. Survival defects of these mutants in the presence of fluconazole were independently validated by either trypan blue exclusion/dilution spotting or colony forming unit assays and a reproducible loss of viability was observed for 20 mutants in these assays. As shown in Figure 3, while ~ 95% of *C. glabrata wt* cells remained viable after 24 h of treatment with fluconazole, fluconazole 'loss of viability' mutants exhibited a survival rate of 18%-68%.

Tn*7* insertion mapping and sequencing analysis of these 20 mutants identified multiple insertions in 7 genes (Table 1). *S. cerevisiae* orthologs of *CgBEM2* and *CgPAN1* are required for organization of actin cytoskeleton while *MED2* and *PGD1* are involved in RNA polymerase II-mediated transcription. In this context, it is noteworthy that Gal11p/MED15 subunit of the mediator co-activator complex has recently been demonstrated to be essential for CgPdr1-regulated expression of multidrug efflux pumps in *C. glabrata.* Slt2 and Bnr1 are downstream targets of Pkc1-mediated CWI pathway and Rho-type GTPases family, respectively in *S. cerevisiae*. *CgERG4* encodes C-24 sterol reductase, an enzyme of ergosterol biosynthesis pathway. Importantly, none of these genes has directly been implicated in calcium signaling pathway, thus, alluding to the contribution of other signaling cascades in fluconazole susceptibility of *C. glabrata*.

Mutants carrying Tn*7* insertions in genes coding for multidrug efflux pumps, CgCdr1 and CgPdr12 showed growth defects in the presence of fluconazole but retained viability. A recent study has reported an essential role for PKC signaling in antifungal drug resistance of *C. albicans via* a circuitry composed of Mkc1, Calcineurin, and Hsp90. Of the seven genes identified in our mutant screen, three genes encode putative constitutents of Rho1-regulated Pkc1-mediated cell wall integrity pathway. *CgBEM2* and *CgSLT2* code for a Rho1 GTPase activating protein (RhoGAP) and a serine/threoine MAP kinase, respectively while *CgBNR1* encodes a formin protein. In *S. cerevisiae*, Bni1, a homolog of Bnr1, is a target of an essential small GTPase Rho1.

Mutant	CAGL-ORF	*S. cerevisiae* ortholog	ORF length (nt)	Position (nt) of Tn*7* insertion
RNA polymerase II mediator complex				
Cgmed2	*CAGL0C04477g*	*YDL005c*	1107	318
Cgpgd1	*CAGL0A01325g*	*YGL025c*	1434	1252
Ergosterol biosynthesis				
Cgerg4	*CAGL0A00429g*	*YGL012w*	1395	170
Actin cytoskeleton organization				
Cgpan1	*CAGL0J01892g*	*YIR006c*	4125	698
Rho1-mediated signaling				
Cgbnr1	*CAGL0H06765g*	*YIL159w*	3885	1747
Cgbem2	*CAGL0I06512g*	*YER155c*	6360	1997
Cgslt2	*CAGL0J00539g*	*YHR030c*	1467	557

Table 1. Mutants identified in a screen for viability loss in the presence of fluconazole

To examine if CgPkc1-mediated CWI pathway regulates antifungal drug susceptibility in *C. glabrata*, we conducted phenotypic profiling analyses on all fluconazole sensitive mutants. Mutants potentially disrupted for PKC signaling exhibited sensitivity to all azole drugs and cell wall damaging agents including caffeine, calcofluor white and congo red, however, no altered sensitivity to a polyene antifungal amphotericin B was observed for any of the mutants. Mutants defective in RNA polymerase II-mediated transcription and multidrug efflux pumps displayed sensitivity to only azoles. Studies are currently underway to elucidate the role of Rho GTPase-mediated signaling and RNA polymerase II mediator complex in *C. glabrata*'s survival during fluconazole stress.

Publications

1. Bairwa G and Kaur R (2011). A novel role for a glycosylphosphatidylinositol-anchored aspartyl protease, CgYps1, in the regulation of pH homeostasis in *Candida glabrata*. ***Molecular Microbiology*** 79: 900-913.

2. Yadav AK, Desai PR, Rai MN, Kaur R, Ganesan K and Bachhawat AK (2011). Glutathione biosynthesis in the yeast pathogens *Candida glabrata* and *Candida albicans*: Essential in *C. glabrata*, and essential for virulence in *C. albicans*. ***Microbiology*** 157: 484-495.

LABORATORY OF IMMUNOLOGY

Understanding the Role of Azadirachtin in Inducing Anti-Inflammatory, Anti-Teratogenic, and Anti-Tumorigenic Activities

Principal Investigator	Sunil K Manna	Staff Scientist
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	Sidharth Mahali	Senior Research Fellow
	S Adeel Husain Zaidi	Senior Research Fellow
	M Raveendra Babu	Junior Research Fellow
	Neeharika Verma	Junior Research Fellow
Other Members	Nune Raviprakash	Proejct Senior Research Fellow
	T Navneeta	Technical Assistant
Collaborators	Usha Naik	Osmania Medical College, Hyderabad
	Chitta S Kumar	SK University, Arunachal Pradesh

Objectives

1. Understanding the term - 'Neem, a Sarvo Rog Hara'
2. Detection of the molecular mechanisms mediated by novel small molecules to induce anti-inflammatory, anti-teratogenic, and anti-tumorigenic responses
3. Regulation of cytokine receptors to regulate tumorigenesis and inflammatory responses.

Summary of work done until the beginning of this reporting year (April 1, 2009 - March 31, 2010)

Doxorubicin is one of the most effective molecules used in the treatment of various tumors. Contradictory reports often open windows to understand the doxorubicin-mediated signaling to exert its apoptosis effect. We provided evidences that doxorubicin induced biphasic induction of nuclear factor kappaB (NF-κB). Late phase induction of NF-κB was observed through interleukin 8 (IL-8), expressed by doxorubicin treatment. Increased amount of IL-8 induced apoptosis via increase in the releases of intracellular Ca^{2+}, activation of calcineurin, nuclear translocation of nuclear factor activated T-cell (NF-AT), and NF-AT-dependent FasL expression (**Charitha *et al*, Breast Cancer Res. Treat., 120: 671-783, 2010**). The compound 5-(4-methoxyarylimino)-2-N-(3,4-dichlorophenyl)-3-oxo-1,2,4-thiadiazolidine (P_3-25) is known to possess anti-bacterial, anti-fungal, and anti-tubercular activities. Here we provided evidence for the first time that P_3-25 interacts with TRAF2 in such manner where recruitment of TANK is completely inhibited and thereby inhibits recruitment of IKKs. Thus, P_3-25 is inhibiting IkBa degradation thereby arresting NF-κB in cytoplasm. It facilitates binding of mitogen activated protein kinase kinase kinase (MEKK) 1 with TRAF2 and thereby activates c-Jun-terminal kinase (JNK) and AP-1. P_3-25 blocks NF-κB-dependent gene transcription by inhibiting p65 phosphorylation. Thus, double sword mechanisms of P_3-25's action are shutting down NF-κB functions completely (**Manna *et al*, J. Biol. Chem., 285: 11617-11627, 2010**). The role of azadirachtin, an active component of a medicinal plant Neem on TNF-induced cell signaling was investigated. Azadirachtin blocks TNF-induced activation of NF-κB. It blocks binding of TNF, but not IL-1, IL-4, IL-8, or TNF-related apoptosis inducing ligand (TRAIL) with its respective receptors. Azadirachtin inhibits TNF binding in both TNFR1 and 2. Further, *in silico* data suggest that azadirachtin strongly binds in the TNF binding site of TNFR (**Thoh *et al*, J. Biol. Chem., 285: 5888-5895, 2010**).

Details of progress in the current reporting year (April 1, 2010 - March 31, 2011)

A. Azadirachtin interacts with retinoic acid receptors and inhibits retinoic acid-mediated biological responses

Considering the role of retinoids in regulation of more than 500 genes involved in cell cycle and teratogenesis, detailed understanding the mechanism and its regulation is useful for therapy.

In this report, we prove the detailed mechanism on the regulation of retinoic acid-mediated cell signaling by azadirachtin, active components of neem extract. Azadirachtin (Figure 1A) repressed all trans-retinoic acid (ATRA)-mediated nuclear transcription factor kappaB (NF-κB) activation, not the DNA binding (Figure 1C) but the NF-κB-dependent gene expression as shown by ICAM1 and Cox2 expression (Figure 1B). It did not inhibit IκBα degradation, IKK activity either by *ex vivo* or *in vitro* (Figure 1D). Azadirachtin inhibited TRAF6-mediated, but not TRAF2-mediated NF-κB activation. It inhibited ATRA-induced Sp1 and CREB DNA binding. Azadirachtin inhibited ATRA binding with retinoid receptors which is supported by biochemical (Figure 1E) and *in silico* (Figure 1F)

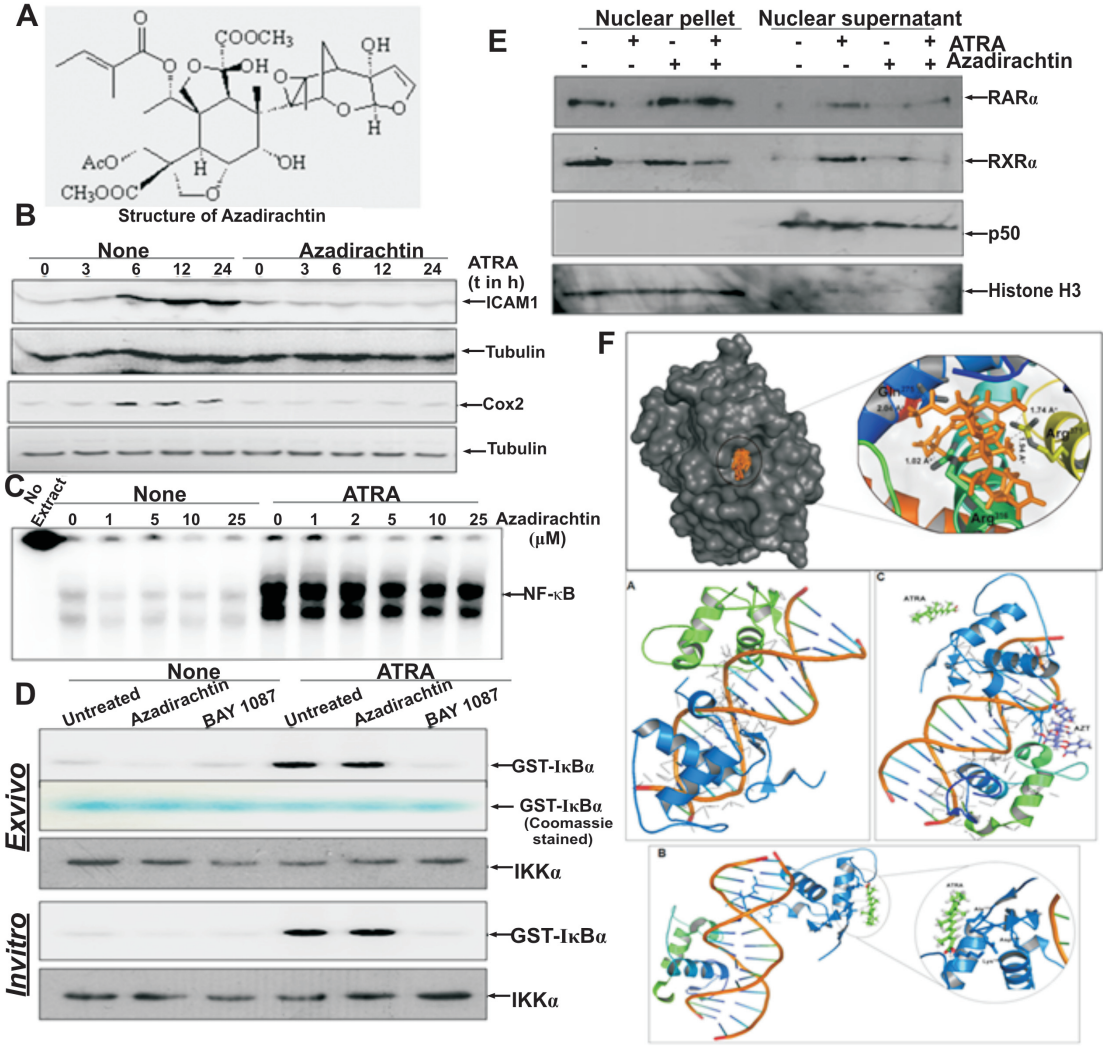

Figure 1. Azadirachtin inhibits ATRA-induced NF-κB activation by downregulating RARα by interacting with ligand binding domain. Structure of azadirachtin (A). Azadirachtin inhibited ATRA-induced ICAM1 and Cox2 activation (B), without much inhibiting NF-κB DNA binding (C). Azadirachtin was unable to inhibit ATRA-induced IKK activation both in *ex vivo* and *in vitro* as shown by in vitro kinase assay using GST-IκBα as substrate (D). A549 cells were treated with azadirachtin for 6 h and then stimulated with ATRA for 24 h. Nuclei were isolated with isotonic lysis buffer and then nuclear pellet were suspended in hypertonic buffer with 100 mM NaCl for 1 h. Nuclear supernatant and nuclear pellet were separated and solubilized with 2x Laemmli buffer and run in 15% SDS-PAGE. RARα and RXRα were detected by Western Blot using 50 μg of proteins. Blots were reprobed for histone H3 and p50 (E). RARα residues Ala^{271}, Gln^{275}, Arg^{316}, Leu^{326} and Lys^{381} showing a hydrogen bonds with AZT (shown in magenta color), where the ATRA (shown in yellow color) showing no interaction with any other amino acid residues in RARα (F, upper panel). RXR-RAR complex with DNA (RXR-RAR showing strong hydrogen bond interaction with DNA) (FA); Binding of ATRA with RXR amino acid residues (zoom view) and this create a very less hydrogen interaction of RXR-RAR with DNA (DNA fall off) (FB); Binding of AZT with RAR (this creates a increase interaction between RXR-RAR with DNA and also AZT doesn't allow ATRA for binding at RAR-RXR complex) (FC)

evidences. Azadirachtin showed strong interaction with retinoid receptors. It suppressed ATRA-mediated removal of retinoid receptors, bound with DNA by inhibiting ATRA binding to its receptors. Overall, our data suggest that azadirachtin interacts with retinoic acid receptors and suppresses ATRA binding, inhibits falling off the receptors and activates transcription factors like CREB, Sp1, NF-κB, etc. and proved to be exerts anti-inflammatory and anti-teratogenic responses.

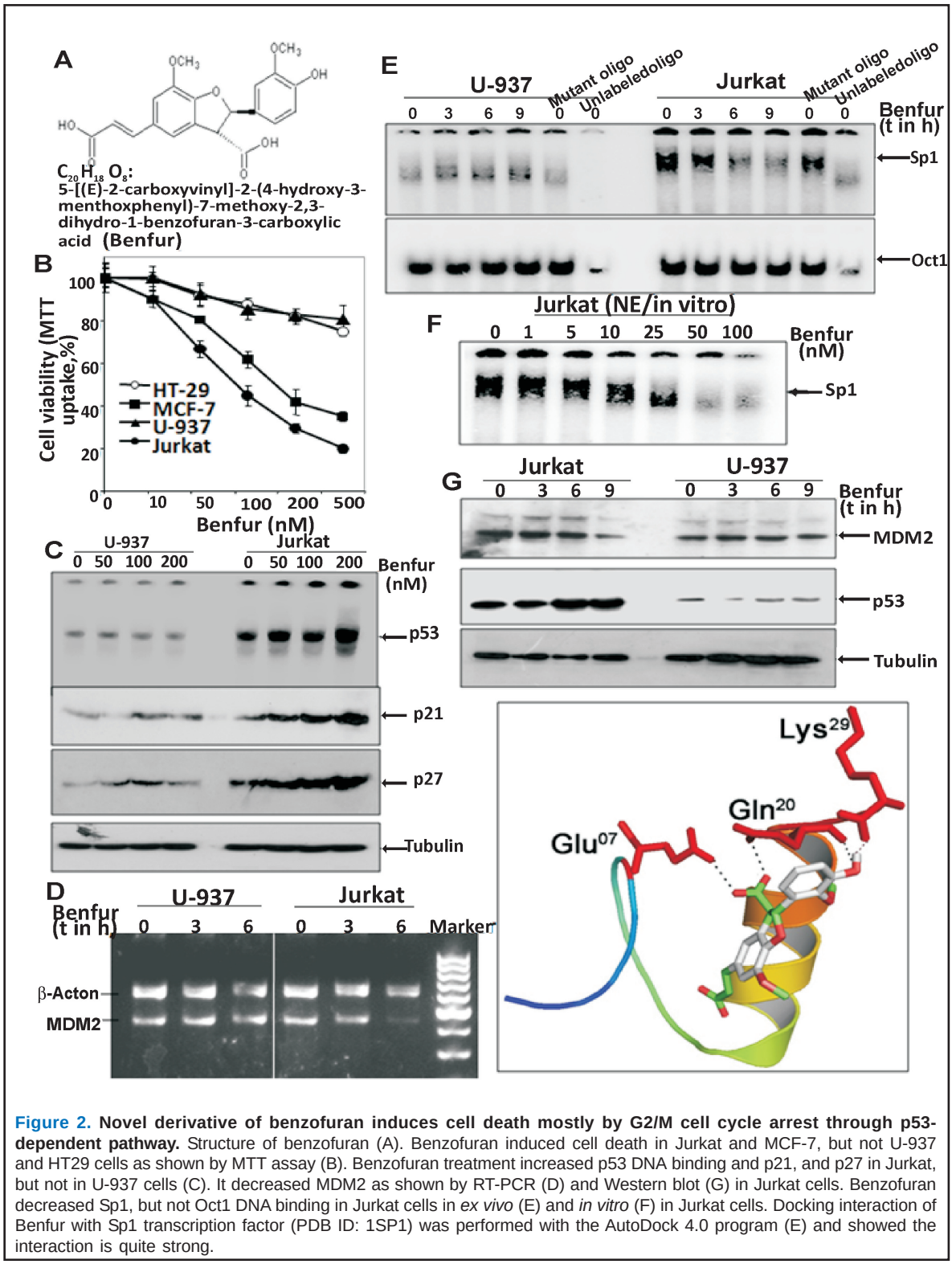

Figure 2. Novel derivative of benzofuran induces cell death mostly by G2/M cell cycle arrest through p53-dependent pathway. Structure of benzofuran (A). Benzofuran induced cell death in Jurkat and MCF-7, but not U-937 and HT29 cells as shown by MTT assay (B). Benzofuran treatment increased p53 DNA binding and p21, and p27 in Jurkat, but not in U-937 cells (C). It decreased MDM2 as shown by RT-PCR (D) and Western blot (G) in Jurkat cells. Benzofuran decreased Sp1, but not Oct1 DNA binding in Jurkat cells in *ex vivo* (E) and *in vitro* (F) in Jurkat cells. Docking interaction of Benfur with Sp1 transcription factor (PDB ID: 1SP1) was performed with the AutoDock 4.0 program (E) and showed the interaction is quite strong.

B. Novel derivative of benzofuran induces cell death mostly by G2/M cell cycle arrest through p53-dependent pathway but partially by inhibition of NF-κB

The *Dracaena* resin is widely used in traditional medicine as an anticancer agent and benzofuran lignin is the active component of it. In this report, we provide evidences that the synthetic derivative of benzofuran lignan (Benfur) (Figure 2A) showed anti-tumor activities. It induced apoptosis in p53 positive cells (Figure 2B). Though it inhibited endotoxin-induced NF-κB activation in both p53 positive and negative cells, the activation of caspase

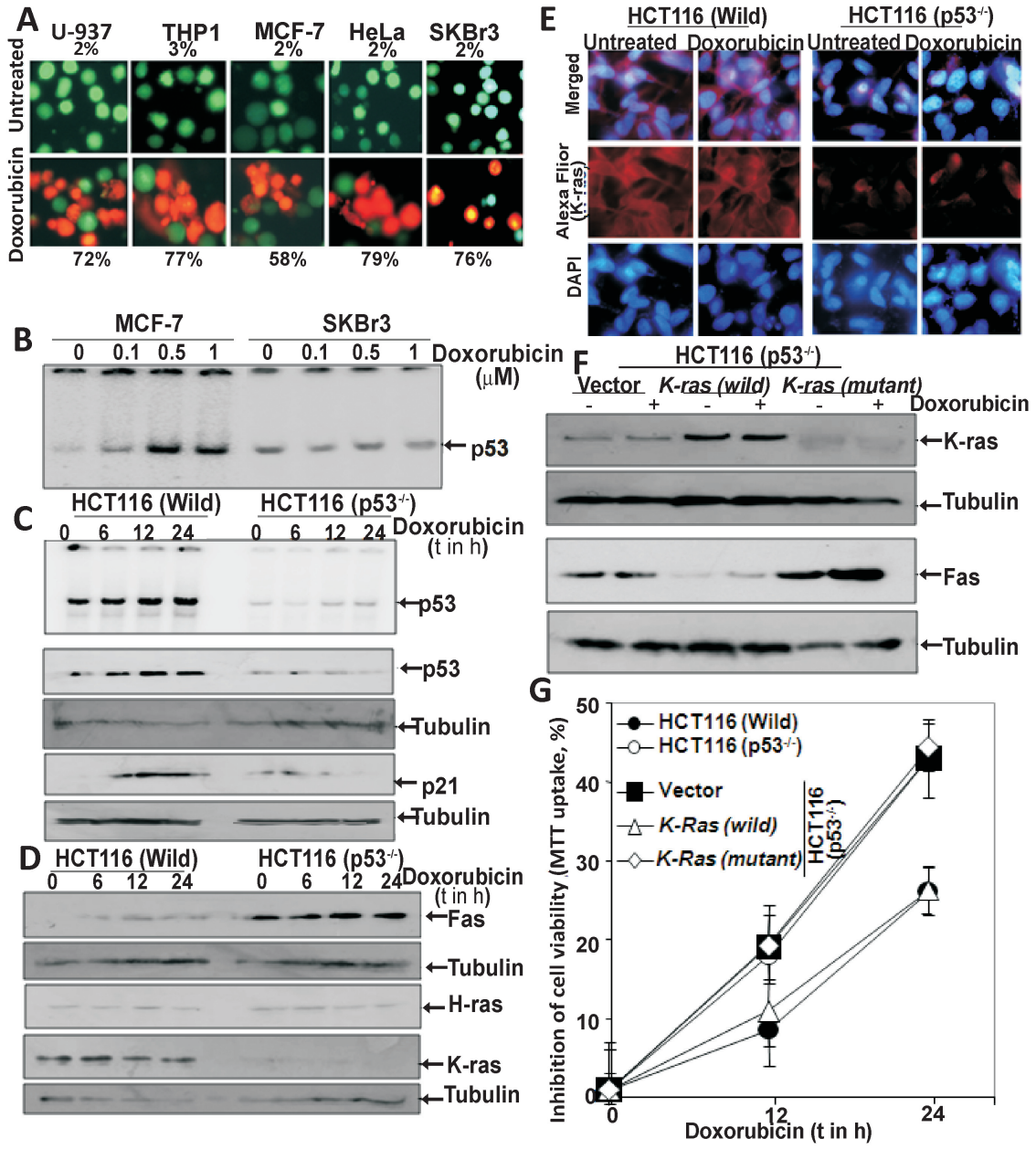

Figure 3. Ras puts brake on doxorubicin-mediated cell death in p53 expressing cells. Doxorubicin induced more cell death in p53 negative cells (U-937, THP1, SKBr3, and HeLa) than p53 positive (MCF-7) cells as shown by Live&Dead assay (A). Doxorubicin increased p53 DNA binding in MCF-7, but not SKBr3 cells (B). Doxorubicin increased p53 DNA binding and p53 and p21 expression in HCT116 p53 positive cells (C). The expression of Fas increased, but K-ras decreased in p53 negative cells as shown by Western blot (D) and immunofluorescence study (E). Overexpression of wild type K-ras in p53 negative cells decreased basal expression of Fas (F). K-ras overexpressed p53 negative cells showed less sensitive to doxorubicin-mediated cell death (G).

3 was observed in p53 positive cells. It showed partial cell death effect in both p53 positive and negative cells through inhibition of NF-κB. Cell cycle analysis using flow cytometry showed that the G2/M arrest in Jurkat T-cells, but not U-937 cells upon benozofuran treatment. It increased amounts of p21 and p27 through p53 nuclear translocation in Jurkat T-cells, but not in U-937 cells (Figure 2C). It inhibited amount of MDM2 (murine double minute 2) (Figure 2D and 2G) by repressing the transcription factor Sp1 *ex vivo* (Figure 2E) as well as *in vitro* (Figure 2F) which was proved *in silico* (Figure 2H) too. It induced cell death in tumor cells, but not in primary T-cells. Overall, our data suggest that Benfur-mediated cell death is partially dependent upon NF-κB, but predominantly dependent on p53. Thus, this novel benzofuran lignan derivative can be effective chemopreventive agent against malignant T-cells.

C. Ras puts brake on doxorubicin-mediated cell death in p53 expressing cells

Doxorubicin is one of the most effective molecules used in the treatment of various tumors. Contradictory reports often open windows to understand the role of p53 tumor suppressor in doxorubicin-mediated cell death. In this report, we provide evidences that doxorubicin induced more cell death in p53 negative tumor cells. Doxorubicin induced cell death in p53 positive cells like U-937, SKBr3, HeLa, and THP1 more aggressively than p53 positive MCF7 cells (Figure 3A) though it induced p53 and dependent genes in p53 positive cells (Figures 3B and 3C). Doxorubicin increased the amount of FasL by enhancing activator protein (AP) 1 DNA binding in both p53 positive and negative cells, but the basal expression of Fas was more in p53 negative cells (Figure 3D). In contrast, the basal expression of Ras oncoprotein was more in p53 positive cells (Figure 3E) that might increase the basal expression of Fas in these cells. Overexpression of Ras decreased the amount of Fas in p53 negative cells (Figure 3F) thereby decreases doxorubicin-mediated aggressive cell death (Figure 3F). Overall, this study will help to understand the much studied chemotherapeutic drug, doxorubicin-mediated cell signaling cascade that leads to cell death in p53 positive and negative cells. High basal expression of Fas might be important determinant in doxorubicin-mediated cell death in p53 negative cells.

Publications

1. Gangadharan C, Thoh M and Manna SK (2010). Late phase activation of nuclear transcription factor kappaB by doxorubicin is mediated by interleukin-8 and induction of apoptosis via FasL. ***Breast Cancer Research Treatment*** 120: 671-683.
2. Manna SK, Babajan B, Raghavendra PB, Raviprakash N and Kumar CS (2010). Inhibiting TNF receptor associated factor 2-mediated activation of nuclear factor kappaB facilitates induction of activator protein-1. ***Journal of Biological Chemistry*** 285: 11617-11627.
3. Manna SK, Bose JS, Gangan V, Raviprakash N, Navneetha T, Raghavendra PB, Babajan B, Kumar CS and Jain SK (2010). Novel derivative of benzofuran induces cell death mostly by G2/M cell cycle arrest through p53-dependent pathway but partially by Inhibition of NF-κB. ***Journal of Biological Chemistry*** 285: 22318-22327.
4. Thoh M, Kumar P, Nagarajaram HA and Manna SK (2010). Azadirachtin interacts with the binding domain of its receptors and inhibits TNF-induced biological responses. ***Journal of Biological Chemistry*** 285: 5888-5895.
5. Kole L, Giri B, Manna SK, Pal B and Ghosh S (2011). Biochanin-A, an isoflavon, showed anti-proliferative and anti-inflammatory activities through the inhibition of iNOS expression, p38-MAPK and ATF-2 phosphorylation and blocking NF-κB nuclear translocation. ***European Journal of Pharmacology*** 653: 8-15.
6. Manna SK, Gangadharan C, Edupalli D, Raviprakash N, Navneetha T, Mahali S and Thoh M (2011). Ras puts brake on doxorubicin-mediated cell death in p53 expressing cells. ***Journal of Biological Chemistry*** 286: 7339-7347.
7. Thoh M, Babajan B, Raghavendra PB, Sureshkumar C and Manna SK (2011). Azadirachtin interacts with retinoic acid receptors and inhibits retinoic acid-mediated biological responses. ***Journal of Biological Chemistry*** 286: 4690-4702.
8. Majumdar S, Dutta K**,** Manna SK, Basu A and Bishayi B (2011). Possible protective role of chloramphenicol in TSST-1 and coagulase positive *Staphylococcus aureus* induced septic arthritis with altered levels of inflammatory mediators. ***Inflammation*** (In press).

LABORATORY OF BACTERIAL GENETICS

Studies on Gene Regulation, Transcription Termination, and Amino Acid and Ion-Transport in *Escherichia coli*

Principal Investigators	J Gowrishankar	Director & Staff Scientist
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	Shivalika Saxena	Senior Research Fellow
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	L Shanthy	Senior Research Fellow
	Amit Pathania	Junior Research Fellow
	Aanisa Nazir	Junior Research Fellow
	Amar Deep Lakra	Junior Research Fellow
	Rajvardhan Madhukar Kamble	Junior Research Fellow (Since Jan. 2011)
Other Members	VK Mishra	Staff Scientist
	K Anupama	Staff Scientist
	J Krishna Leela	Technical Officer III
	TS Shaffiqu	Technical Assistant
	Vimala Allada	Project Associate
	P Hima Bindu	Project Associate
	S Mahalakshmi	Project Assistant

Objectives

1. To study the ArgP regulon and the mechanism of ArgP-mediated transcriptional regulation of the arginine exporter ArgO
2. To test the model of and mechanisms mediating R-loop formation from nascent untranslated transcripts
3. To investigate an unusual phenomenon of K^+ toxicity in *hns trx* double mutant strains
4. To understand biological functions of the stringent response factors (p)ppGpp/DksA
5. To delineate roles of transketolase function in *E. coli* physiology.

Summary of work done until the beginning of this reporting year (April 1, 2009 - March 31, 2010)

The work undertaken in earlier years on each of the objectives has been summarized in the first parts of the corresponding descriptions below.

Details of progress made in the current reporting year (April 1, 2010 - March 31, 2011)

1. Studies on Rho-dependent transcription-termination and the R-loop model

a. In work from this laboratory that had been described in the earlier reports, we had shown that a newly identified missense mutation (R258C) in the gene encoding the transcription elongation factor NusA confers phenotypes of defective factor-dependent transcription termination (also called polarity relief) and lethality with plasmid pACYC184 similar to mutations affection the Rho or NusG proteins (Rho-A243E and NusG-G146D, respectively). Furthermore, we had found that the polarity relief phenotypes of the *rho, nusG* or *nusA* mutations could be suppressed or reversed by a variant of the 137-amino acid-long DNA-binding nucleoid protein H-NS that is truncated after residue

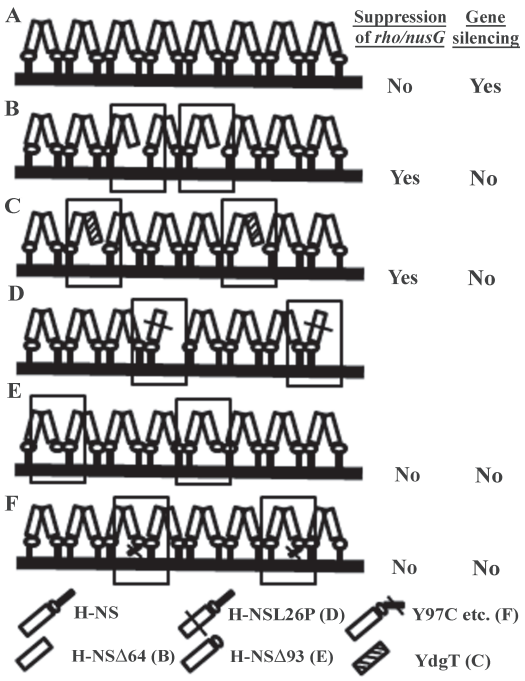

Figure 1. Diagram representation of the interrupted polymeric scaffold model to explain modulation of Rho-dependent termination by some but not all H-NS variants and by YdgT. DNA is denoted by the horizontal line in all panels, and given in the key are the protomer depictions of H-NS and its variants and of YdgT (with the panel in which each of the variants is inserted mentioned in parentheses). For H-NS, the N-terminal domain (residues 1-63), linker or intermediate region (residues 64-92), and DNA-binding domain (residues 93-137) are represented by the rectangle, oval, and solid bar, respectively. (A) Wild-type H-NS uses two inter-subunit contact motifs to form the polymer scaffold from which the DNA-binding domains extend to interact with DNA. Insertion into the scaffold of H-NSΔ64 (B) or YdgT (C) on the one hand, or L26P (D) on the other, leads to its interruption in two alternative ways; insertion of H-NSΔ93 (E) or the other H-NS variants such as Y97C, I119T or P116S (F) does not affect the scaffold continuity but interferes only with DNA binding. Sites of such insertions into the scaffold are boxed in each panel. Also shown are corresponding effects with respect to (a) suppression of *rho* and *nusG* phenotypes, and (b) ability to silence *proU* gene expression.

63 (designated H-NSΔ64), as also by overexpression of YdgT which is a member of the H-NS family of proteins that shares structural similarity and interacts with the N-terminal half of H-NS.

In the current year, we tested a set of H-NS variants in addition to H-NSΔ64 for their ability to suppress the transcription termination defects of the *rho*, *nusG,* and *nusA* mutants. All of these H-NS variants are known to be dominant negative for the gene silencing functions of H-NS, for example on repression of *proU* expression, which we confirmed in this study. Of the H-NS variants tested, L26P and E53G/T55P behaved like Δ64 in suppressing the polarity relief and pACYC184 lethality phenotypes, whereas others including Δ93, Y97C, P116S or I119T were ineffective for such suppression. Multicopy-*ydgT*$^{+}$ (which suppresses polarity relief) was also derepressed for *proU* expression.

The data above therefore indicate that mutants of H-NS that are uniformly defective for gene silencing functions can nevertheless be subdivided into two categories that can or cannot suppress defective transcription termination. Accordingly, we have proposed a new model that is based in part on the recent findings from other labs that H-NS forms a linear polymeric scaffold through an alternating sequence of site 1-site 1 interactions (involving residues 2 to 47) and site 2-site 2 interactions (involving residues 58 to 84) between adjacent H-NS protomers (note that C-terminal residues from 93 to 137 comprise the DNA-binding domain of H-NS). According to our model, it is the interruption of the scaffold structure caused by the recruitment of protomers of Δ64 or L26P that is correlated with polarity relief suppression, whereas C-terminal domain variants such as Δ93, Y97C etc. exhibit a normal scaffold structure and are not suppressors of polarity relief (although all are defective for gene silencing). A diagram representation of this model is shown in Figure 1.

We also tested the effects of combining two or more of the mutations in *rho*, *nusG* and *nusA* to test for synthetic phenotypes, if any. In this part of the work, we also used two new transcription termination-defective mutations that we had identified, namely Rho-Q32R and Rho-R102S,A243E. The results showed that various combinations of the *rho*, *nusG*, and *nusA* mutations are synthetically lethal and that the lethality is suppressed by expression of H-NSΔ64. Thus, it appears that, by combining different mutations in *rho, nusG* and *nusA*, along with expression of YdgT or of variants of H-NS such as H-NSΔ64, one can generate a wide spectrum of efficiencies of Rho-dependent termination *in vivo*. As depicted schematically in Figure 2, the corresponding

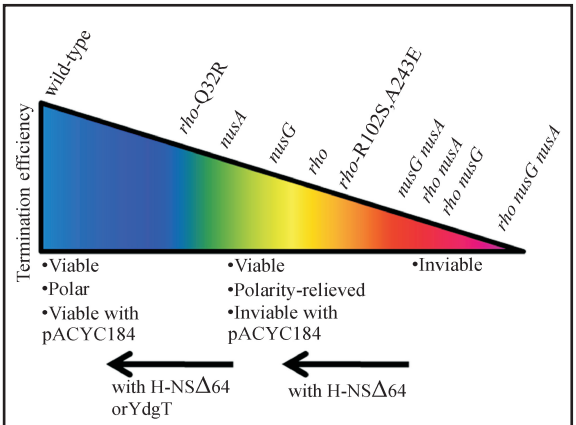

Figure 2. Spectrum of Rho-dependent transcription termination efficiencies in different mutants, and the effects of H-NSΔ64 or YdgT thereon. The designations *rho, nusG* and *nusA* without suffixes refer, respectively, to *rho*-A243E, *nusG*-G146D, and *nusA*-R258C mutations.

phenotypes would extend from viable cells exhibiting full transcriptional polarity (highest efficiency) through viable but polarity-relieved cells (intermediate efficiency) to inviable cells (lowest efficiency). Perturbations involving the H-NS family of proteins, as with expression of H-NSΔ64 or of YdgT, are associated with a shift in the spectrum from lower to higher efficiency, such as to convert synthetic lethal combinations to viable but polarity-relieved states, and polarity-relieved derivatives to those exhibiting full polarity.

b. In last year's Report, we had described the results of genetic experiments to show that whereas the single mutants RNase E- ΔCTH (deleted for the C-terminal half of the 1061-amino acid-long protein), RppH (enzyme RNA 5'-pyrophosphohydrolase that converts 5'-triphosphate in RNA to 5'-monophosphate) or RNase-R169Q (mutated in the 5'-sensor domain so that the enzyme is no longer activated by 5'-monophosphate in the RNA substrate) are viable, the combinations RNase E-ΔCTH ΔRppH or RNase E-R169Q, ΔCTH were synthetically lethal. Furthermore, both lethalities were suppressed by mutations in *rho* or *nusG* that conferred a transcription termination-defective phenotype. The *rho* and *nusG* mutations could also suppress the inviability of Δ*rppH* strains in which the *rne* gene for RNase E was placed downstream of the P_{lac} or P_{ara} promoters in culture media not supplemented with inducer (IPTG or arabinose, respectively).

In the current year, we showed that the *nusA*-R258C mutation defective for transcription termination is also a suppressor of ΔRppH RNase E-ΔCTH synthetic lethality. We measured bulk mRNA decay rates in the single and double mutants (by employing a conditional lethal approach for the synthetic lethal combinations). The data indicate that (i) the single mutant RNase E-ΔCTH exhibits moderate increase in bulk mRNA half-life, consistent with the results from other groups whereas ΔRppH is not different from the wild-type strain; (ii) the synthetic lethal combination of RNase E-ΔCTH with ΔRppH is more severely compromised for mRNA degradation; and (iii) the *rho* suppressor mutation partially reverses the mRNA degradation defect in the synthetic lethal double mutant.

We also examined the processing of tRNA and rRNA precursors in the cultures above. As with bulk mRNA degradation, processing of $tRNA^{Cys}$ and $tRNA^{His}$ was defective in the synthetic lethal mutant under the restrictive conditions (with evidence for accumulation of precursor species in the cells), and was rendered normal in the absence of wild-type Rho (that is, under the permissive conditions). On the other hand, maturation of 5S rRNA from its 9S RNA precursor was apparently unaffected in the ΔRppH RNase E-ΔCTH double mutant strain even in the restrictive conditions.

RNase E expression is transcriptionally autoregulated, such that β-galactosidase expression from a single-copy *rne-lac* fusion is inversely related to the activity of RNase E in the strain. We observed that *rne-lac* expression was elevated in the RNase E-ΔCTH strain compared to that in the strain with full-length RNase E which is consistent with the earlier data, and that the expression was not affected by Δ*rppH, rho* or *nusG* mutations. Thus, the *rho* and *nusG* mutations do not alter the *in vivo* activity of RNase E or RNase E-ΔCTH. Western blot experiments also demonstrated that the immunoreactive RNase E polypeptide levels, in both rne^{+} and *rne*-ΔCTH strains, were unaltered by the mutations that affect Rho-dependent termination and by ΔRppH.

We also undertook immunoblot experiments with anti-RNase E antibody in the *rho* derivative of the P_{lac}-*rne* strain that was able to grow in medium without IPTG. The data revealed that the RNase E level in the *rho* strain grown without IPTG addition was even lower than that in *rho*$^+$ *rne-lac* control at 3 μM IPTG, indicating that the suppression had not been achieved by gratuitous expression of RNase E in the strain.

Taken together, these results have permitted us to formulate a model which states that (i) RNase E has two pathways of cleavage that are, respectively, 5'-end-dependent (lost in ΔRppH or R169Q mutants) and CTH-dependent (lost in RNase E-ΔCTH); (ii) whereas strains with loss of any one of the two pathways are viable, those with both pathways defective are inviable; and (iii) mutations (in *rho*, *nusG* or *nusA*) affecting transcription termination serve to suppress the inviability associated with loss of both RNase E pathways, by providing a bypass mechanism involving R-loops or RNA-DNA hybrids for mRNA degradation in these strains. We further suggest that the operation of this bypass mechanism would have a sparing effect on the scarce RNase E which is now made available to catalyze the maturation reactions in tRNA in these cells. Thus, our results would suggest that the essentiality of RNase E in *E.coli* is dictated not just by a single category of reactions catalyzed by it, but instead by the need for a certain minimum level of activity that is sufficient for all its reactions.

2. ArgP regulon and mechanism of ArgO exporter function

a. In the work reported last year on the ArgP transcriptional regulator, we had described the identification of the gene encoding the LysP permease for Lys uptake as a transcriptional target of ArgP. Thus, *lysP* transcription *in vivo* is activated 35-fold by ArgP and the 5-fold repressive effect of Lys on *lysP* expression is also mediated by ArgP.

In the current year, we undertook electrophoretic mobility shift assays (EMSAs) to determine binding of ArgP to the *cis* regulatory region of *lysP*. Our results indicate that ArgP binds to the *lysP* regulatory region with a K_d of around 35 nM in the absence of Lys and that the binding affinity is greatly diminished (K_d > 150 nM) upon Lys addition.

Given the findings so far that ArgP mediates activation by Arg of *argO* and repression by Lys of several genes including *argO*, *lysP, gdhA* and *dapB*, we undertook a candidate gene approach to identify additional genes involved in Lys and Arg metabolism that may be regulated by ArgP. For this purpose, we constructed promoter-*lac* fusions to quantitate β-galactosidase expression in *argP*$^+$ and *ΔargP* strains, as also in a panel of *argP*^{d} mutants (ie, *argP*-dominant) that had earlier been isolated as constitutive for *argO* expression. We also performed EMSAs to determine *in vitro* ArgP binding to the *cis* regulatory regions of the genes.

The data from these experiments have indicated that in addition to *argO*, *gdhA* and *dapB* identified earlier and *lysP* above, several genes that are in the pathway of Lys biosynthesis are also ArgP-regulated, including *lysC, asd, dapD* and *lysA*. In all cases, ArgP activates transcription around 3- to 5-fold and mediates Lys repression as well. In EMSAs, ArgP binds to these regulatory regions with K_ds of around 50 – 150 nM, and this binding is Lys-sensitive. Some other candidate genes that were tested, such as *artJ, artP* and *argT* (all involved in Arg uptake), were unaffected by ArgP both *in vivo* and *in vitro.*

We also tested the effects of the panel of *argP*^{d} mutations on expression of these genes. Although all the *argP*^{d} mutants had been obtained on the basis of increased expression in them of *argO*, they exhibited different effects on the other target genes with regard both to the degree of activation relative to *ΔargP* and to the degree of repression upon Lys supplementation. Thus, for example, the variants P108S and L294F were the most effective of all in activating *gdhA* (7-fold) and *lysC* (6-fold), but these two variants were also the only ones to be defective for repression by Lys of *lysP*; two other variants V144M and P217L were unable to activate *asd* or *dapD*; and finally, P274S was completely ineffective for activation of *lysC, asd, dapD, gdhA* and *dapB* and partially so for *lysP*, whereas it was indeed the most effective of all the *argP*^{d} mutants for *argO*

activation. On the other hand, for the genes such as *artJ* or *argT* that are not ArgP-regulated, there was no difference in expression between the Δ*argP* derivative and any of the *argP*^{d} mutants.

The results also indicate that of the different genes under the control of ArgP *in vivo*, the regulation of *argO* appears to be unique in at least two ways. First, it is the only gene that requires Arg as co-effector for its activation. Second, it is also the only example in which ArgP's binding to the *cis* regulatory region is not Lys-sensitive, so that repression by Lys is achieved by an RNA polymerase-trapping mechanism at the *argO* promoter. The differences between *argO* and the other target genes, with regard to the features of their regulation by ArgP, are also reflected in their differential responses to the *argP*^{d} mutations.

In earlier *in vitro* studies, ArgP has also been implicated in regulation of DNA metabolism and DNA replication including transcriptional regulation of *dnaA* and *nrdA*. We found in our work that ArgP does not regulate *dnaA* or *nrdA in vivo* although it does bind *in vitro* to the regulatory regions of these genes with a K_d of around 200 nM in a Lys-insensitive manner.

Taken together, therefore, our studies point to ArgP as a non-canonical transcriptional regulator that mediates all Lys-liganded repression in *E. coli*.

b. We have also undertaken functional studies on Arg export mediated by ArgO. ArgO is an inner membrane protein that mediates export of Arg and its toxic analogue L-canavanine and is a member protein belonging to the LysE family of exporter proteins, whose activities mediate export of a variety of solutes. To study the mechanism of ArgO exporter function, we have earlier reported extensive mutagenesis studies to identify amino acid residues critical for ArgO function wherein we have obtained multiple amino acid substitutions in the first, second, fourth, fifth transmembrane segments and one substitution in the fourth periplasmic hydrophilic loop, that lead to significant impairment of in vivo ArgO activity without affecting its levels. To obtain a view of the topological distribution of residues critical for ArgO function we have initiated an experimental validation of the topology of ArgO in the inner membrane. Bioinfomatic analyses have suggested that ArgO possesses six putative transmembrane segments, three cytoplasmic hydophilic loops and two periplasmic hydrophilic loops. Guided by this initial topological map we have generated gene fusions of signal-sequenceless alkaline phosphatase (ss*phoA*) at several positions in the *argO* ORF. Our preliminary analysis suggests that both the N and C termini of ArgO are localized to the periplasm, and that the amino acid residues identified by mutagenesis studies are located in the transmembrane segments of ArgO.

Finally, we have investigated the inter-relationship between ArgP and ArgO of *E. coli* on the one hand and their respective orthologs LysG and LysE of *Corynabacterium glutamicum* on the other. As with the ArgP-ArgO system, LysG activates LysE transcription. The differences are that whereas ArgO exports Arg and is activated by Arg and repressed by Lys, LysE exports both Arg and Lys and is activated by both amino acids. We constructed a *lysE-lac* fusion and also cloned *lysG* to undertake regulation experiments in *E. coli*. Our results indicate that (i) regulation by the cognate activator is demonstrable ie., *lysE* by LysG (notwithstanding that LysG is interacting this case with heterologus *E. coli* RNA polymerase) and *argO* by ArgP, but not cross-regulation; and (ii) *lysE* is indeed activated by both co-effectors Arg and Lys, unlike *argO*. Most interestingly, several *argP*^{d} mutants were also able to activate *lysE* expression in *E. coli*, indicating that ArgP and LysG are indeed functionally similar to each other.

3. Potassium toxicity of *E. coli* mutants

Research in this project is directed towards understanding the physiological defect present in an *E. coli* strain doubly defective for *trx* and *hns* (TH strain), a defect that renders it sensitive to external concentrations (> 40 mM) of the essential cellular cation K^+. Towards this end we have performed extensive genetic analyses of a large collection of mutations that suppress the K^S (K toxicity / sensitivity) phenotype of

the TH strain and have reported their effects earlier. Our studies have shown that the TH strain bears an altered allele of the wild-type *spoT* gene (*spoT1*), whose presence is associated with the manifestation of the K^S phenotype, because the biological activity of SpoT1 leads to production of high cellular levels of ppGpp and that its mutational inactivation leads to both lowered levels of ppGpp and suppression of the TH strain's K^S phenotype. Mutations in a number of loci other than *spoT1* have been found to suppress the K^S phenotype of the TH strain and we have shown that these suppressor mutations can be grouped into two general categories, one that mediates its suppressive effects by lowering cellular ppGpp levels whereas the other does so regardless of the presence of high cellular ppGpp level contributed by the *spoT1* allele.

Further genetic studies have shown that in addition to high cellular ppGpp, there is a second determinant required for manifestation of the K^+ sensitivity displayed by the TH strain, which is a high cellular level of the alternative sigma RpoS. The presence of *trx* and *hns* mutations results in cells bearing high cellular levels of RpoS. Deletion of *rpoS* suppresses the K^S phenotype of the TH strain, without causing a significant reduction in cellular ppGpp levels. Furthermore, mutations in genes whose products stimulate cellular RpoS levels or activity such as the *cspC* and the *crl* genes respectively, lead to suppression of the TH strain's K^S phenotype. On the other hand removal of RssB, a protein that mediates the normal regulated proteolytic degradation of RpoS and thus maintains physiological levels of RpoS, leads to the generation of the K^S phenotype in combination with the *hns* mutation but not with the *trxA* or the *trxB* mutations.

In *E. coli*, there is evidence that the induction of the OxyR regulon leads to a down regulation of the activity of RpoS, mainly by reducing the translation of its mRNA, an effect caused by increased levels of the *oxyS* RNA, a non coding RNA that is a member of the OxyR regulon. Consistent with this we find that a lack of OxyS and OxyR generates K^+ sensitivity in combination with the *hns* mutation and furthermore that suppression of the K^S phenotype of the TH strain mediated by the *ahpC* null and the *oxyR2* mutations (suppressor mutations reported previously) is eliminated by the removal of OxyS. This has permitted the inference that the TH strain may suffer the physiological consequences of high cellular RpoS activity and that the outcome of an activated OxyR regulon is to mediate its reduction. It is known that H-NS is a repressor of RpoS translation; thus in the *hns* mutant, RpoS levels are higher than normal. Studies in this project thus suggest that the *trxA* (or the *trxB*) mutations may act in some manner to lower the activity of OxyR, leading to increased RpoS levels via the OxyS pathway. This implies that the *hns* and the *trx* mutations may act additively to increase cellular RpoS levels. Current studies in this project are directed towards testing the role of the *trx* mutations in OxyR activation and obtaining quantitative estimates of RpoS levels in the TH strain and in its derivatives that bear the various suppressor mutations. Furthermore, the interrelationships between cellular RpoS levels, ppGpp and intracellular K^+ concentrations are also being sought.

4. (p)ppGpp/DksA regulated functions in *E. coli*

a. Regulation of proline transport

Genetic evidence obtained implicates a role for ppGpp in the regulation of proline transport as described below. An *E. coli* strain lacking the proline transporter PutP and incapable of proline biosynthesis grows in rich medium such as LB or minimal medium containing glucose and all amino acids. However, a *relA* derivative of this strain shows significantly retarded growth in these same media. Notably, the growth defect was not observed in minimal media containing glucose and only proline at concentration sufficient to satisfy auxotrophic requirements (40-50 μg/ml). Supplementation of the growth media with fairly high concentrations of proline (≥400 μg/ml) reversed the growth defect. Taken together the results indicate that in a proline auxotroph that lacks the proline/sodium symporter PutP, the nutrients in the growth media (mainly amino acids) regulate proline transport into the cell using the RelA protein which is required for ppGpp synthesis following amino acid starvation. The

phenotypes described above for the *relA* mutant can also be reversed by the addition of NaCl/KCl/ sucrose to the growth media. Furthermore, suppression of the growth defect by NaCl is alleviated by the addition of compatible solute glycine betaine possible by competing for proline transport since they share common transporters. These results indicate a proline uptake defect in the *relA putP proA* mutant that can be corrected by an osmotic upshift or an increase in external proline concentration. Further studies have also shown that the growth defect of the *relA putP proA* strain in minimal media containing glucose and all amino acids is phenocopied by the *putP proA proP* mutant suggesting a role for the proline proton symporter ProP in the *relA* mediated regulation of proline transport in minimal medium. The molecular mechanisms of the regulation are being investigated.

b. (p)ppGpp/DksA mediated transcriptional regulations *in vivo*

A synthetic lethal screen revealed that the ribosome rescue/protein tagging machinery in *E. coli* composed of a RNA component encoded by *ssrA* and a protein component encoded by *smpB* is conditionally essential for survival of an *E. coli* strain lacking ppGpp ($ppGpp^0$) but not of the wild-type strain. This phenotype is suppressed by increasing the growth temperature of the strain. Strains lacking ppGpp are known to have transcriptional defects although the nature of the defects *in vivo* are not entirely understood. Using a set of mutations in RNA polymerase (RNAP) some of which have been isolated as suppressors of the growth defect of the $ppGpp^0$ strain in minimal media, we tested their ability to suppress the synthetic lethal phenotype. Our results indicate that the speed of RNA polymerase could be an important contributor to the synthetic lethal phenotype; thus, while a slow-moving RNAP mutant is able to suppress the phenotype, a faster moving mutant appears to accentuate the synthetic lethal phenotype. These results are consistent with the idea that ppGpp can influence the elongation rate of RNAP. We are also trying to test the role of ppGpp on RNAP elongation rate *in vivo* by using a naturally occurring attenuator that functions based on the relative speed of RNAP with respect to that of translating ribosomes. The attenuator would be used to make transcriptional fusions with the *lacZ* reporter gene and used to study the effects of ppGpp on attenuation with an aim to understand how it regulates the elongation properties of RNAP.

5. Genetic analysis of transketolase deficient *E. coli* strain

Two isoforms of transketolase enzyme, namely, TktA and TktB have been identified in *E. coli*. Expression of TktB is regulated by (p)ppGpp/RpoS and is elevated during stationary phase, while TktA is the major transketolase during exponential growth. Transketolase activity is required for the transfer of two-carbon units between sugar molecules and provides the link between glycolysis and the pentose phosphate pathway. The *tktA tktB* double mutant of *E. coli* shows severe growth deficiency in LB, an undefined rich growth medium that is widely used. Suppressor mutations that improved the growth of the strain were identified and studied in order to understand the metabolic defect(s) leading to slow growth of the transketolase deficient strain.

Three transposon insertions (*glpF*::Tn*10*dCm, *deoB*::Tn*10*dCm and *deoD*::Tn*10*dCm) and one multicopy suppressor clone from an *E. coli* plasmid library, each of which improved the growth of the transketolase mutant were identified and characterized. The *glpF*::Tn*10*dCm insertion at the end of *glpF* (glycerol permease) eliminates the last eight codons of the gene and increases the expression of the downstream gene *glpK* (glycerol kinase) of the *glpFKX* operon. Further studies showed that the increased expression of *glpK* and the presence of a functional *glpD* (glycerol-3-phosphate dehydrogenase) are essential for suppression of growth defect by this insertion.

The *deoB*::Tn*10*dCm and *deoD*::Tn*10*dCm insertions interrupt the *deoB* (phospho-pentomutase) and *deoD* open reading frames in the *deoCABD* operon and possibly eliminate enzyme activities required for the degradation (salvage) of purine/pyrimidine

ribo/deoxyribonucleotides and cellular PRPP (phosphoribosylpyro-phosphate) biosynthesis. DeoB catalyses the reversible conversion of the final product of the salvage pathway, namely, ribose-1-phosphate to ribose-5-phosphate, the latter being the substrate for transketolase in the pentose phosphate pathway. DeoD is a purine nucleoside phosphorylase which generates ribose-1-phosphate from purine nucleosides. Transketolase mutants cannot utilize pentose sugars as a sole source of carbon for growth, as their catabolism requires a functional pentose phosphate pathway. Based on the suppression of the growth defect by *deoB*::Tn*10*dCm and as well as the Δ*deoB*::Kan insertions, it is possible to speculate that during growth in LB, the accumulation of ribose-5-phosphate in the transketolase mutant is growth inhibitory and that the *deoB* mutation alleviates this through inactivation of the salvage pathway.

Based on the suppression of growth defect and increased *glpK* expression conferred by the *glpF*::Tn*10*dCm insertion in the transketolase mutant, we examined the regulation of the *glpFKX* operon *in vivo* in the transketolase deficient strain (*tktA* mutant) using a *lacZ* reporter fusion. This study indicates a positive regulation of the operon by transketolase, although it is presently not clear if this effect is direct or indirect. Another interesting observation obtained using the fusion was the regulation of the operon by ribose and the details of such regulation are being investigated.

A third suppressor of the growth defect was obtained by screening a library of *E. coli* genes on medium copy number plasmid and identified to be *pntA* and *pntB* both of which constitute an operon and code for the two subunits of the membrane-bound proton-translocating pyridine nucleotide transhydrogenase. PntAB is a major source of NADPH in the cell. The mechanism of suppression by multicopy *pntAB* is currently under investigation.

Publications

1. Kumar S, Sardesai AA, Basu D, Muniyappa K and Hasnain SE (2010). DNA clasping by Mycobacterial HU: The C-terminal region of HupB mediates increased specificity of DNA binding. ***PLoS One*** 5, e12551, 1-10.

2. Nandineni, MR, Prasad SPR, Goud Ch V, Negi DS, Nagaraju J and Gowrishankar J (2010). DNA-based identification of victims of the Mangalore air crash of May 2010. ***Current Science*** 99: 341-342.

3. Sabareesh V, Sarkar P, Sardesai AA and Chatterji D (2010). Identifying N60D mutation in ω subunit of *Escherichia coli* RNA polymerase by bottom-up proteomic approach. ***Analyst*** 135: 2723-2729.

Other publication

1. Gowrishankar J (2010). Craig Venter, and the claim for 'synthetic life'. ***Current Science*** 99: 152.

Patents

1. Gowrishankar J and Nandineni MR. A microbial process for arginine production.

   (i) US Patent 7749738 B2, granted 6 July 2010.

   (ii) European Patent 1574566, granted 15 September 2010

2. Gowrishankar J and Harinarayanan R. A method of altering levels of plasmids.

   Indian Patent 246791, granted 16 March 2011.

LABORATORY OF COMPUTATIONAL BIOLOGY

Computational Studies on Protein Structure, Function and Interactions

Principal Investigator	HA Nagarajaram	Staff Scientist
PhD Students	Tabrez Anwar Shamim	Senior Research Fellow (Till Oct. 2010)
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Objectives

1. Studies on human nsSNPs: Classification of nsSNPs into disease (deleterious) and neutral categories
2. Studies on protein-protein interaction networks:

a. Analysis of Human-Virus PPI (HU-Vir PPI) network

b. Studies on spatio-temporal dynamics of human interaction networks

c. Structural and functional characterization of hubs in human PPI network.

Summary of work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

1. Position specific probability ($\widehat{P_{ab}}$) of an amino acid residue *a* at a given position *b* calculated using Dirichlet mixture of priors was tested for prediction of disease nsSNPs and neutral nsSNPs. A value of ($\widehat{P_{ab}}$) <0.05 indicates that amino acid residue a at position b is not preferred whereas a value >0.05 indicates preference. When tested on a known set of disease and neutral nsSNPs it was found that ($\widehat{P_{ab}}$) correctly predicts 80% of 3103 disease and 60% of 18407 neutral human nsSNPs.
2. Enzyme-centric protein-protein functional linkage networks were constructed for *E. coli* DH10B, *Saccharomyces cerevissiae* and *Methanococcus jannaschii* from the three Kingdoms Prokarya, Eukarya and Archea respectively. Various topological properties viz., degree distribution, betweenness distribution, and motif abundances were calculated and analyzed.

Details of progress made in the current reporting year (April 1, 2010 - March 31, 2011)

Project 1: Classification of human nsSNPs into deleterious (disease) and benign catergories: Development of a new method called Hansa

Having found the predictive value of ($\widehat{P_{ab}}$) for identification of diseae nsSNPs and neutral nsSNPs we resorted to develop a method for accurate prediction of disease and neutral amino acid substitutions as implicated by nsSNPs. In addition to ($\widehat{P_{ab}}$) we used nine other features (Table 1) as the disease-neutral nsSNPs discriminatory features. The ten features (Table 1) include position specific probability scores calculated using Dirichlet mixture of prior information as well as Gribskov's approach, predicted solvent accessibility and secondary structural features, BLOSUM62 substitution scores and change in free energy changes associated with both wild-type and mutant amino acid residues. These 10 features were incorporated into a support vector machine learning classifier which was trained and tested on a set of 12,473 "Disease" nsSNPs mapping on to 1029 human proteins and 7623 nsSNPs annotated as "polymorphisms" (and considered here as neutral) mapping on to 2940 proteins. We carried out 10-fold cross validation test and the results obtained are shown in Figure 1 in the form of ROC curve. Figure 1 also shows ROC curves obtained for other known methods which had been tested on the same dataset. We named our new method as Hansa and this yields a prediction accuracy of 83% (at 0.2 FPR) which is more than 10% as compared to the best available method.

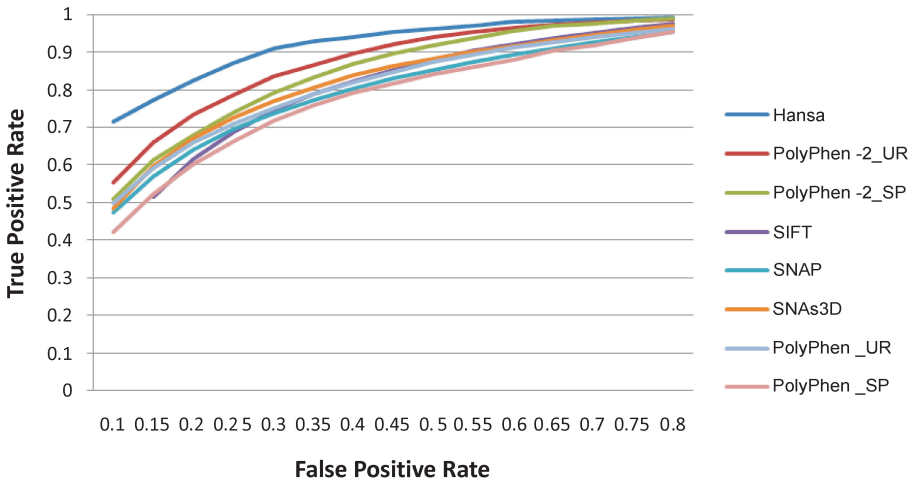

Figure 1. The comparison of Receiver Operating Characteristics (ROC) curves generated for Hansa and the other popular tools viz., SIFT, PolyPhen, SNPs3D, SNAP and PolyPhen-2. The data for these tools have been taken from Adzhubei *et al*, 2010.

Position-specific features	Position-specific probability score of the wild-type amino acid residues (p_{ab}^{WT}).
	Position-specific probability score of the mutant-type amino acid residues (p_{ab}^{MT})
	Difference between position –specific probabilities score of the Wild and the Mutant amino acid residues i.e., diff ($p_{ab}^{WT} - p_{ab}^{MT}$)
	Gribskov's Score of the wild-type amino acid residues (G_{ab}^{WT})
	Gribskov's Score of the mutant-type amino acid residues (G_{ab}^{MT})
	Difference between Gribskov's Score of the wild-type and the mutant amino acid residues i.e., diff ($G_{ab}^{WT} - G_{ab}^{MT}$)
Structure-based Features	Solvent accessibility status of the amino acid at the mutation site&&; 1 if it is buried (solvent accessible surface area is <10%);0 if it is exposed.
	Secondary structural status of the amino acid residue at the mutation site**; 1 if it is a part of alpha-helix; 2 if it is a part of extended strand or 0 for other types.
Amino acid based Features	Difference in transfer free energy values of wild type and mutated type from inside to surface of the protein@@
	BLOSUM62 Substitution scores for Wild-type ->Mutated type amino acids.

Table 1. Details of the ten discriminatory features used in Hansa

&& Solvent accessibility calculated from ACCpro4.0 [Cheng *et al*, 2005]

** Secondary structure prediction calculated from SSpro v4.5 [Cheng *et al*, 2005]

@@ Transfer in free energy values from inside to outside of a globular protein [Janin, 1979]

Project 2: Analysis of human and virus protein-protein interaction (Hu-Vir PPI) networks

Pathogens employ various strategies to invade host, acquire nutrients and escape from host immune system for their survival and multiplication. Infection of a host by a pathogen is mediated by a number of protein-protein interactions (PPIs) between the pathogen and its host. As a part of our investigations on human-pathogen PPI networks we have undertaken a systematic computational analysis of Human-Virus (Hu-Vir) PPIs with special emphasis on the role of intrinsically disordered proteins (IDPs). IDPs are an interesting class of proteins which lack stable tertiary structure. In order to carryout our analysis we used Hu-Vir PPI data from VirusMINT (Chatr-aryamontri *et al,* 2009), Pathogen Interaction Gateway (PIG) (Driscoll *et al*, 2009) and Zhang *et al*, (2009). Disorder in human and viral proteins was predicted using DISOPRED2. When the interacting proteins were studied, it was found that about 60% of human proteins interacting with viral proteins are highly disordered whereas only 25% of viral proteins interacting with human proteins are disordered (Figure 2(a) and (b)). In the bipartite network of Hu-Vir PPI it was observed that human proteins either have degree < 60 or >130. There was no preference seen for human IDPs to have either high degree or low degree. Functional enrichment analysis revealed that human IDPs interacting with viral proteins are involved in important functions such as DNA or RNA binding, cell cycle regulation and protein synthesis. Further studies are underway.

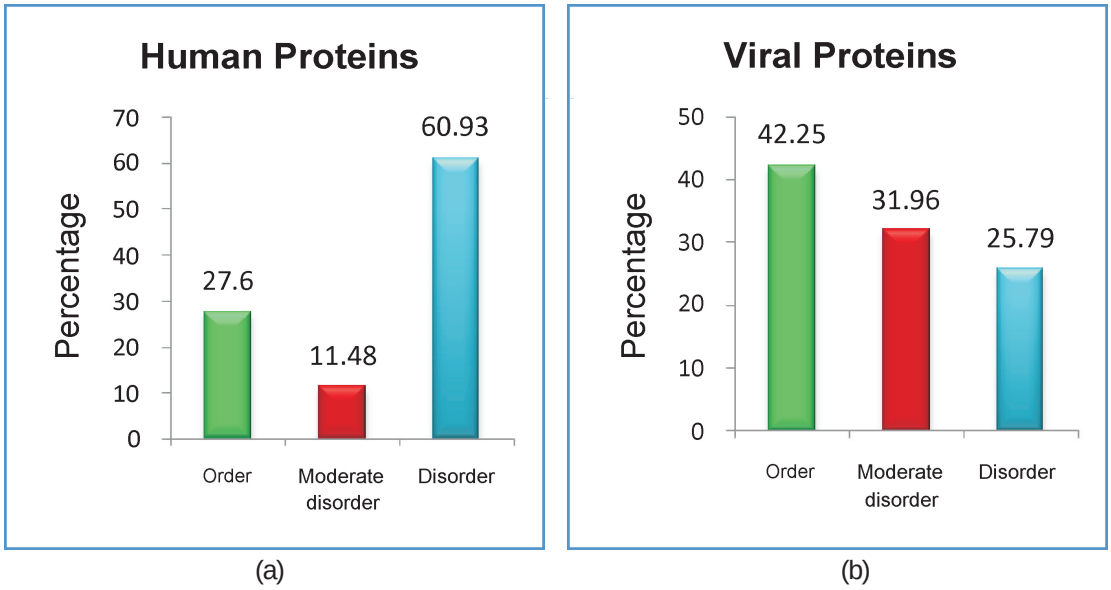

Figure 2. Distribution of human (a) and viral (b) proteins interacting with viral and human proteins respectively into three categories of structural disorder.

Project 3: Studies on spatio-temporal dynamics of human PPI networks

Literature abounds with a large number of reports involving human PPI networks. Most of these studies have considered static network. However, PPI networks are not static and show variation from tissue to tissue (spatial) and also from one developmental stage to another (temporal) as a consequence of tissue-wise and development-wise protein expressions. We have undertaken comparative studies on tissue-wise PPI networks. We constructured 79 tissue-wise networks from the data provided by Bossi & Lehner (2009) and investigated various topological properties such as degree, betweenness and clustering coefficient of protein products of housekeeping as well as tissue-specific genes. We found that proteins expressed in specific tissues make fewer connections however, with a few exceptions that make tissue-specific hubs. Furthermore, tissue-specific proteins avoid occurring in shortest paths and possess less interconnected partners. In contrast, widely expressed proteins establish most of the interactions and act as global hubs in various tissues. These results reconfirmed earlier observations made from an analysis of a smaller set of tissue-wise networks (Lin *et al*, 2009). Moreover, widely expressed proteins occur in the shortest paths and hold highly interconnected

partners. Our study also revealed that protein products of housekeeping genes are found to establish both tissue-specific interactions as well as those prevailing in various tissues. Further studies are underway.

Project 4: Structural and functional characterization of hubs in human PPI network

As stated in the previous report, we examined the relation between degree and the number of splice variants of nodes in human PPI network and found a weak positive correlation between the two. We further extended our studies to decipher the relationships between degree and unstructuredness of the nodes. The extent of unstructuredness in all the protein sequences in the *Homo sapiens*.GRCh37.56.pep.all file from ENSEMBL was predicted using DISOPRED2. For each gene an average disorderedness value was computed using the disorderedness values of individual splice variants of that gene. Contrary to the previous reports, only a weak positive linear correlation was found between the degree of gene/node and the average unstucturedness of all its splice variants. Studies were also carried out to examine the relationship between the extent of splice variation and the average unstructuredness of protein products. All the protein products (splice variants) of all the genes were binned into three categories with respect to their unstructuredness values: **structured** proteins (<10 % of residues in the unstructured region/s), **moderately unstructured** proteins (10% - 30% of residues in the unstructured region/s), and **unstructured** proteins (> 30% of residues in the unstructured regions). When the ratio of the unstructured variants to the total number of variants in each splice variation bin was plotted against the bin size a significant linear positive correlation was observed. Further studies are underway wherein we are investigating the relationship between the number of constitutive exons and the degree of nodes.

Future plans and directions

1. Integration and analysis of human nsSNP data on protein-protein interaction networks
2. Analysis of viral-human bridged PPI network
3. Studies on tissue-wise PPI networks integrated with drug-protein interaction data
4. Further studies on structural and functional characterization of hubs in huam PPI networks.

Publications

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LABORATORY OF MOLECULAR CELL BIOLOGY

Signal Transduction Pathways in Macrophages and Host-Pathogen Interaction in Tuberculosis

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Objectives

1. Signal transduction pathways in macrophages regulating its innate-effector functions
2. Studying how various candidate proteins of *Mycobacterium tuberculosis* interfere with macrophage signaling cascades to modulate host's protective responses against the bacilli.

Summary of work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

In our previous studies, we found that heat shock protein 60 (Mtbhsp60) primarily targets the TLR2 signaling cascades to inhibit nuclear translocation of c-rel and consequently decrease the production of IL-12 p40 in PPD-activated macrophages. It appears that interaction of Mtbhsp60 with TLR2 plays an important role in inducing a dominant Th2-type response during *M. tuberculosis* infection that favors the intracellular survival of the bacilli. One of the possible mechanisms by which Mtbhsp60 blocks IL-12 p40 production involving TLR2 could be through induction of anti-inflammatory mediators like IL-10 since IL-10 is known to inhibit IL-12 p40 induction in macrophages primarily by targeting the c-rel transcription factor. Earlier, we also found that interaction of Mtbhsp60 with TLR4 but not TLR2 resulted in increased production of IL-12. Therefore, it appears that Mtbhsp60 is unique in orchestrating anti-inflammatory and proinflammatory responses depending on its specific interaction with TLR2 or TLR4. In this study we examined in details the mechanisms involved in the regulation of anti- and pro-inflammatory responses in macrophages by Mtbhsp60. This study hints at the possible mechanisms of regulation of both anti-inflammatory and proinflammatory responses in tuberculosis involving the TLRs which might be useful in devising strategies to tailor macrophage innate-responses to induce protective host immunity.

Details of progress made in the current reporting year (April 1, 2010 - March 31, 2011)

Project 1. Understanding the mechanism of regulation of anti- and proinflammatory responses by heat shock protein 60 of *Mycobacterium tuberculosis*

Interaction of Mtbhsp60 with TLR2 receptors is important for induction of IL-10 in macrophages. IL-10 induction in macrophages was analyzed by treating PMA-differentiated THP-1 macrophages with Mtbhsp60 and IL-10 expression was checked either by RT-PCR or by enzyme immunoassay (EIA). The recombinant Mtbhsp60 protein was found to activate IL-10 production in THP-1 macrophages in dose-dependent manner. Since hsp60 is known to interact with both TLR2 and TLR4 receptors, we next aimed to identify the TLR receptor involved in the activation of IL-10 by Mtbhsp60. Therefore, TLR receptors of the PMA-differentiated THP-1 macrophages were blocked with either anti-TLR2 or anti-TLR4 or isotype-matched control Ab and subsequently treated with Mtbhsp60 and the levels of IL-10 produced by these macrophages were measured by RT-PCR or EIA. It was found that compared to the group treated with medium alone, a robust IL-10 gene expression by Mtbhsp60 was observed predominantly in groups treated with either anti-TLR4 mAb or isotype-matched control Ab. In contrast, treatment with anti-TLR2 mAb resulted in very little IL-10 gene expression in the presence of Mtbhsp60. Similar responses were also observed when IL-10 was measured at the protein level by EIA. Again, silencing of the TLR2 but not TLR4 (by TLR-specific siRNA-mediated gene silencing) resulted in downregulation of IL-10 in Mtbhsp60-treated cells. Collectively, these data suggest that IL-10 induction by Mtbhsp60 is predominantly mediated through TLR2-induced signaling.

IL-10 activation by Mtbhsp60 is dependent on endocytosis of Mtbhsp60 via TLR2 receptors. We observed that receptor-mediated, clathrin-dependent endocytosis of Mtbhsp60 is required for IL-10 induction in macrophages. Since, in the previous experiments, we observed a direct role of TLR2 in the Mtbhsp60-mediated activation of IL-10; we next examined whether internalization of Mtbhsp60 was actually mediated through the TLR2 receptor and this process was important for Mtbhsp60-mediated activation of IL-10. Therefore PMA-differentiated THP-1 macrophages were pre-treated with 10 µg/ml of anti-TLR2 or anti-TLR4 mAb to block the TLR2 or TLR4 receptors respectively and then incubated with Mtbhsp60-FITC (10 µg/ml) for 15 min at 37^{0}C. Using confocal immuno-fluorescence microscopy, we found that macrophages pre-treated with anti-TLR2 mAb showed impaired Mtbhsp60 endocytosis as compared to macrophages pre-treated with either anti-TLR4 mAb or isotype control Ab (Figure 1A). This indicates that internalization of Mtbhsp60 is predominantly mediated *via* TLR2 pathway (Figure 1A) and interaction of Mtbhsp60 with TLR4 predominantly results in cell surface accumulation of the protein (Figure 1A). Next, we examined whether IL-10 activation by Mtbhsp60 required TLR2-mediated endocytosis. We observed that IL-10 induction was strongly inhibited when TLR2-mediated endocytosis was inhibited by treating cells with Monodansylcadaverine MDC (Figure 1B). On the other hand, interaction of Mtbhsp60 with TLR4 induced a dominant proinflammatory response characterized by higher TNF-α production possibly because of poorer internalization of Mtbhsp60 (Figure 1A) when interacted through TLR4 thereby leading to higher surface-bound Mtbhsp60 (Figure 1C). Interestingly, we observed inhibition of TLR2-mediated endocytosis by MDC resulted in increased cell surface accumulation of Mtbhsp60 and in such situation we found an increase in the TNF-α production (Figure 1C). These results together indicate that retention of Mtbhsp60 on the cell surface (when Mtbhsp60 interacted with TLR4 or TLR2 in the presence of MDC) is sufficient to trigger TNF-α induction and induction of IL-10 by Mtbhsp60 requires clathrin-dependent endocytosis of this protein.

Differential activation of p38 MAPK and ERK 1/2 was observed during interaction of Mtbhsp60 with TLR2/TLR4. TLR ligands are known to activate various MAPKs, mainly the p38 MAPK and the ERK 1/2. We and others have shown that p38 MAPK and ERK 1/2 signaling is crucial in the regulation of anti-inflammatory and proinflammatory cytokines in macrophages. While p38 MAPK is crucial for IL-10 induction, ERK 1/2 predominantly regulates TNF-α signaling. Therefore, we compared the phosphorylation status of p38 MAPK and ERK 1/2 in situation where Mtbhsp60 is endocytosed by interacting with TLR2 to a situation where it is sequestered to the cell surface like interaction with TLR4 or TLR2 in the presence of MDC. A rapid internalization of Mtbhsp60 through TLR2 was found to be associated with an increased phosphorylation of p38 MAPK whereas engagement of TLR4 by Mtbhsp60 induced predominantly ERK 1/2 phosphorylation. Again, blocking the TLR2-

mediated endocytosis of Mtbhsp60 by MDC resulted in attenuation of p38 MAPK phosphorylation with concomitant enhancement of ERK 1/2 phosphorylation. Therefore, it appears that dichotomous nature of signal transduction through TLRs is governed primarily by the divergent MAPK signaling transmitted from the endosome against those from the membrane.

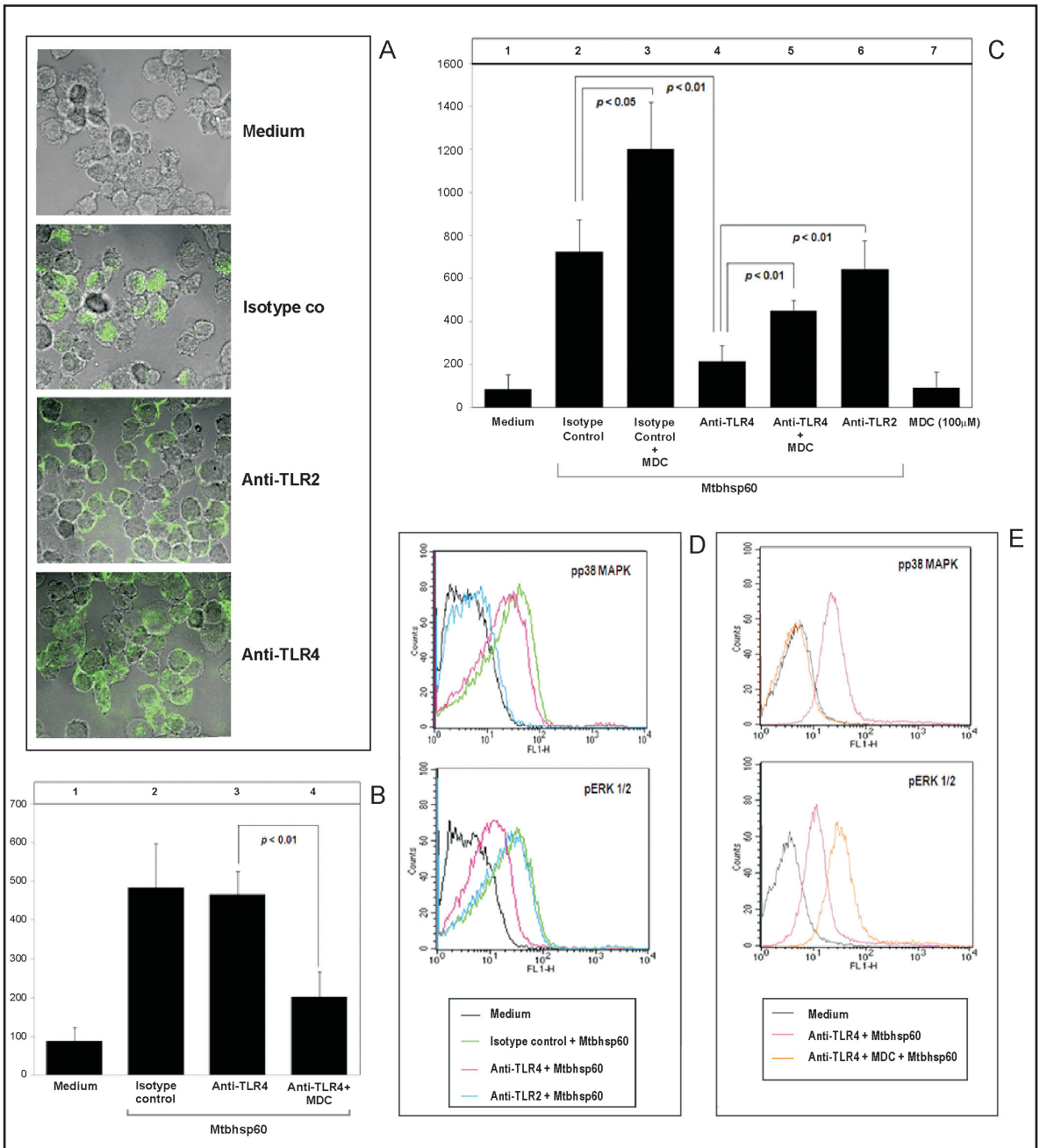

Figure 1. IL-10 activation by Mtbhsp60 is dependent on endocytosis of Mtbhsp60 through the TLR2 receptors wbile TNF-alpha induction by Mtbhsp60 is dependent on retention of Mtbhsp60 on cell surface when interacted with TLR4 or with TLR2 in the presence of MDC. PMA-differentiated THP-1 macrophages were pre-treated with 10μg/ml of anti-TLR2 mAb or anti-TLR4 mAb or isotype-matched control Ab for 1 h and further incubated with Mtbhsp60-FITC (10μg/ml) at 37°C for 15 min. Cells were fixed, washed and the endocytosis was examined by confocal laser-scanning microscope (A). PMA-differentiated THP-1 macrophages were pre-treated with 10μg/ml of anti-TLR2 or anti-TLR4 mAb or istotype-matched control Ab for 1h and then incubated with 3 μg/ml of Mtbhsp60 in the absence or presence of 100 μM MDC. After 48 h of incubation, IL-10 (B) or TNF-α (C) level was measured by EIA in various culture supernatants. hosphorylation status was compared between p38 MAPK and ERK ½ mediated by Mtbhsp60 in situations where Mtbhsp60 interacts with TLR2 and TLR4 receptors (D) or with TLR2 in the presence of MDC (E).

Project 2. Functional characterization of *M. tuberculosis* ESAT-6 proteins involved in modulation of macrophage functions

This modulation of host immune response may be carried out by secretion of *M. tuberculosis* proteins into the macrophage cytoplasm. The RD1 region of *M. tuberculosis* encodes a novel protein secretion system, which is absent from the attenuated *M. bovis* BCG (BCG), and *M. microti* and is responsible for the export of culture filtrate proteins ESAT-6 and CFP-10. The importance of this RD1 region for pathogenicity has been shown by reintroduction of the extended RD1 region into BCG, and by deletion of RD1 from *M. tuberculosis*. Several effects related to pathogenicity have also been found associated with expression of ESAT-6 in *M. tuberculosis*. These include suppression of proinflammatory responses, interaction with TLR2, cytotoxicity, necrosis, phagosome maturation arrest and granuloma formation. However, not much is known about the mechanism by which ESAT-6 affects some of these functions. We will be using yeast two hybrid screening, GST pulldown assay, co-immunoprecipitation (Co-IP) assay to identify the interacting partner of ESAT-6 in the macrophage proteome, interaction with which leads to modulation in the behavior of macrophage allowing *M. tuberculosis* to survive and spread.

Expression of ESAT-6. The mycobacterial ESAT-6 was cloned into the yeast two-hybrid bait vector (pGBKT7) in-frame, with the Gal4 BD. Sequencing using the T7 forward primer confirmed that the fusion construct was in-frame. The bait protein construct was then tested for auto-activation of interaction reporters (ADE2, HIS3, lacZ, MEL1) and toxicity. Both of these not been observed proper expression of bait fusion protein in yeast was confirmed by Western blotting using c-Myc monoclonal antibody on protein extracts prepared from yeast transformed with the bait construct.

Screening the library for protein-protein interactions by yeast mating. The bait transformed in MATa yeast strain AH109 and the prey library transformed in MAT-α strain Y187 was mated overnight in YPDA .The entire culture was then plated onto QDO (SD/–Ade/–His/–Leu/–Trp) medium and incubated at 30°C for 8 days. On the 8th day about 275 colonies which appeared were picked up and sub streaked onto QDO plates, 44 of these sub-streaked colonies failed to grow or showed very poor growth leaving about 231 colonies that grew well on the QDO plates. These colonies were then analyzed for the activation of other two reporters Mel1 and LacZ, of the 231 colonies 211 showed expression of LacZ and 216 showed expression of Mel1 with 196 clones showing expression of all the four interaction reporters ADE, HIS, MEL1 and LacZ. These 196 positive clones were sub-streaked about 5 times to allow for the loss of nonspecific library plasmids, from these clones genuine positives which require both the bait and prey for activating the Gal4 responsive reporters were picked up as opposed to the false positives which activate the reporter genes even in the absence of bait plasmids. Bait plasmid isolated from the diploid positives were retransformed back into AH109 in the following combinations; 1) Bait + prey, 2) Prey alone, 3) Empty bait vector + prey. True positive clones show reporter activation only in transformation 1, while false positives will have reporter activation in transformation 2 and 3. Only two of the 196 clones showed colonies for transformation 2 and 3. Insert from these 194 clones will be identified by sequencing.

Future plans. We would like to study in details the mechanisms involved in the regulation of anti- and proinflammatory by Mtbhsp60. Also, we would like to identify the interacting partner of ESAT-6 in the macrophage proteome and the role of ESAT-6 in the pathophysiology of tuberculosis.

Publications

1. Alam K, Ghousunnissa S, Nair S, Valluri VL and Mukhopadhyay S (2010). Glutathione-redox balance regulates c-rel-driven IL-12 production in macrophages: Possible implications in antituberculosis immunotherapy. ***Journal of Immunology*** 184: 2918-2929.
2. Das A and Mukhopadhyay S (2011). The evil axis of obesity, inflammation and type-2 diabetes. ***Endocrine, Metabolic and Immune Disorders - Drug Targets*** 11: 23-31.
3. Mukhopadhyay S and Balaji KN (2011) The PE and PPE proteins of *Mycobacterium tuberculosis*. ***Tuberculosis*** (In press).
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LABORATORY OF STRUCTURAL BIOLOGY

Structural and Biochemical Characterization of Some *M. tuberculosis* Proteins

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	Abhijit A Sardesai	CDFD, Hyderabad
	Sanjeev Khosla	CDFD, Hyderabad

Objectives

1. Identification of important proteins of *Mycobacterium tuberculosis* for crystallographic and biochemical analysis
2. Expression and biochemical characterization of the chosen proteins. X-ray structural analysis of the chosen proteins
3. Develop applications of graph theory to understand genome-wide protein: protein interactions.

Summary of work done until the beginning of this reporting year (April 1, 2009 - March 31, 2010)

Three broad categories of proteins from *Mycobacterium tuberculosis* were chosen for biochemical and structural work. They are:

Redox proteins	• Thioredoxin and thioredoxin reductase • Glutaredoxin
Heat shock proteins	• Chaperonin-60 family (Cpn60.1, Cpn60.2 and Cpn10) • Heat shock protein 70 family (Hsp70, Hsp40)
Other proteins including proteins involved in transcription processes	• cAMP Receptor Protein • YefM:YoeB toxin-antitoxin complex

Chaperonins

We had demonstrated earlier GroEL-1 is capable of binding to DNA without any sequence specificity. The affinity of DNA recognition by GroEL-1 is sufficiently high in the range of 100-200 nM suggesting that the protein has naturally evolved to bind DNA. This property of GroEL-1 was proposed to be due to its participation in nucleoid formation in *M. tuberculosis*.

Details of progress made in the current reporting year (April 1, 2010 - March 31, 2011)

Project 1: Structural characterization of Glutaredoxin

Glutaredoxin gene was cloned in the pET23a vector, overexpressed and purified using metal affinity chromatography with the Ni^{2+}-NTA resin. The protein could be purified to homogeneity. This protein has been crystallized and diffraction data has been collected. Structure solution is in process.

Project 2: Molecular characterization of Chaperonins

During the period under review, we have carried out ChIP-chip experiments in *M. tuberculosis* using monoclonal antibody raised against GroEL-1. For this, we treated mycobacterial cells with formaldehyde, harvested and lysed them gently. The chemically crosslinked DNA-protein complexes were immunoprecipitated using monoclonal anti-GroEL1 antibody. The immunoprecipitated DNA was hybridized on a high density microarray chip containing approximately 240,000 overlapping probe DNA fragments, each of about 60 oligonucleotide length. The scanned microarray data were analysed using Chip Analytics software of Agilent Technologies, and by locally written scripts.

The analysis of microarray data revealed that out of the 240,000 probes, approximately 2400 probes are enriched for binding. Gene-based enrichment showed that this corresponds to 357 genes out of the ~4000 genes in the genome of *M. tuberculosis*. An interesting outcome of this analysis was that the GroEL1 binds predominantly to the coding region, and to GC-rich regions. Enrichment in the coding region of the PE-PGRS genes was also observed. The results of ChIP-chip were confirmed by PCR amplifications of the bound probes, and by electrophoretic mobility shift assays of identified consensus sequences.

These were results were further confirmed by Surface Plasmon Resonance with the oligonucleotide sequences designed using the consensus obtained from ChIP-chip analyses. The SPR experiments revealed that GroEL-1 binds to these oligonucleotides with an affinity in the range of 1-10 nM.

Project 3: Structural studies on cAMP Receptor Protein

Crystal structure of cAMP Receptor Protein was determined in the absence of cAMP. In order to gain further understanding into allosteric changes brought about by cAMP, Normal Mode Analyses were also carried out. The crystallographic analyses combined with NMA have yielded interesting insight into the allosteric mechanism of this protein.

Project 4: Application of graph theory to genome-wide protein: protein interactions

We had earlier proposed a set of genome-wide functional linkage in *E. coli*. Using this data, during the period under review, we have proposed a method, where the gene expression data can be understood in the context of genome-wide functional linkages. These data were used to construct 467 subnetworks in *E. coli*, which are unique to each of the expression conditions. These subnetworks have been subjected to modularity analysis and further work is in progress.

Future plans and direction

We plan to determine the structure of glutaredoxin of *M. tuberculosis* and its relevant complexes with cognate electron transfer partners.

Publications

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LABORATORY OF MAMMALIAN GENETICS

Epigenetic Mechanisms Underlying Developmental Pathways

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	Amitava Basu	Senior Research Fellow
	Rachana Roshan Dev	Junior Research Fellow
	Imtiyaz Yaseen	Junior Research Fellow
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	Vaishnavo Pai	Project Associate
	Bindu Bhargavi	Project Assistant
	N Vanitha	Project Assistant
	Ranjani Subramanian	Project Assistant (Till Sep. 2010)
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	Shekhar C Mande	CDFD, Hyderabad
	Rakesh Mishra	CCMB, Hyderabad
	Vinay K Nandicoori	NII, New Delhi

Project 1: *DNMT3L*: Epigenetic correlation with cancer

Summary of work done until the beginning of this reporting year (April 1, 2009 - March 31, 2010)

Previously, we had reported loss of DNA methylation at the *DNMT3L* promoter in cervical cancer samples. This loss of *DNMT3L* promoter DNA methylation correlated with its expression. Furthermore, *DNMT3L* overexpression stimulated cellular proliferation in HeLa and SiHa cells and induced nuclear reprogramming both at morphological and molecular level.

Details of progress made in the current reporting year (April 1, 2010 - March 31, 2011)

DNMT3L and cancer

DNA methylation analysis on a larger cohort of cervical cancer samples has validated our previous observation of loss of DNA methylation in a few cervical samples. More importantly, the loss of DNA methylation at the *DNMT3L* promoter was also observed in tongue, esophagus and colorectal cancer samples (Figure 1). This could suggest that the process of carcinogenesis might be following a similar pathway involving loss of DNA methylation at DNMT3L promoter in different cell types. Further work is required to validate this hypothesis.

Role of *DNMT3L* promoter in regulation of it transcription

DNMT3L is transcriptionally silent in most tissues (except germ cells and during early embryogenesis) and work from our own laboratory indicates that the DNMT3L promoter is normally hypermethylated (in the tissues we have examined, see Figure 1). To gain further insight into the regulatory mechanisms underlying the transcription of *DNMT3L*, we have asked the following questions:

1. Do the cis-elements present within the *DNMT3L* promoter have activating or silencing potential;
2. Apart from DNA methylation are there any other factors that contribute to the silencing of *DNMT3L*?
3. What are the factors that contribute to activation of *DNMT3L* transcription in some tissues?

To identify the regulatory potential of *DNMT3L* promoter, transgene reporter gene assay in Drosophila was initiated wherein the promoter region flanked by loxP sites, was inserted upstream of the hsp70 promoter driven mini-white reporter gene containing P-element vector pCaSpeR. The comparison of eye color for the transgenic lines

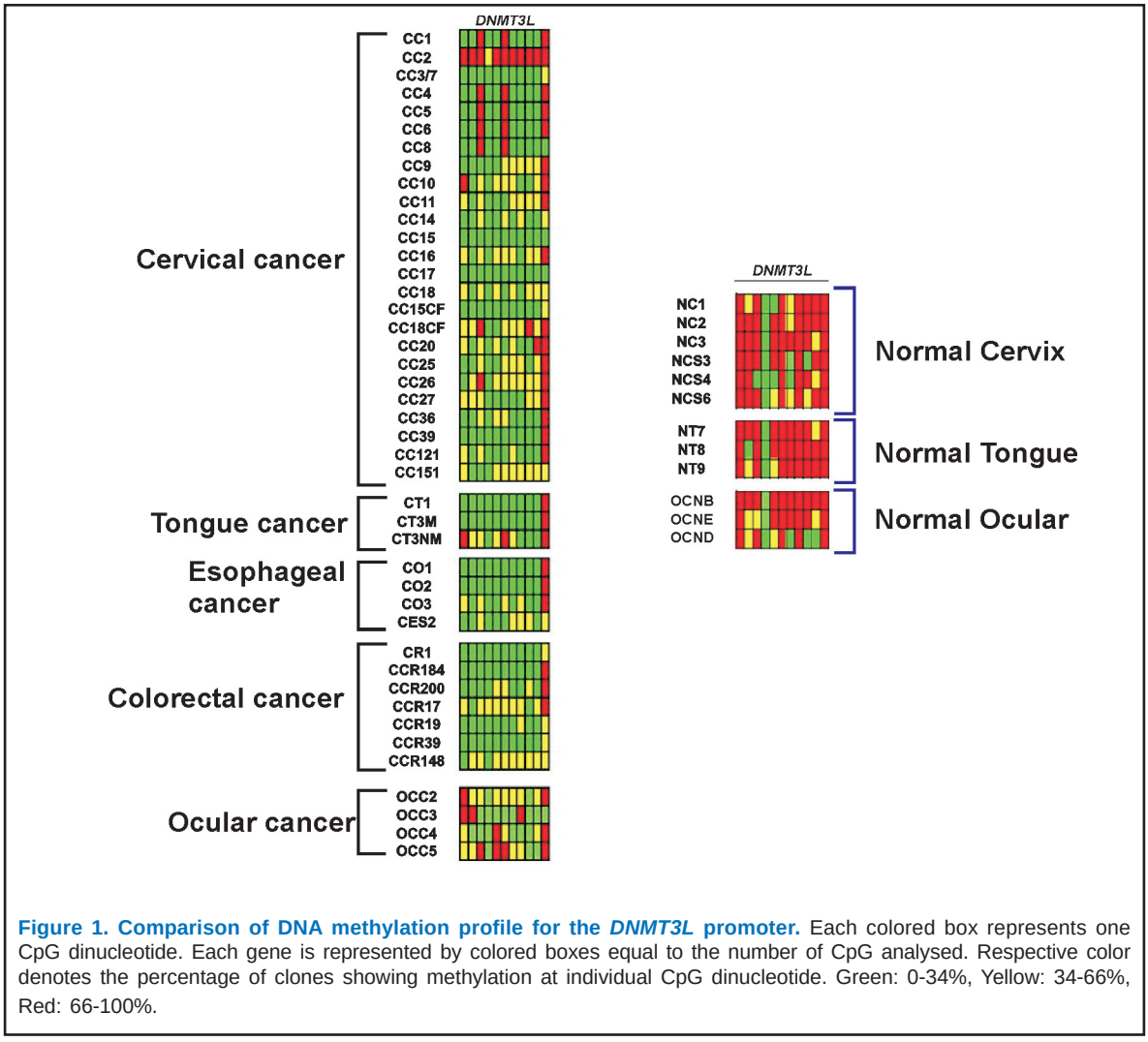

Figure 1. Comparison of DNA methylation profile for the *DNMT3L* promoter. Each colored box represents one CpG dinucleotide. Each gene is represented by colored boxes equal to the number of CpG analysed. Respective color denotes the percentage of clones showing methylation at individual CpG dinucleotide. Green: 0-34%, Yellow: 34-66%, Red: 66-100%.

with lines which don't contain the promoter would indicate whether it is as an activator or repressor of transcription.

Project 2: *Dnmt2* and RNA processing

Summary of work done until the beginning of this reporting year (April 1, 2009 - March 31, 2010)

Though it has all the domains specific for methyltransferases, *Dnmt2* has failed to show significant DNA methylation *in vitro* and *in vivo* conditions. Studies from our laboratory have shown that Dnmt2 is involved in RNA processing during cellular stress.

Details of progress made in the current reporting year (April 1, 2010 - March 31, 2011)

Dnmt2 collaborates with other Dnmts

The localization of GFP-Dnmt2 fusion protein to stress granules and P-bodies in the cytoplasm and the relocalization of endogenous Dnmt2 to these cytoplasmic foci under stress pointed to the role of Dnmt2 in the stress management machinery of the cell. Since Dnmt2 is the only known DNA methyltransferase to be conserved across various species, it is possible that methylation function of Dnmt2 is part of a primitive mechanism by which a cell deals with environmental challenges. To test whether Dnmt2 relocalisation to P-bodies has any bearing on the localization of other DNA methyltransferases, we studied localisation of Dnmt1, Dnmt3a and Dnmt3l upon overexpression of *Dnmt2*. While Dnmt3a localization is not affected by overexpression of *Dnmt2*, both Dnmt1 and Dnmt3l are relocalized (Figure 2) suggesting that Dnmt2 role in RNA processing may be correlated with the action of other DNA methyltransferases. Further work to confirm the same is underway.

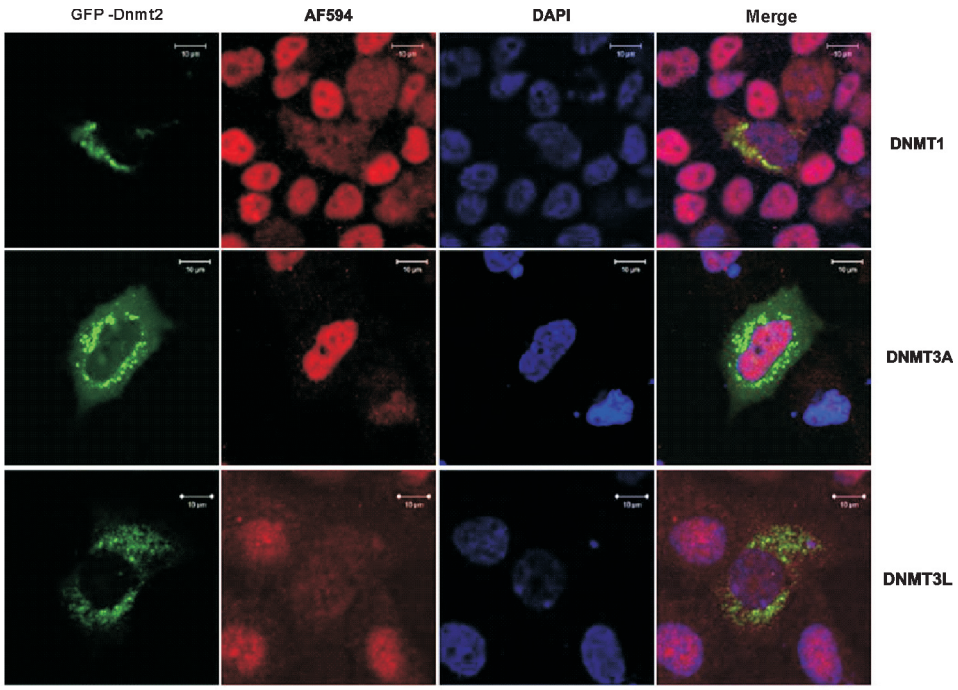

Figure 2. Colocalization of GFP-Dnmt2 with other DNA methyltransferases. Transiently transfecting *GFP-Dnmt2* were immuno-stained with antibody to DNMT1,DNMT3A and DNMT3B as indicated. Secondaryantibody conjugated to Alexafluor594 was used. Nuclei were counter stained with DAPI. Bar is ~10 µM.

Project 3: Host epigenetic response to infection

Summary of work done until the beginning of this reporting year (April 1, 2009 - March 31, 2010)

To influence the epigenetic circuitry of the human host cells, a mycobacterium needs to possess factors (proteins/RNA) which could interact or influence the effectors of epigenetic modifications. Bioinformatically we had identified 29 putative methyltransferases in *Mycobacterium tuberculosis* genome. This list was pruned to 21 putative DNA/RNA methyltransferases based on literature and further bioinformatic analysis. 17 of these were cloned for further analysis.

Details of progress made in the current reporting year (April 1, 2010 - March 31, 2011)

To further narrow down our search the following criteria was set:

1. The gene should be a DNA methyltransferase
2. The gene product should be secreted out of the mycobacterium
3. Upon infection it should also localize to the nucleus.

Of the 17, protein overexpression was achieved for 7 genes. Of these 7, 3 showed DNA methyltransferase activity in 3 different assay systems. Biochemical analysis to quantify the methyltransferase activity of these 3 proteins is underway.

Out of these 3 proteins, one of the gene products has been found to be secreted out of *Mycobacterium smegmatis*. Results for others have been inconclusive. Efforts are on to confirm the secretory potential for the remaining two gene products and also to determine the secretory potential for all the 3 in *M. tb* and *M. bovis*.

To examine whether a mycobacterial protein is able to localize to the host nucleus, the best way would be to infect host cells with Mycobacteria and check whether the test protein relocalises to the host nucleus. In absence of a clear candidate to test for this criterion, we decided to perform a pilot study wherein we transfected GFP fusion constructs of the 20 putative mycobacterial methyltransferases into HeK and PMA treated Thp1 cell lines. 8 of the transfected mycobacterial gene products localized to the cytosol, 8 showed localization to both cytosol and nucleus and 4 showed localization only to the nucleus in HeK cells. Similar localization was seen

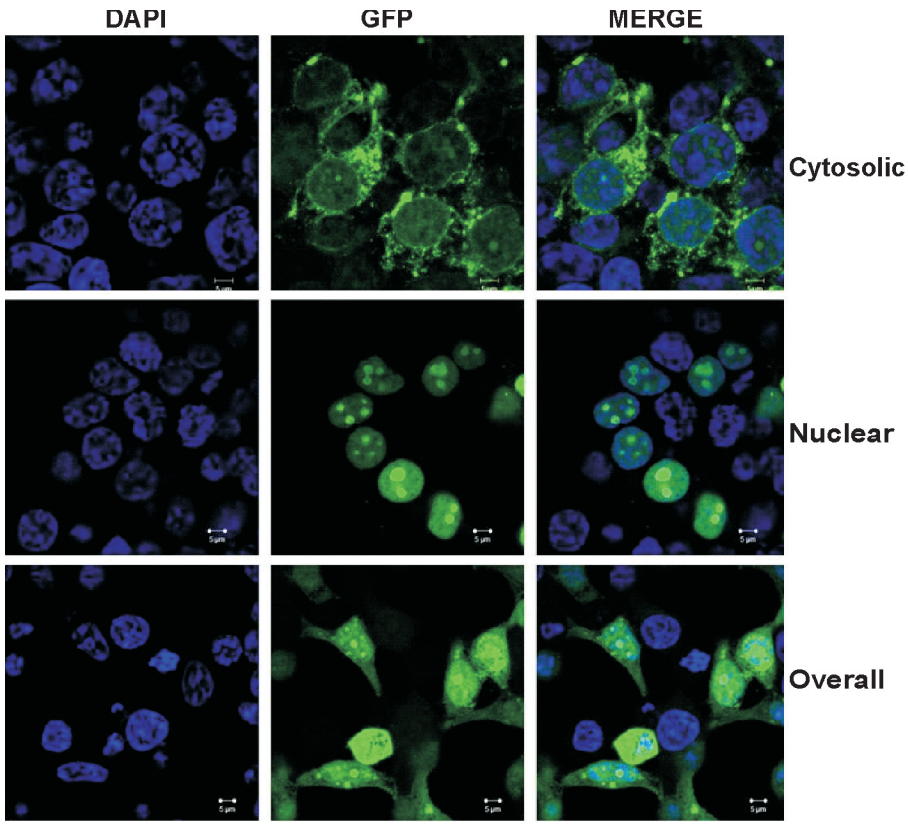

Figure 3. Subcellular localization of Mycobacterial proteins upon transfection of GFP-fusion constructs. Transiently transfecting *GFP-Mycobacterial gene* constructs were counterstained with DAPI and observed under a confocal microscope. Each panel is a for a specific Mycobacterial protein. Bar is~10 μM.

in Thp1 cells for a few of the genes that were tested. Representative pictures showing localization of some fusion proteins is shown in Figure 3.

Project 4: Specialized chromatin structures as epigenetic imprints to distinguish parental alleles

Summary of work done until the beginning of this reporting year (April 2009 - March 31, 2010)

We obtained, through a collaboration with CDB, Kobe and NCBS, Bangalore, mice which had the second intron of *Neuronatin* replaced by a Neo-cassette at its endogenous locus. In the previous year, we had initiated appropriate cross of these mice with wild type C57BL/6 mice to analyse the transcriptional status of *Neuronatin* in the knocked–out allele.

Details of progress made in the current reporting year (April 1, 2010 - March 31, 2011)

Functional analysis of neuronatin's second intron

Examination of the second intron in a transgene based reporter assay in Drosophila had indicated it to be a transcriptional activator. To test the possibility that the second intronic region of *Neuronatin* is a transcriptional activator even in mammals, mice in which the second intron of *Neuronatin* had been deleted were generated. The knock-out mice were crossed with wild type mice producing offspring inheriting either a maternal or paternal copy of the deletion. If the role of second intron was that of a transcriptional activator then heterozygotes inheriting the deleted locus from the father (+/NnatΔI^2) would be expected to show loss of *Neuronatin* expression, whereas mice inheriting the deletion from mother (NnatΔI^2/+) would not show any effect on *Neuronatin* expression. As shown in Figure 4, deletion of intron 2 does lead to loss of *Neuronatin* expression when this deletion is inherited from the father. Moreover, we find that this deletion leads to change in the DNA methylation levels at the *Neuronatin* promoter suggesting a role for it in controlling the imprinting status of this gene.

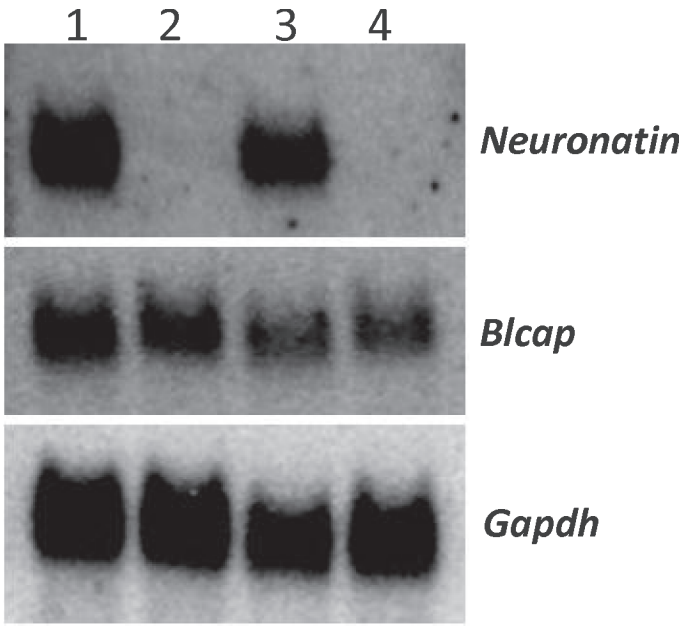

Figure 4. Northern Blot analysis to examine transcriptional status of *Neuronatin* gene. RNA isolated from 1: Wild type C57BL/6; 2: Paternal heterozygote (+/NnatΔI2); 3: maternal heterozygote (NnatΔI2/+) 4: homozygous (NnatΔI2/NnatΔI2) was electrophoresed, blotted and probed for the indicated genes. Probes used for hybridization are indicated on the side of each panel. *Neuronatin* is located within the first intron of the *Blcap* gene.

Publications

1. Manderwad GP, Gokul G, Kannabiran C, Honavar SG, Khosla S and Vemuganti G (2010). Hypomethylation of the DNMT3L promoter in Ocular Surface Squamous Neoplasia (OSSN). ***Archives of Pathology and Laboratory Medicine*** 134: 1193-1196.

2. Thiagarajan D, Dev RR and Khosla S (2011). The DNA methyltranferase Dnmt2 participates in RNA processing during cellular stress. ***Epigenetics*** 6: 103-113.

3. Singh NP, Madabhusi SR, Srivastava S, Senthilkumar R, Neeraja C, Khosla S and Mishra RK (2011). Epigenetic profile of the euchromatic region of human Y chromosome. ***Nucleic Acids Research*** (In press).

LABORATORY OF MOLECULAR ONCOLOGY

Genomics and Molecular Genetics of Cancer and Human Genetic Disorders

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Objectives

1. Identification and characterization of important deregulated genes/pathways in cancers prevalent in India
2. Identification and characterization of disease causing mutations in genetic disorders.

Summary of work done until the beginning of this reporting year (April 1, 2009 - March 31, 2010)

Colorectal cancer (CRC)

Work on the identification and characterization of major deregulated pathway(s) in early-onset CRC was continued. Our initial analysis revealed a significantly reduced frequency of Wnt activation but not microsatellite instability (MSI) in early-onset CRC. Array based comparative genomic hybridization (aCGH) was performed on eighteen samples; a recurrent deletion at 1p36.21 and a recurrent amplification at 19q13.12-13.32 were identified specifically in Wnt- samples.

Pancreatic cancer

Analysis of aCGH data generated from pancreatic cancer xenografts revealed a novel amplification located at 18q11.2 that included the gene coding for *GATA6*. *GATA6* gene copy number correlated significantly with transcript abundance in several pancreatic tumor samples. We used statistical approaches to determine transcriptional targets of *GATA6* which surprisingly revealed genes belonging to the oxidative phosphorylation cycle of mitochondria.

Hypohidrotic/Anhidrotic ectodermal dysplasia (H/AED)

We analyzed thirteen H/AED families and five harbored mutation in the *Ectodysplasin A* (*EDA*) gene and eight in the *Ectodysplasin A Receptor*

(*EDAR*) gene. A total of six novel mutations were identified; two in *EDA* and four in *EDAR*. Interestingly, the *EDAR* p.G382S mutation was identified in four independent families. Sequence and structure analysis of novel *EDA* mutations *viz.* p.Y304C and p.M279R was also performed.

Details of progress made in the current reporting year (April 1, 2010- March 31, 2011)

Project 1: Molecular genetic analyses of early-onset sporadic CRC

The colon and rectum possess several distinguishing features with respect to embryonic origin, histology, organ physiology, etc. Differences in etiology of colonic and rectal tumors have also been revealed. Recent reports indicate an increased rectal cancer incidence worldwide. Unfortunately, due to a tendency to consider colonic and rectal cancer as a single entity, very few specific studies on rectal cancer have been performed. Our earlier studies had revealed a reduced occurrence of Wnt activation in early-onset CRC. Work carried out during the current reporting year indicated specific biological differences in tumors occurring in rectum and colon especially in young patients. The reduced occurrence of Wnt activation in early-onset CRC was more pronounced in rectal tumors as compared to colonic tumors. In addition, K-Ras mutation frequency was significantly reduced in rectal cancer occurring in the young but not in the older patients unlike colonic cancer. No significant difference was however observed with respect to p53 status; neither between the two age groups nor between colon and rectum. In order to determine chromosomal instability (CIN) status we have analyzed DNA copy number alterations (CNAs) in Wnt- and Wnt+ CRC samples. The Wnt- samples exhibited significant chromosomal aberrations indicating presence of CIN in the absence of Wnt activation (Figure 1). Interestingly, the CNAs identified in Wnt- samples were distinct from those identified in the Wnt+ samples. Our results point towards involvement of novel pathways for tumor initiation and progression in early-onset rectal cancer.

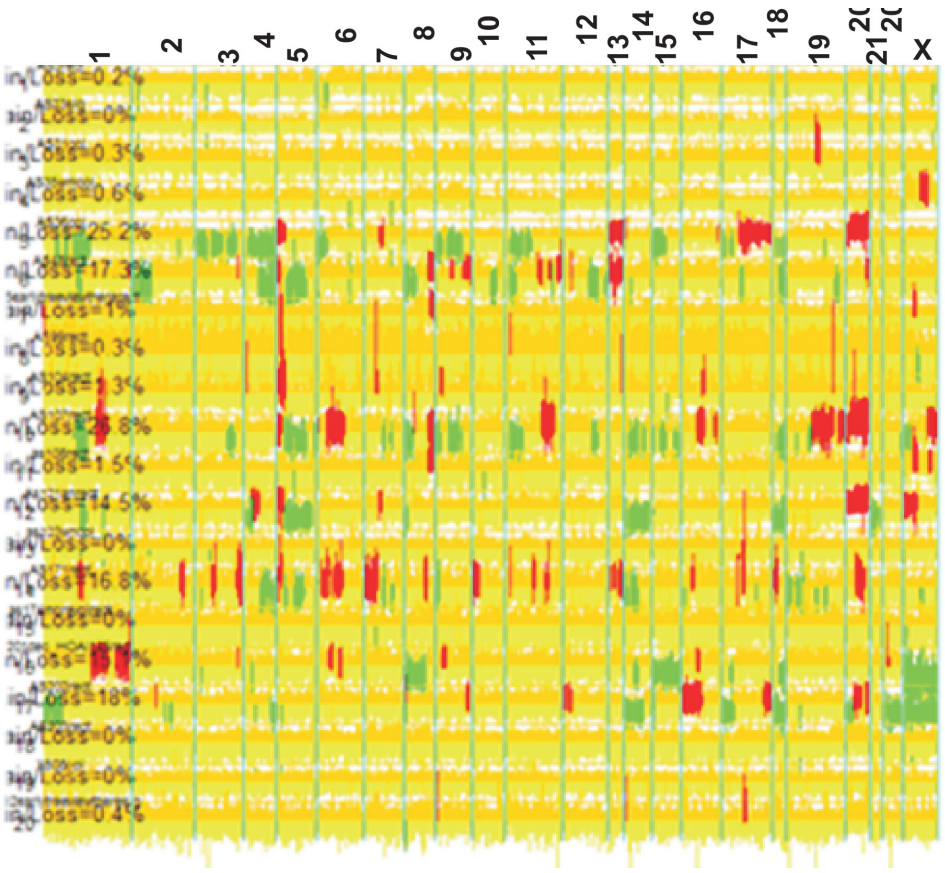

Figure 1. Graphic representation of DNA copy number alterations identified in 20 Wnt- CRC samples. Each row represents one sample and each column represents one chromosome (numbered at the top).

Project 2: Identification of Mismatch repair (MMR) gene mutations in suspected Hereditary Non-Polyposis Colorectal Cancer (HNPCC) patients from India

HNPCC is an autosomal dominant familial syndrome that predisposes individuals to early-onset CRC. It is caused mainly due to mutational inactivation of any one of several MMR genes which in turn results in a form of genetic instability called microsatellite instability (MSI). Screening guidelines have been established in the West to identify potential HNPCC patients that include Immunohistochemistry (IHC)-based identification of loss of MMR protein expression as well as detection of MSI in the tumor samples. The guidelines have helped in improving patient outcome since HNPCC tumors warrant alternate therapeutic regimen unlike other forms of CRC. Since, these guidelines were set for the Western population, they may not necessarily apply to the Indian population. In order to better understand HNPCC in our population, we have initiated the first large scale analysis of suspected HNPCC patients from India. Out of 900 CRC patient samples we first shortlisted 44 early-onset samples from patients who either exhibited HNPCC specific family history or harbored multiple primary tumors. Out of 41 samples screened, 38 exhibited high MSI (MSI-H) which were then subjected to IHC to determine expression of two important MMR proteins *viz.* MLH1 and MSH2. Loss of MLH1/MSH2 expression accounts for about 70-80 % of all HNPCC cases in the West. Surprisingly, only 16 samples (42 %) were negative for MLH1/MSH2 protein expression. We have identified mutation in *hMlh1*/*hMsh2* in 10 out of 11 samples screened; six in *hMsh2* and four in *hMlh1* (Table 1). Five mutations were novel; four in *hMsh2* and one in *hMlh1.* Out of the remaining 22 samples, only 3 were negative for MSH6 expression (*hMsh6* is the third most commonly mutated gene in HNPCC) out of which we identified mutation in one (Table 1). The instability profile of the five microsatellite markers differed depending on which MMR gene was inactivated (Table 1). At least three mutations generated a premature termination codon and the resultant mutant transcript is expected to be degraded through nonsense mediated decay. Quantitative reverse transcription PCR based analysis revealed a drastic reduction in transcript level in tumor as compared to normal sample confirming loss of expression of the second allele. Loss of heterozygosity appeared to be the most common mode of somatic inactivation of the second allele (Table 1).

	Age/ Gender	Tumor location / Grade	Family status	MSI	Mutation	Exon / Intron	LoH
hMsh2							
	32 / F	Anal Canal / WDAC[1]	Father (Brain)	3/5	p.L244S; **Novel**	E4[2]	Yes
	53 / M	Right colon; stomach; bladder / MDAC[3]	No	3/3	p.P349L	E6	??
	40 / F	Right Colon / Mucinous	Maternal Uncle (colon)	5/5	p.R406X	E7	Yes
	40 / M	Right Colon / MDAC	Father (colon)	3/5	p.D603V; **Novel**	E12	Yes
	37 / M	Right colon / MDAC	No	5/5	c.2136delA; **Novel**	E13	Yes
	38 / M	Right colon / WDAC	Father (gastric)	ND	p. E901X; **Novel**	E16	??
hMlh1							
	44 / M	Rectum / WDAC	Sister (colon)	3/4	p.C77Y	E3	Yes
	35 / M	Left colon / MDAC	Brother (colon)	5/5	p.T117M	E4	??
	45 / F	Right colon / WDAC	Son (colon)	4/4	p.R385C	E12	??
	45 / M	Right colon / MDAC	No	5/5	c.1516del7; **Novel**	E13	Yes
hMsh6							
	47 / M	Right colon / MDAC	Grandfather, Grandmother (both colon)	2/5	IVS4+3A>T; **Novel**	I4[4]	ND

Table 1. Clinical and molecular details of HNPCC patients
[1]Well differentiated adenocarcinoma; [2]E, Exon; [3]moderately differentiated adenocarcinoma; [4]I, Intron

Project 3: Identification and characterization of novel pancreatic cancer genes

We had earlier characterized two novel oncogenes that were identified based on an aCGH screen carried out on pancreatic tumor samples. During the current reporting year, we have characterized a novel tumor suppressor gene for pancreatic cancer based on analysis of a homozygous deletion located at 6q25.3, which included only one annotated gene *viz. ARID1B.* ARID1B is a component of the human SWI/SNF chromatin remodeling complex. Other components of this complex have been shown to have a tumor suppressor role in several cancers. We cloned the *ARID1B* gene in pcDNA3.1HisC expression vector and introduced the recombinant plasmid into the MiaPaCa2 pancreatic cancer cell line which harbors a homozygous deletion for *ARID1B*. Permanent transfectants harboring the gene exhibited reduced ability to form colonies in liquid (colony forming assay; Figure 2A) as well as solid (soft agar assay; Figure 2B) culture when compared to transfectants harboring the vector alone. The *ARID1B* transfectant also exhibited a reduced motility in wound healing assays. However, there was no significant difference in growth as determined by MTT and crystal violet staining. We detected elevation of *ARID1B* transcript upon treatment with 5'-Azacytidine in several pancreatic cancer cell lines harboring a single allele deletion of *ARID1B*, indicating that the second allele might be repressed through promoter hypermethylation. A CpG island was identified in the *ARID1B* promoter and Bisulphite sequencing revealed extensive hypermethylation. These results appear to indicate a possible tumor suppressor role for *ARID1B* leading credence to previous reports that ascribe a similar role to other components of the human SWI/SNF complex.

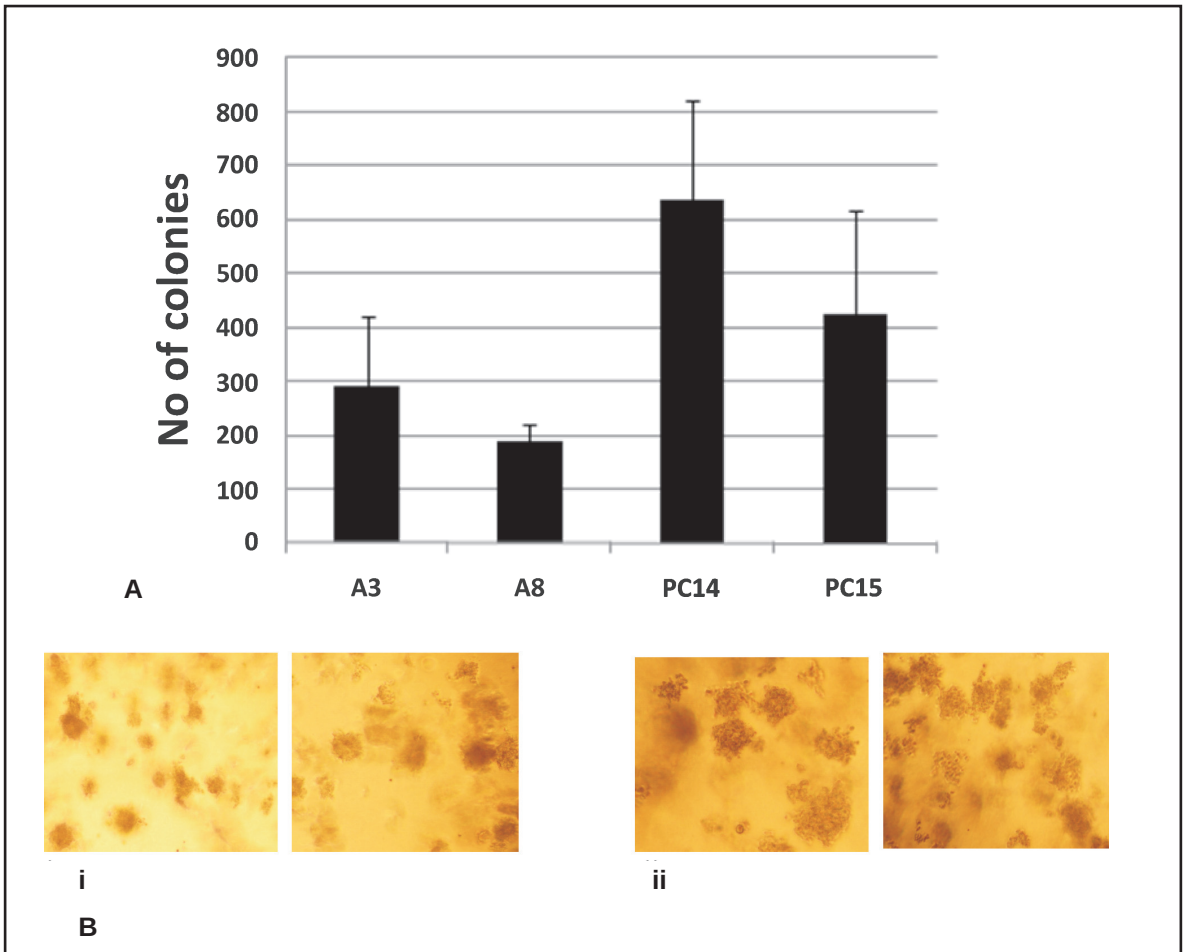

Figure 2. *ARID1B* represses tumor-related phenotype in pancreatic cancer cell lines. Panel A; MiaPaCa2 pancreatic cancer cell line permanent transfectant generated from *ARID1B* cloned in pcDNA3.1HisC vector forms less no. of colonies in liquid culture (A3 and A8) as compared to vector alone (PC14 and PC15); p=0.0158. Panel B; similar results for soft agar assay; i, *ARID1B* and ii, vector.

Project 4: Identification of mutations in Hypohidrotic/Anhidrotic ectodermal dysplasia patients (H/AED)

We had earlier identified mutations in thirteen H/AED patients; during the current year we have analyzed ten additional patients. Details of all 23 patients are given in Table 2. Twelve patients harbored mutation in *EDAR* while only eleven harbored mutation in *EDA*. This is in contrast to studies performed in other countries where *EDAR* accounts for less than 25% of the cases. Of the nineteen mutations identified, twelve were missense mutations (seven in *EDA* and five in *EDAR*), four were insertion/deletion mutations (two each in *EDA* and *EDAR*), two were splice mutations (one each in *EDA* and *EDAR*) and one a nonsense mutation in *EDA*. A total of eleven novel mutations were identified; six in *EDA* and five in *EDAR*. All patients harboring mutation in *EDAR* exhibited an autosomal recessive mode of inheritance and among these only one exhibited compound heterozygosity indicating a high degree of consanguinity. One other patient harbored two mutations in *EDA*. We also detected two *de novo* mutations; one each in the two genes. Interestingly, we identified the *EDAR* p.G382S mutation in five independent families. By using three polymorphic microsatellite markers located close to the gene we showed a possible founder effect for the mutation. The founder effect explains the unusually high frequency of *EDAR* mutations in Indian H/AED patients.

Future plans and direction

1. aCGH will be continued and expression profiling will be carried out to determine deregulated pathway(s) in Wnt- rectal cancer samples.

EDAR				
Patient No.	**Mutation[1]**	**Exon/Intron**	**Mutation type**	**Mode of inheritance**
1	p.C71Y	Exon 4	Missense	AR
2	**p.C113Y**	Exon 4	Missense	AR
3	**c.478delC**	Exon 6	Deletion	AR
4	**IVS6+5G>A**	Intron 6	Splice	AR
5	c.719_722delAAGA	Exon 8	Deletion	AR
6	**p.V340L**	Exon 11	Missense	AR
7	p.G382S	Exon 12	Missense	AR
8	p.G382S	Exon 12	Missense	AR
9	p.G382S	Exon 12	Missense	AR
10	p.G382S	Exon 12	Missense	AR
11	p.G382S	Exon 12	Missense	AR
12	**p.R98W[2];** **p.V340L**	Exon 4; Exon 11	Missense; Missense	AR; AR
EDA				
Patient No.	**Mutation**	**Exon/Intron**	**Mutation type**	**Maternal carrier status**
13	**p.G45D**	Exon 1	Missense	Carrier
14	**p.T57A**	Exon 1	Missense	NA[3]
15	**IVS1+2T>C**	Intron 1	Splice	NA[3]
16	p.R155C	Exon 3	Missense	Carrier
17	**p.R244X**	Exon 6	Nonsense	NA[3]
18	**p.M279R**	Exon 8	Missense	Carrier
19	p.G291R	Exon 8	Missense	Carrier
20	p.Y304C	Exon 8	Missense	Carrier
21	**c.947_952delACTTTG**	Exon 9	Deletion	Carrier
22	**c.1149dupATC**	Exon 9	Insertion	Carrier
23	p.G299S[2]	Exon 3; Exon 8	Missense; Missense	Carrier; Non-carrier

Table 2. Mutations identified in H/AED patients.
[1]Novel mutations are shown in bold face; [2]*de novo* mutation; [3]not available

2. Specific mutations in MMR genes occurring in HNPCC patients will be characterized.

3. Further characterization of the *ARID1B* and its transcriptional targets with respect to pancreatic cancer will be carried out.

Publications

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2. Bashyam MD, Chaudhary A, Reddy E, RamaDevi A, Savithri G, Ratheesh R, Bashyam L, Mahesh E, Sen D, Puri R, Verma I, Nampoothiri S, Vaidyanathan S, Chandrasekhar M and Kantheti P (2010). Phenylalanine hydroxylase gene mutations in phenylketonuria patients from India: Identification of novel mutations that affect PAH RNA. ***Molecular Genetics and Metabolism*** 100: 96-99.

3. Purushotham G, Madhumohan K, Anwaruddin M, Nagarajaram HA, Hariram V, Narasimhan C and Bashyam MD (2010). The MYH7 p.R787H mutation causes hypertrophic cardiomyopathy in two unrelated families. ***Experimental and Clinical Cardiology*** 15: e1-e4.

4. Yabaluri N* and Bashyam MD* (2010). Hormonal regulation of gluconeogenic gene transcription in the liver. ***Journal of Biosciences*** 35: 473-484.

**Shared corresponding authorship*

LABORATORY OF CANCER BIOLOGY

Understanding the Mechanism of Cellular Senescence

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	Renu Wadhwa	AIST, Japan

Objective

Telomere attrition is a well known cause for cellular senescence. However, oxidative damage can accelerate ageing leading to premature senescence. In this context we had earlier proposed a role of wild type Ras in growth arrest (Arvind *et al*, FASEB 2005). Infact senescence is now considered an important growth arrest mechanism in context of neoplastic transformation. We are currently focusing on two main aspects (a) to understand the role of both Ras and histone deacetylases, Sirtuins (SIRT7), in context of both cellular proliferation and senescence and (b) role of redox in accelerating senescence.

Summary of work done until the beginning of this reporting year (April 1, 2009 - March 31, 2010)

We had earlier reported that wild type Ras can induce growth arrest by arresting cells in G1/G0 phase of cell cycle or by inducing features similar to cellular senescence. In context of Histone deacetylase (SIRT7) we had shown a gradual decline in SIRT7 expression in senescent cells. In addition we had started a new project on role of redox in accelerating senescence.

Details of progress made in the current reporting year (April 1, 2010 - March 31, 2011)

1. Role of wild type Ras in hepatocellular carcinoma

To gain insight into role of wild type Ras in carcinogenesis we evaluated the expression and functionality of Ras in HBV mediated hepatocellular carcinomas (HCC). We found that mutations in *ras* are a rare event in etiology of HCC development and progression. In absence of its mutation, an unusual observation was significantly low amounts of wild type Ras-p21 in HCC compared to both normal and chronic liver disease (cirrhosis and chronic hepatitis) as revealed by immunoblot, immunohistochemistry, RT-PCR analysis and Ras-GTP functionality assay (Sujoy *et al,* 2011). Considerable heterogeneity amongst the tumors was noted in the tumors with respect to Ras mediated signaling events (pRaf, pMAPk and pAKT). In contrast we noted a significant upregulation in Ras mediated signaling events in the *in vitro* HCC cell lines viz., HepG2 and Hep3B.

2. Role of SIRT7 in proliferation and ageing

Sirtuins are a class of histone deacetylases III which are at crossroads of ageing and cancer. In mammalian system there are seven different isoforms of Sirtuins (SIRT1-7) of which very little is known about the functioning of nucleolar SIRT7. Since in organisms like yeasts and worms there is a close connection between ageing and SIR2, we asked the question if:

(a) Expression of nucleolar SIRT7 varies during the process of ageing?

(b) Overexpression of SIRT7 provides any growth advantage to fibroblasts?

(a) Expression level of SIRT7 following ageing

We did not find any significant change in levels of SIRT7 in ageing mice tissues (1 week , 6 months and 1 year old) collected from different organs, however it's expression declined significantly in

senescent primary fibroblasts cultures (P10) in comparison to young primary fibroblasts (P1). In addition, we found by immunofluorescence a prominent nucleolar localization of SIRT7 in young primary cultures which disappearance in the senescent cells. The disappearance of nucleolar SIRT7 was observed in a variety of primary cell cultures viz, WI38, MRC5 and TIG3. Senescence in primary cell culture is due to telomere shortening, however oxidative stress can also lead to Stress induced premature senescence (SIPS). We therefore asked the question if SIRT7 localization

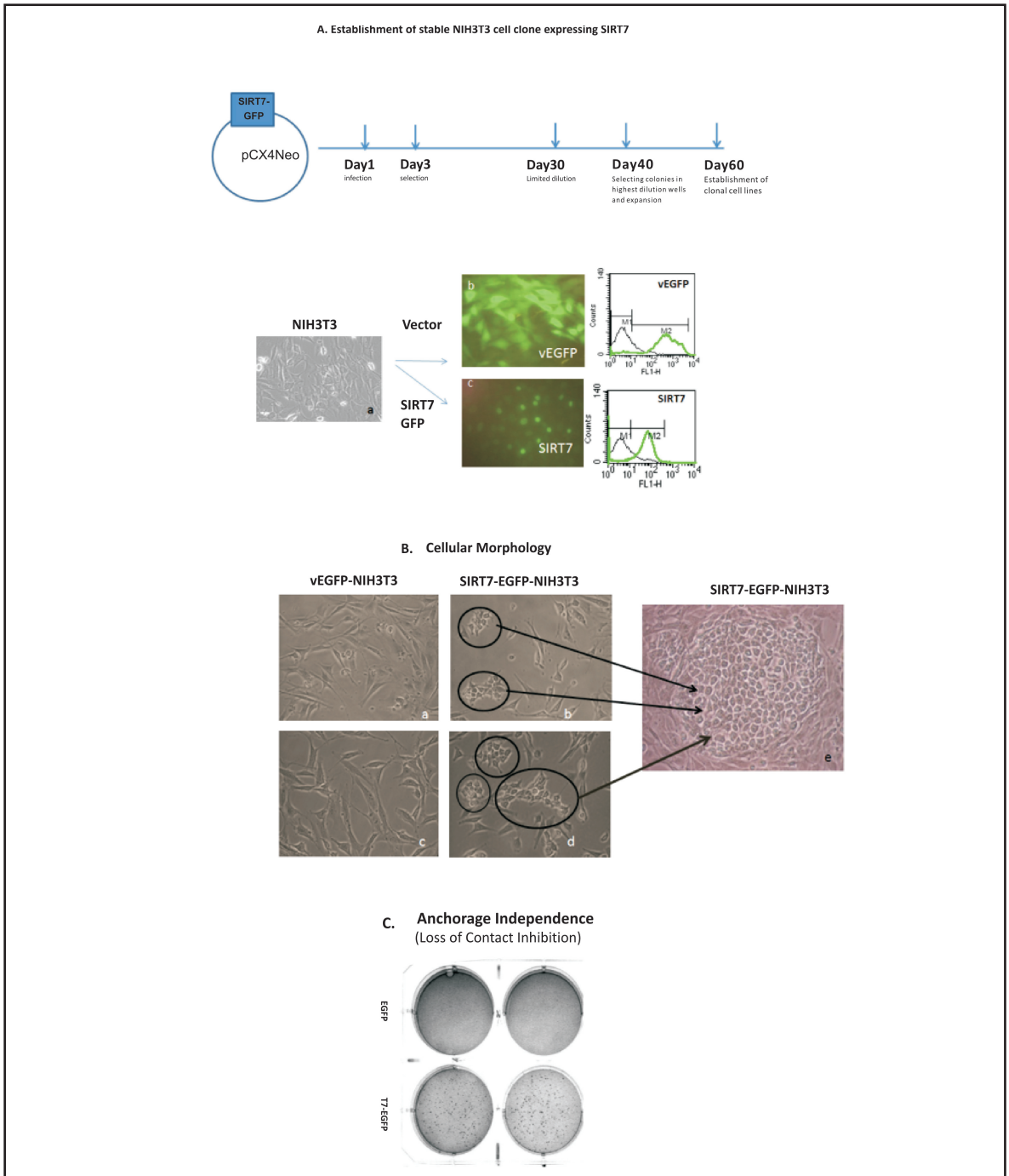

Figure 1. Establishment of SIRT7 overexpressing NIH3T3 cells. (A) NIH3T3 cells were transfected with pCXneo4 retroviral construct expressing EGFP or SIRT7. Various clones were selected following selection in genticin. Two stable clones expressing EGFP or SIRT7 were selected. The GFP expression was also checked by FACS analysis. (B) SIRT7 overexpressing cells on continuous passage showed changes in cellular morphology (b,d) which in turn grows as distinct colonies (e). (C) SIRT7 overexpressing clones can row on soft agar indicative of anchorage independence.

is also affected in SIPS? We induced SIPS in osteosarcoma cell lines (U2OS) by treating with adriamycin and found no disappearance of nucleolar SIRT7. This indicated that disappearance of SIRT7 from nucleoli is specific only to replicative senescence because of telomere shortening.

(b) Role of SIRT7 in cellular proliferation

Based on our observation on declining levels of SIRT7 expression in senescent cells, we hypothesize that SIRT7 may have a role in cellular proliferation. In order to gain insight if SIRT7 gives any growth advantage, we cloned human SIRT7 in EGFP-C3 mammalian expression vector and also the pCXneo retroviral system. Overexpression of SIRT7 in HEK293T cells resulted in no significant changes in the growth in general. We next tried overexpressing SIRT7 in immortalized mouse fibroblasts, NIH3T3, by retroviral transfection. SIRT7 overexpressing clones showed no significant difference in growth profiles. Interestingly, we find that some of the SIRT7 overexpressing clones show a drastic change in cellular morphology accompanied by growth on soft agar (Figure 1). Characterizations of various SIRT7 expressing cell- clones are currently underway.

3. Cellular model with changes in redox states to study cellular senescence

In continuation with the previous studies on SIRT7 and ageing, we are also trying to establish cell culture systems where senescence can be induced so as to study various biochemical and cellular changes associated with ageing. Treatment of cells with a variety of cytotoxic agents usually at sub-lethal doses can induce premature senescence. These include oxidizing agents, ionizing radiation, DNA-damaging agents, microtubule-damaging agents, retinoids, mitogens, cytostatic agents. H_2O_2 is the most preferred oxidant for studying SIPS and is

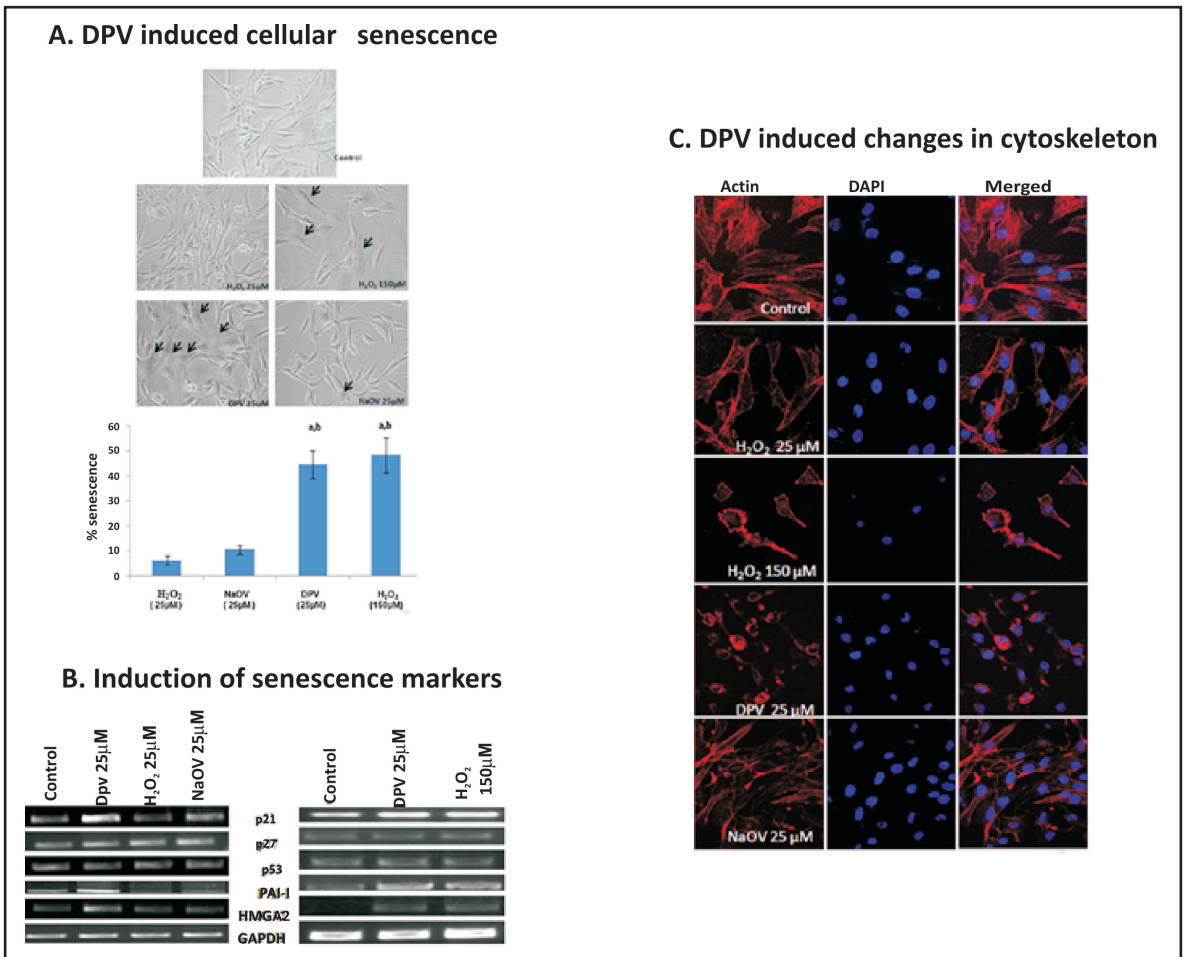

Figure 2. Cellular senescence in immortalized fibroblasts cells (NIH3T3). (A) DPV (25µM) induces SIPS at concentrations 6 fold lower than H_2O_2 (150µM), while equimolar concentrations of orthovanadate (NaOV) and H_2O_2 had no effect. (B) DPV induced senescence markers like p21, PAI and HMGA2 more prominently than H_2O_2 and sodium orthovanadate. (C) DPV induced cellular senescence is preceded by changes in cytoskeletal organization as revealed by actin-phalloidin staining.

also considered a unifying ageing mediator. However, studies on the cellular effects of H_2O_2 are constrained by the need for high concentrations and long duration of treatment because cells are abundantly equipped with catalase and glutathione peroxidase that rapidly deplete intracellular H_2O_2. Earlier it has been reported that single pulse of sub-lethal dose (150–250 mM) led to cell cycle arrest/ apoptosis/senescence in human cells. Prolonged exposure to low levels of H_2O_2 also led to SIPS-like state. Availability of sufficient peroxide in intracellular milieu appears to be a prerequisite for cellular ageing. H_2O_2 forms a stable peroxo- complex with orthovanadate, diperoxovanadate (DPV), at pH 7.0, and its peroxo groups are relatively slowly degraded by catalase. If DPV can act as a good oxidant because of an active and stable peroxo-group, we hypothesized that DPV can substitute for H_2O_2 mediated SIPS at much lower concentrations. The major highlight of the study is treatment, of mouse fibroblasts, with DPV induced growth arrest similar to senescence with increased expression of senescent markers (p21, HMGA2, PAI-1) more efficiently than a similar dose of either H_2O_2 or vanadate (Figure 2 A, B). A characteristic feature of DPV treatment was rapid cellular rounding accompanied by apparent cytoskeletal reorganization (Figure 2C) and also a striking relocalization of Cyclin D1 protein from nucleus to cytoplasm in the senescent cells. The same effects were obtained with H_2O_2 at much higher concentration. Our findings therefore suggest that inorganic peroxides can act more efficiently in place of H_2O_2 to accelerate the process of senescence. In addition, DPV can serve as a useful tool in studies on plethora of cellular effects mediated by H_2O_2, because of its definitive, faster responses.

Publications

1. Vedantham H, Silver MI, Kalpana B, Rekha C, Karuna BP, Vidyadhari K, Mrudula S, Ronnett BM, Vijayaraghavan K, Ramakrishna G, Sowjanya P, Laxmi S, Shah KV and Gravitt PE; CATCH Study Team (2010). Determinants of VIA (Visual inspection of the cervix after acetic acid application) positivity in cervical cancer screening of women in a peri-urban area in Andhra Pradesh, India. ***Cancer Epidemiology, Biomarkers and Prevention*** 19: 1373-1380.

2. Bose S, Sakhuja P, Bezawada L, Agarwal AK, Kazim NS, Khan LA, Sarin SK and Ramakrishna G (2011). Hepatocellular carcinoma with persistent hepatitis B virus infection shows unusual downregulation of Ras expression and differential response to Ras mediated signaling. ***Journal of Gastroenterology and Hepatology*** 26: 135-144.

LABORATORY OF COMPUTATIONAL AND FUNCTIONAL GENOMICS

Computational and Functional Genomics of Microbial Pathogens

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	Suhail Yousuf	Junior Research Fellow
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Project I: Genome analysis and functional characterization of the genomes of microbial organisms

1. Characterization of the promoter and transcription factor binding sites in *M. tuberculosis*

Adaptation to the various conditions encountered by the pathogen during the establishment of an infection is thought to require strict gene expression control. In prokaryotes, much of this control is at the level of transcription. There are thirteen sigma factors encoded in the genome of *Mycobacterium tuberculosis*. Although some of these have been characterized, many remain to be characterized in terms of the promoter recognition specificities and their physiological roles. Furthermore, over 140 putative transcriptional regulators are presumably involved in gene expression modulation in this pathogen.

Objectives

1. To study gene expression and regulation in mycobacteria, with special emphasis to pathogenesis, using the non-pathogenic and relatively fast growing *Mycobacterium smegmatis* as a model organism
2. To predict promoter sequences and to sort them into individual sigma factor dependent regulons
3. To use *in vitro* assays for the study of dynamics of RNA polymerase activity and specificity, circumventing the problems posed by live infectious cultures employed for *in vivo* experiments
4. To study the promoter context of mycobacterial transcription factors in order to further understand and expand their regulons.

Summary of the work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

A database of putative *M. tuberculosis* promoters was constructed using the already published consensus sequences of sigma factors, which were used to search for occurrences in the genome. Binding sites of the IdeR repressor were used to generate putative binding sites using Predict Regulon, thus potentially augmenting the number of genes known to be regulated by IdeR.

Cellular responses to environmental conditions are governed by the fine tuning of functional and physical interactions in the proteome. A number of methods have been proposed for the prediction of these Protein-Protein Interactions (PPI), which are based on genomic contexts and Expression Similarity (ESM).

Objectives

1. To develop an integrated approach for the prediction of functional and physical interactions in the proteome

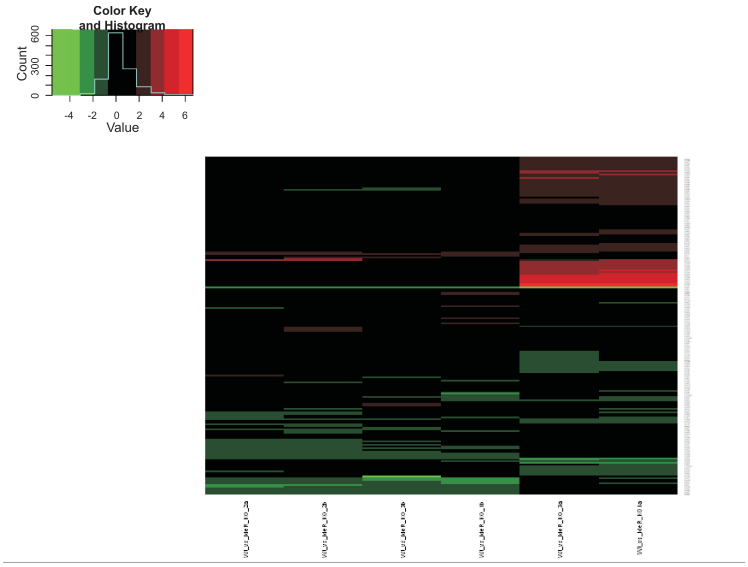

Figure 1. Heatmap of gene expression data from the top 5% most variable genes, of IdeR KO strains, compared to WT strain, under high and low iron conditions.

Details of progress in the current reporting year (April 1, 2010 – March 31, 2011)

PredictRegulon has revealed novel genes putatively regulated by the IdeR regulator. Incorporation of gene expression data would serve to confirm this. To demonstrate that IdeR regulates the genes identified, heat maps were generated from the gene expression data for the gene neighborhood. Figure 1 shows a heat map for the 5% most variable genes, and demarcates a cluster of IdeR regulated genes. The heat maps demonstrate that these genes have a differential expression pattern from their immediate neighborhood. In addition, for some genes, downstream genes show a similar pattern of gene expression, suggesting that these genes are co-regulated, and may occur as an operon.

2. Reconstruction of a genome-wide protein-protein functional linkage map: A machine learning approach to understand cellular physiology

1. To compare and contrast the predictive power of PPI prediction methods using various Machine Learning Classifiers (MLC).

Summary of the work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

Six PPI prediction methods which includes gene cluster, gene order conservation, gene neighbor, phylogenetic profile, improved mirrortree method and gene expression similarity were evaluated in terms of predictive power, their ability to discriminate various types of interactions from non-interacting ones. We have used seven MLCs to predict the PPI network in *E. coli* by integrating the above mentioned six PPI prediction methods.

Details of progress in the current reporting year (April 1, 2010 – March 31, 2011)

We derived the whole genome protein functional linkage map of *Escherichia coli* K12 using a

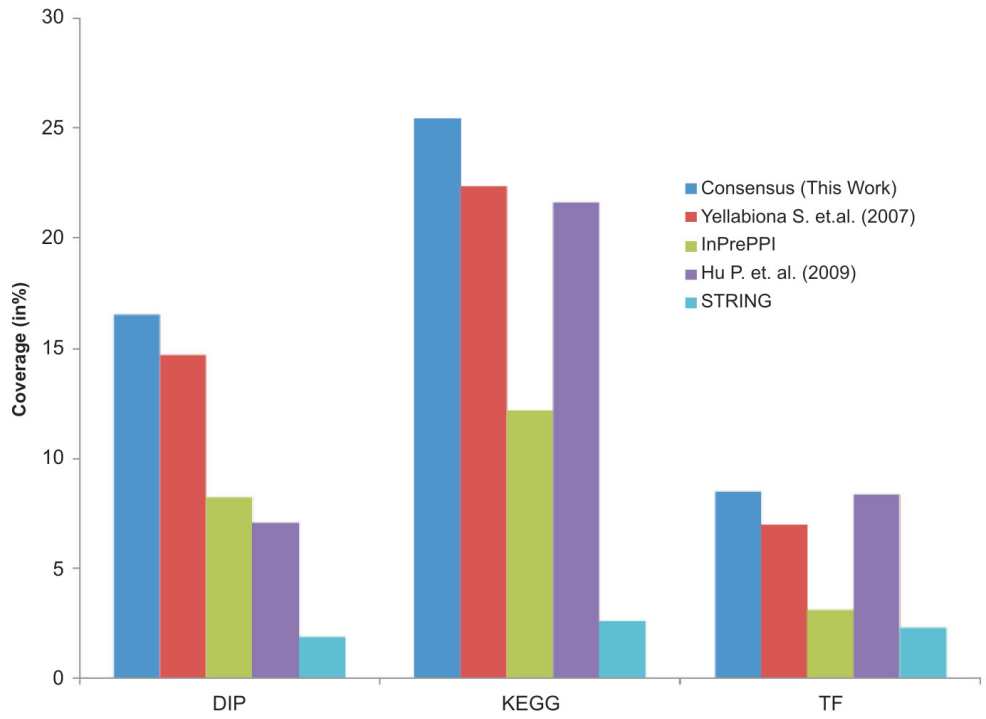

Figure 2. Comparative analysis of the coverage of known physical (DIP), co-pathway (KEGG) and regulatory (TF) interactions by our method and published methods.

consensus of seven MLCs. As a proof of concept, we show that the predicted network has highest coverage of known interactions than previously published four methods (Figure 2). A number of interactions predicted by individual MLCs are varied greatly though accuracy of them is quite similar. The topological property of networks shows remarkable improvement over previous reports. These are closer to estimated topological properties of cellular network using genetic analysis and other experimental data. Our network has modularity value of 0.5 which suggests the network has many small components that are highly connected among themselves than rest of the proteins in network. The small components were analyzed using gene expression data for example as given in Figure 3, which shows the antagonistic behavior of biofilm associated proteins to that of cell division and outer membrane biosynthesis.

Project II: Genome analysis and functional characterization of *Plasmodium falciparum*

1. Study of the *Plasmodium falciparum* genome and the effect of AT-richness on its proteome

Some of the genomes exhibit a non uniform usage of nucleotides; one of such extreme organisms is *Plasmodium falciparum,* which consists of a nuclear genome of 23.3 megabases (Mb) organized into 14 chromosomes and is an extremely AT-rich organism. The biasness of the genome can extend across all regions including both the coding and noncoding (Table 1).

One possible consequence of the biasness in the coding regions is the variation in the amino acid composition of the corresponding proteome.

S. No.	Regions	No. of exons/introns	AT content (%)
1	Coding	13,739	75.44
2	Noncoding	7,958	86.78

Table 1. AT content of the coding and noncoding regions of the genome of *P. falciparum*

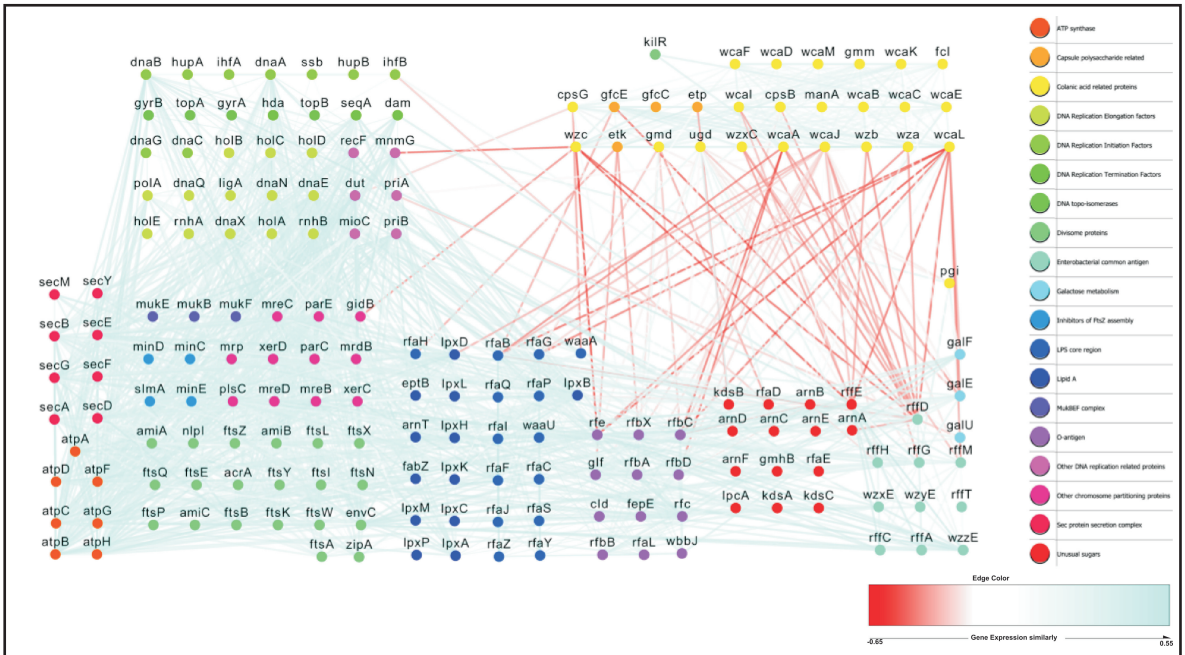

Figure 3. Inverse gene expression relationship of biofilm and cell division, peptidoglycan synthesis associated proteins. We also show that the Sec protein-translocation pathway is tightly linked with fts locus proteins which can be clarify by the fact that SecA and FtsZ both binds to inner membrane in the presence of $MgCl_2$. Majority of inner membrane component are indeed part of this network.

Objectives

1. Is there any difference in the dinucleotide correlations of the coding and noncoding regions of an AT-biased genome like *P. falciparum*?
2. Are there any selection pressures, acting either at the nucleotide or at the amino acid level of this biased organism?

Summary of the work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

Our work suggests that the correlations follow a similar pattern as that of the natural language and there has been an influence of AT-richness on these correlations. The existence of these correlations in the genome is a result of the expansion and modification of some regions of the genome, which have introduced certain mutations that are not found to be lethal for the organism and yet maintain the functionality of the genes.

Details of progress in the current reporting year (April 1, 2010 – March 31, 2011)

Dinucleotide analysis of the coding and noncoding regions of *P. falciparum* exhibit a significant demarcation in their correlations values with the noncoding regions having higher correlations than the coding regions (Figure 4). The dinucleotides, TA, TG, AT and AG are found to be highly correlated in the exonic sequences where as the dinucleotides, AT, TA, AA and TT are found to be highly correlated in the intronic sequences (Figure 5). These results suggest that since exons are coding, they are under the pressure to maintain the codon usage levels of both the AT-rich and GC-rich codons. The intronic sequences are not directly under the pressure of the codon usage, since they are noncoding, which makes them lenient to maintain high AT-richness (86%). The amino acid

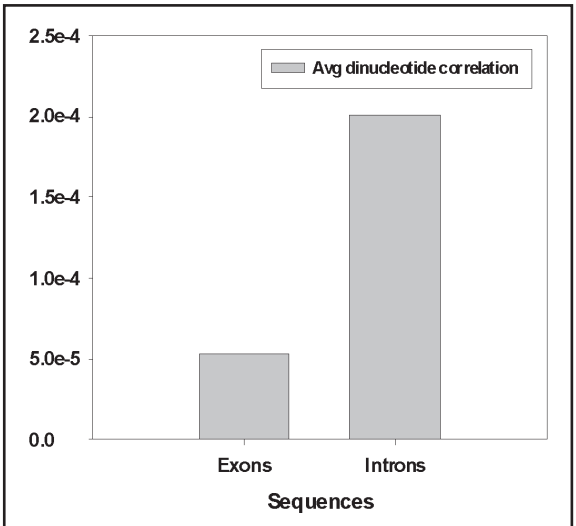

Figure 4. Average dinucleotide correlation of the 16 dinucleotides of the complete coding and noncoding regions of *P. falciparum*

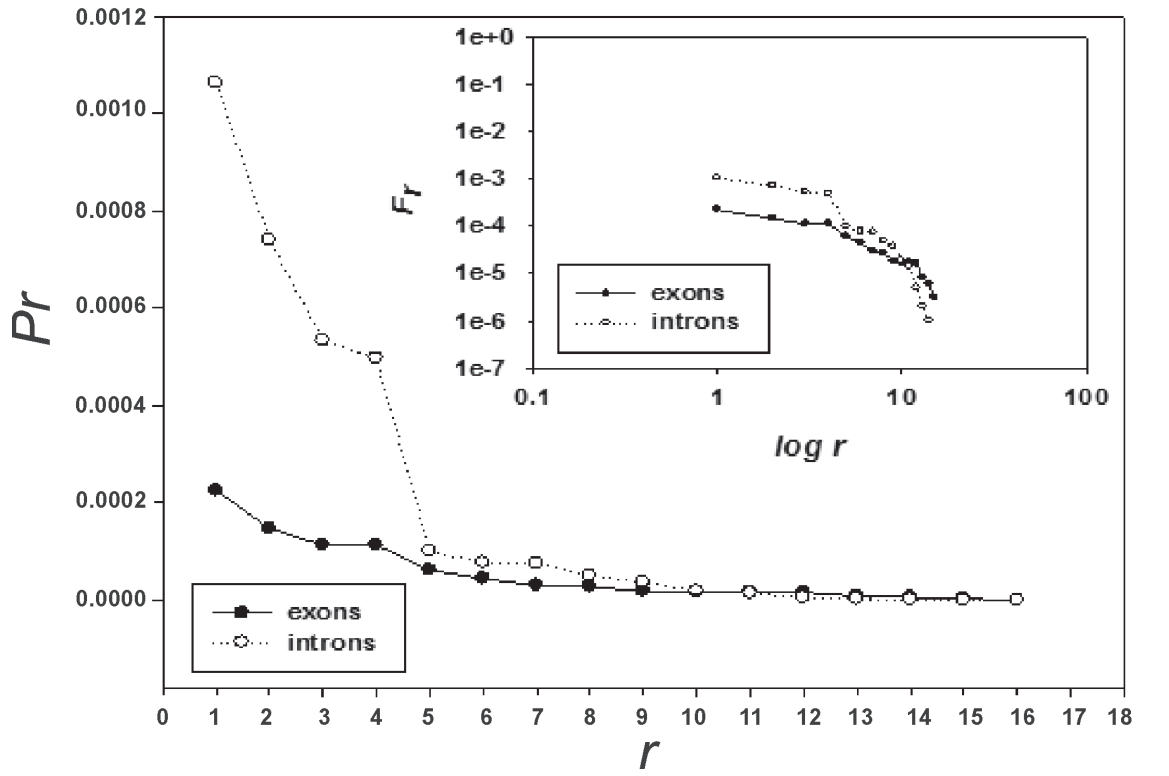

Figure 5. Correlations of the coding and noncoding sequences *vs.* its rank of all the 14 chromosomes of *P. falciparum.*

analysis suggests that the amino acid composition of an organism is not exactly a direct consequence of its genome and is under the constraints of various selection pressures. We have observed that the organism tries to maintain a balance between the constraints that the nucleotide sequence imposes on its amino acid sequence and the constraints the amino acids impose on the nucleotide sequences.

2. Role of multiple Acyl CoA binding protein paralogues in *Plasmodium falciparum*

Acyl-coenzyme A binding proteins (ACBPs) are a family of 86 to 103 residues (~10 kD) proteins with conserved amino acid sequences. There are experimental evidences from diverse sources suggesting their role in modulation of fatty acid biosynthesis, regulation of the intracellular acyl-CoA pool size and many more basic metabolic processes. The knockout/down studies in *Trypanosoma brucei* and HeLa cell lines have proved that ACBP is essential.

Objectives

1. To study the binding preferences of all Pf ACBPs and also to study stage specific expression of different Pf *acbp* genes
2. To study the oligomerisation state of ACBPs using mass spectrometry and gel filtration chromatography.

Summary of the work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

We have cloned and expressed all the four ACBPs as histidine-tagged recombinant proteins and purified them by Ni-NTA affinity chromatography. The ACBPs were further purified by gel filtration on Superdex-75 column.

Details of progress in the current reporting year (April 1, 2010 – March 31, 2011)

ACBPs are highly conserverd even in a highly diverged eukaryote like *Plasmodium falciparum*. We hypothesized that there should be some additional function of ACBP in *P. falciparum* apart from binding to acyl CoAs. It is a well known fact that the lipid contents of normal and infected RBCs are different form each other. The maximum expression stage of ACBP is merozoite in which these lipid changes are observed. We wanted to know whether Pf ACBP has anything to do with lipid changes in merozoite

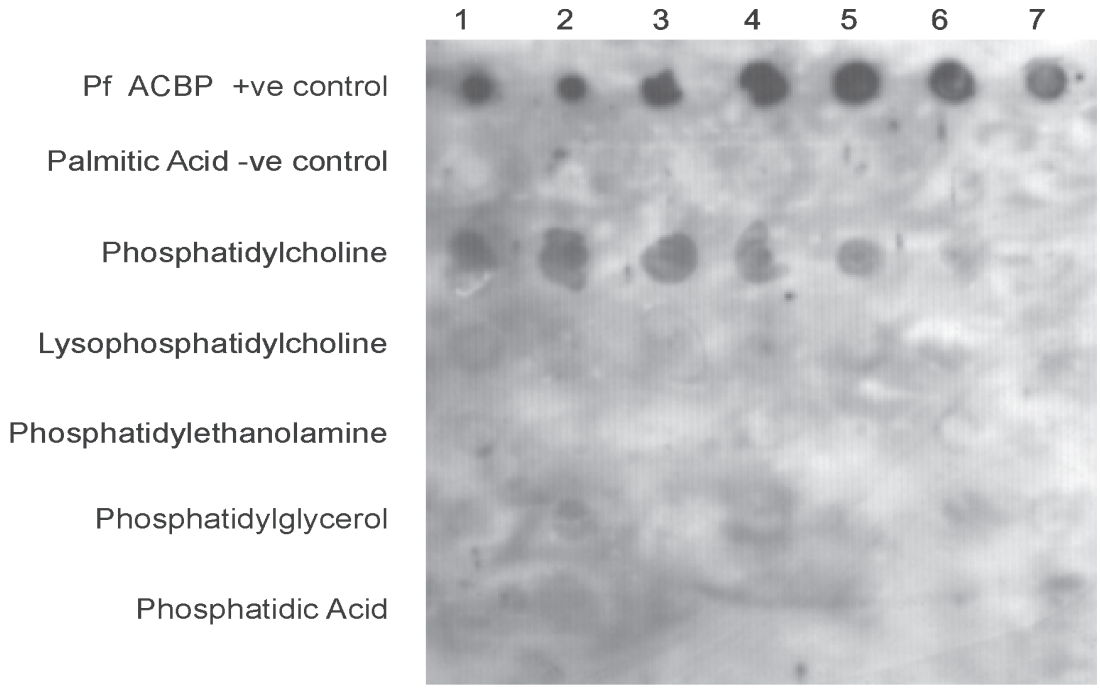

Figure 6. Phosphatidylcholine binding by PF14_0749. The different lipids were spotted on nitrocellulose membrane and it was blocked with fat-free BSA. The lipid coated membrane was incubated with 1 µg/ml pure recombinant Pf ACBP at 4 C overnight. ACBP binding to lipid was detected by anti-ACBP antibodies followed by HRP-conjugated secondary antibodies. Membrane was washed extensively (10-12 times) after each incubation.

stage or not. We checked the binding of Pf ACBP with different phospholipids using Protein Lipid Overlay assay, a technique similar to western blot used for detecting protein-lipid interactions. Pf ACBP can bind phosphatidylcholine but not other lipids used in this assay (Figure 6). Till now, there is only one report of ACBP in case of *Arabidopsis thaliana* for phosphatidylcholine binding.

LABORATORY OF TRANSCRIPTION

Mechanism of Transcription Termination and Antitermination in *Escherichia coli*

Principal Investigator	Ranjan Sen	Staff Scientist
PhD Students	Ghazala Muteeb	Senior Research Fellow
	Amitabh Ranjan	Senior Research Fellow
	Rajesh Sashni	Senior Research Fellow
	Sourav Mishra	Junior Research Fellow
	Mohd Zuhaib Qayyum	Junior Research Fellow
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	Sapna Godavarthi	Technical Officer I
	Nanci R Kolli	Technical Assistant (Till Jun. 2010)
	Shalini Mohan	Project Assistant
	Shrutika Wadgaonkar	Project Assistant (Till Oct. 2010)
Collaborators	Udayaditya Sen	SINP, Kolkata
	V Nagaraja	IISc, Bangalore

Objectives

Transcription must terminate at the end of each operon. In *E. coli*, end of 50% of the operons consist of intrinsic termination signal that codes for a hairpin followed by a U-rich stretch in mRNA. Rest of the operons does not have any signature sequence and it is possible that termination of these operons depend on a factor called Rho. On the other hand, these termination signals can be overcome in response to certain type of modifications in the elongation complex and process is termed as antitermination. Mechanism of these termination and antitermination processes is still not very clear and offers an exciting subject for study. In my laboratory, studies in the following areas are in progress.

1. Mechanism of action of transcription termination factor, Rho
2. Molecular basis of Rho-NusG interaction
3. Mechanism of transcription antitermination by N protein at Rho-dependent terminators
4. Mechanism of action of transcription antitermination of Rho-dependent termination by an anti-rho factor Psu
5. Physiological significance of Rho dependent termination.

Summary of the work done until the beginning of this reporting year (April 1, 2009 - March 31, 2010)

1. We made a detailed *in vitro* characterization of the Rho protein from *Mycobacterium tuberculosis.* We established that this Rho protein unlike that from *E. coli* is less dependent on its ATPase and translocase activities to perform the termination function (JMB, 2010)
2. We have defined the interacting regions involved in the complex formation between transcription elongation factor NusG with the terminator Rho using mutational and biochemical analyses (JMB, 2011).

Details of the progress in the current reporting year (April 1, 2010 - March 31, 2011)

A. Generalized existence of the kinetic coupling in the *in vivo* Rho-dependent termination

The conventional model of Rho-dependent transcription termination in bacteria requires a "kinetic coupling" between the elongation complex and the translocating Rho on the nascent mRNA. This model has been recently challenged by a radical view, wherein Rho binds to the elongating RNA polymerase prior to loading onto the mRNA. This view questions the relevance of the kinetic coupling which was proposed from an observation of the suppression of a Rho-mutant (*rho201*) by a slow-elongating RNA polymerase. The generality of this concept has never been tested. Using growth assays, micro-array analyses and reporter based transcription termination assays *in vivo*, we showed that slowing down of the transcription elongation rate suppressed the termination defects of five Rho mutants, three NusG mutants defective for Rho-binding and the defects caused by the two Rho-inhibitors, Psu and Bicyclomycin. These results established the generality of the existence of the kinetic coupling in the *in vivo* Rho-dependent termination which also strongly suggests that Rho translocates along the RNA and does not piggy-backs the elongation complex *in vivo*. Furthermore, these results indicated that one of the major roles of NusG in *in-vivo* Rho-dependent termination is to enhance the RNA-release speed from the elongation complex.

B. An inhibition-antitermination mechanism for overcoming Rho-dependent termination by N

Lamdoid phages have evolved an antitermination system to overcome the Rho-dependent transcription termination in bacteria. N protein from these phages modifies the host-transcription machinery to overcome both the Rho-dependent and the -independent termination. N binds to a specific site called *nut* site on the mRNA, which also overlaps with the Rho-loading site (the *rut* site of the *tR1*terminator), on the same RNA, using its N-terminal ARM motif and interacts with the elongating RNA polymerase (RNAP) through its C-terminal domain. We hypothesized that the mechanism of overcoming the Rho-dependent termination by N should at least involve two steps; inhibition of Rho by blocking its entry at the nut-site and an antitermination mechanism by

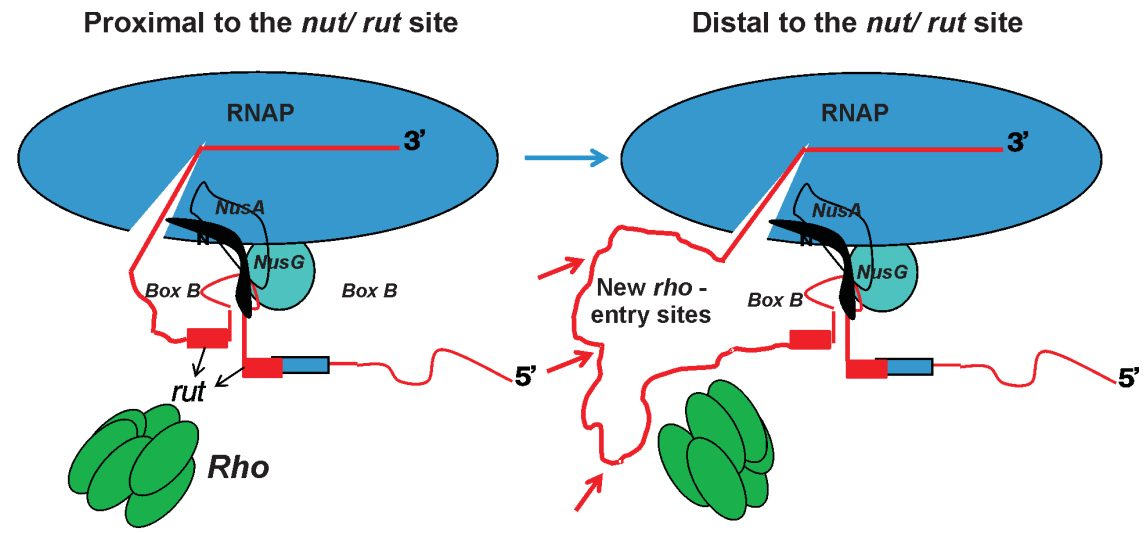

Figure 1. Possible mechanisms of overcoming the Rho-dependent termination by N.

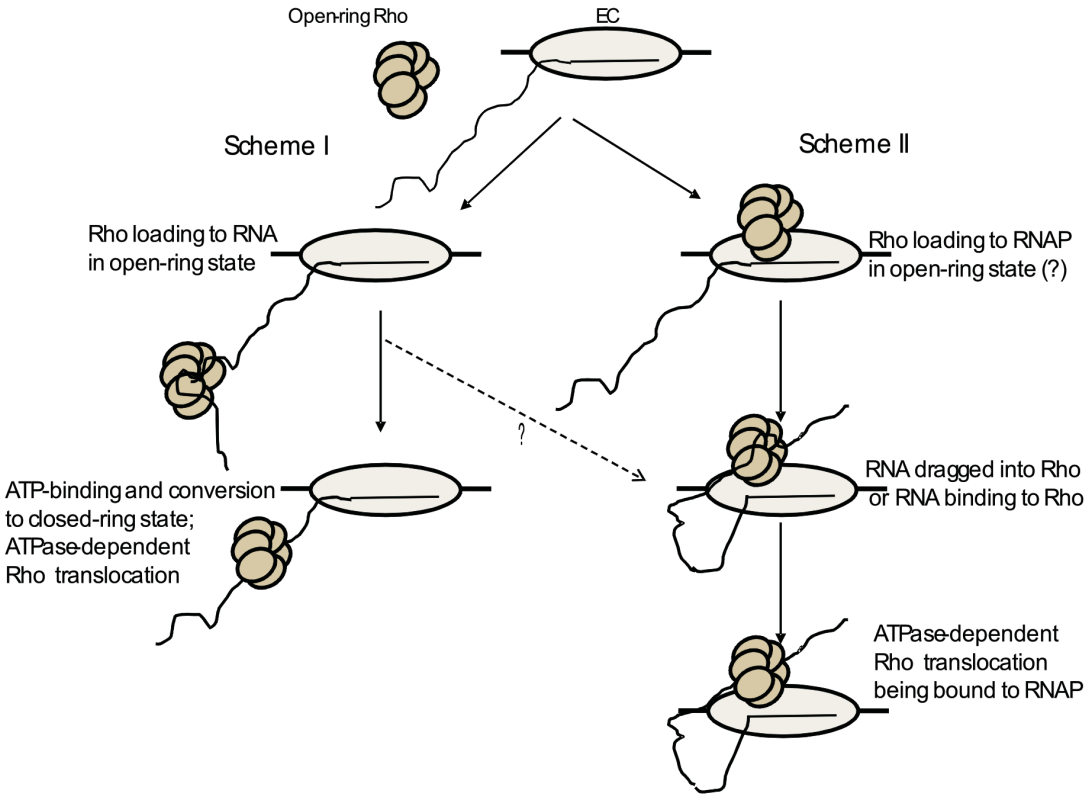

Figure 2. Rho recruitment models of the transcription elongation complexes.

modifying the RNAP most-likely at the RNA exit channel which could be the access point for Rho. Here we tested these hypotheses by using the N protein from a Lamdoid phage H-19B. We observed that the N-boxB interaction is sufficient for N to overcome Rho when the elongation complex is near the nutR/tR1 sites whereas N-RNAP interaction becomes more important when the EC travelled further away from the nut site and the looped out nascent RNA contains many potential Rho-loading sites. Rho function is inhibited even from the N-modified stalled elongation complexes indicating that enhancement of transcription elongation rate is not the major reason for overcoming Rho. The rate of RNA-dependent ATPase activity on the RNA with a nutR/tR1 site by Rho was reduced in the presence of N. But the direct binding studies revealed that N and Rho co-exist at the NutR/tR1 site. Most likely N delays the Rho binding at the rut site and subsequent isomerization steps and Rho eventually overcomes the N-effect. We propose that the antiterminator N uses an inhibition-antitermination hybrid mechanism to overcome the Rho-dependent termination (Figure1).

C. RNA binding is pre-requisite for Rho to be recruited to the elongation complex

In the conventional model of the Rho-dependent transcription termination, the hexameric RNA-binding protein Rho binds to and translocate along the nascent RNA (at the rut sites) prior to make possible interactions with the elongating RNAP to exert the termination function. Even though the interaction between Rho and isolated RNAs were studied in great details, the same has never been shown with the nascent RNA of a transcription elongation complex. Direct demonstration of the RNA binding with the nascent RNA becomes even more important because of a recently proposed alternative view which proposes that the Rho loads onto the RNA polymerase prior to the formation of the nascent RNA. Here we have measured the direct interaction of Rho with a stalled elongation complex. We observed that the association of Rho with the elongation complex is only dependent on the presence of rut site containing long nascent RNA, and *in vitro* Rho does not get associated with either free RNAP or RNAP-promoter binary complex or elongation complexes formed near the promoter.

RNA-footprinting assays also revealed that Rho protects the rut site of a nascent RNA in the absence of ATP hydrolysis. We concluded that the nascent RNA loading of Rho is a pre-requisite for its recruitment to the transcription complex and NusG does not play any role in this binding step (Figure 2).

Publications

1. Kalarickal NC, Ranjan A, Kalyani BS, Wal M and Sen R (2010). A bacterial transcription terminator with inefficient molecular motor action but with a robust transcription termination function. ***Journal of Molecular Biology*** 395: 966-982.
2. Khamurai S, Ranjan A, Pani B, Sen R and Sen U (2010). Crystallization and preliminary X-ray analysis of Psu, an inhibitor of bacterial transcription terminator, Rho. ***Acta Crystallographica Section F Structural Biology and Crystallization Communication*** 66: 204-206.
3. Muteeb G and Sen R (2010). Random mutagenesis using mutator strain. ***Methods in Molecular Biology*** 634: 411-419.
4. Chalissery J, Muteeb G, Nisha CK, Mohan S, Jisha V and Sen R (2011). Interaction surface of the transcription terminator Rho required to form a complex with the C-terminal domain of the antiterminator NusG. ***Journal of Molecular Biology*** 405: 49-64.
5. Swapna G, Chakraborty A, Kumari V, Sen R and Nagaraja V (2011). Mutations in β' subunit of *E. coli* RNA polymerase perturb the activator polymerase functional interaction required for promoter clearance. ***Molecular Microbiology*** (In press).

LABORATORY OF CELL SIGNALLING

Investigating the Role of Inositol Pyrophosphates in Eukaryotic Cell Physiology

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	Jadav Rathan Singh	Senior Research Fellow
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	P Srilakshmi	Research Associate (Till May 2010)
	Ruth Manorama Ravoori	Technical Assistant
	Dharmika Kumar	Project Junior Research Fellow
	Somadri Ghosh	Project Junior Research Fellow
	CP Unnikannan	Project Junior Research Fellow
	Kurchi Bhattacharya	BITS Trainee (Since Jan.2011)
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	Satish Kumar, CCMB, Hyderabad	
	Sagar Sengupta, NII, New Delhi	
	Nagaraj Balasubramanian, IISER, Pune	
	Keykavous Parang, University of Rhode Island, USA	

Objectives

1. Examine the role of inositol pyrophosphates in yeast ribosome biogenesis
2. Understand the cellular functions of mammalian inositol hexakisphosphate kinase 1
3. Generate tools to detect inositol pyrophosphate mediated protein pyrophosphorylation.

Summary of work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

Inositol pyrophosphates are derivatives of inositol that contain pyrophosphate or diphosphate moieties in addition to monophosphates. They include diphosphoinositol pentakisphosphate (PP-IP_5, or IP_7) and bis-diphosphoinositol tetrakisphosphate ($[PP]_2$-IP_4 or IP_8), which are implicated in diverse biological functions, including cell growth, vesicular trafficking, apoptosis, DNA recombination and osmotic regulation. We have earlier demonstrated that the beta phosphate group of inositol pyrophosphates can be transferred to pre-phosphorylated serine residues on proteins to form pyrophosphoserine. Pyrophosphorylation occurs on several proteins within the cell, including proteins involved in ribosome biogenesis and vesicular trafficking. 5PP-IP_5 (IP_7) is synthesised from inositol hexakisphosphate (IP_6) and ATP by IP_6 kinases, three isoforms of which are present in mammals (IP6K1, IP6K2 and IP6K3). IP6K1 knockout mice display low body weight compared with wild type mice, low insulin levels and defective spermatogenesis.

Our aim is to understand the biochemical link between protein pyrophosphorylation and cellular phenomena regulated by inositol pyrophosphates.

We utilise *S. cerevisiae,* mammalian cell lines, and knockout mouse strains as model systems to investigate the signalling and metabolic pathways that are altered when inositol pyrophosphate levels are perturbed.

Since IP_7 pyrophosphorylates nucleolar proteins involved in ribosome biogenesis, we examined whether cells with altered IP_7 levels display defects in ribosome synthesis. We observed that *S. cerevisiae* strains lacking the IP_6 kinase *kcs1* display slow growth, sensitivity towards antibiotics that inhibit ribosome function, and have reduced levels of ribosomes. Steady state levels of 35S precursor rRNA are lowered by 50% in *kcs1*Δ cells, suggesting that there may be a defect in rRNA transcription in yeast lacking IP_7. These observations suggest that protein pyrophosphorylation by IP_7 may control ribosome biogenesis, and thereby regulate cell growth and proliferation.

To understand the role of IP_7 in the regulation of mammalian physiology, we utilise IP6K1 knockout (KO) mice, as well as mouse embryonic fibroblasts (MEFs) derived from these mice as model systems. We have established a colony of IP6K1 heterozygous mice and are breeding wild type and knockout litter mates for further analysis. IP6K1 KO MEFs have 70% reduced levels of IP_7 compared with WT MEFs. We carried out a gene expression microarray analysis of IP6K1 KO MEFs, comparing them with WT MEFs, and observe dysregulated expression of several genes in IP6K1 KO cells. Analysis of this data using pathway analysis tools designed to interpret gene expression microarray data revealed that a significant number of genes encoding proteins involved in cell signalling pathways display altered expression in IP6K1 KO cells.

Serine pyrophosphorylation by IP_7 occurs on pre-phosphorylated serine residues present in acidic serine sequences, *i.e.* a stretch of two or more serine residues interspersed with Glu and/or Asp residues. Such sequences occur commonly throughout the proteome of all eukaryotic organisms. We have identified several candidate proteins that may be pyrophosphorylated by IP_7, but in order to investigate whether they are pyrophosphorylated *in vivo*, we require a reagent to detect pyrophosphoserine residues in cellular proteins. Pyrophosphoserine synthesised by our collaborator will be used to screen a DNA aptamer library and obtain specific aptamers that recognise pyrophosphoserine, but not phosphoserine.

Details of progress made in the current reporting year (April 1, 2010 - March 31, 2011)

Project 1: Regulation of yeast ribosome biogenesis by IP_7

Having observed a decrease in ribosome levels in *kcs1*Δ yeast, we examined protein synthesis rates in these strains. The incorporation of ^{35}S-Met into proteins is 50-60% lower in yeast lacking IP_7 compared with wild type yeast. The lowered levels of 35S pre-rRNA in *kcs1*Δ yeast could be due to a decrease in rRNA transcription or rapid processing. We therefore monitored RNA polymerase I-mediated rRNA transcription, and processing of 35S pre-rRNA to mature 25S and 18S rRNA, in wild type and *kcs1*Δ cells (Figure 1a). The incorporation of radiolabelled uracil into rRNA is substantially lowered in *kcs1*Δ yeast (Figure 1b). Run-on transcription analysis suggests that the rate of rRNA transcription is also reduced (Figure 1c,d). There is however no obvious change in the rate at which pre-rRNA is processed to 25S and 18S rRNA (Figure 1b).

Future directions

We are conducting chromatin immunoprecipitation analyses to monitor occupancy of the rDNA promoter by RNA polymerase I in *kcs1*Δ yeast. The next stage in this study will be to identify the molecular mechanism by which IP_7 regulates ribosome synthesis. Several components of the RNA polymerase I core complex and accessory factors possess acidic serine sequence motifs that could be pyrophosphorylated by IP_7. These proteins will be tested to determine which of them are phosphorylated by IP_7, and the pyrophosphorylated Ser residues will be identified by site directed mutagenesis.

Project 2: Cellular functions of mammalian inositol hexakisphosphate kinase 1 (IP6K1)

We have conducted a gene expression microarray analysis to compare the levels of different transcripts in WT and IP6K1 KO MEFs. The expression of 373 genes is up regulated and 887 genes are down regulated in IP6K1 KO cells. Pathway analysis tools applied to this gene expression data predict that the 'regulation of the actin cytoskeleton' is one of the potentially altered signalling pathways in KO MEFs. To investigate this possibility, we examined the pattern of polarized migration in WT and KO MEFs plated on fibronectin coated surfaces, and observe an altered migration pattern in the IP6K1 KO MEFs. Our investigations show that KO MEFs spread more slowly on fibronectin coated surfaces

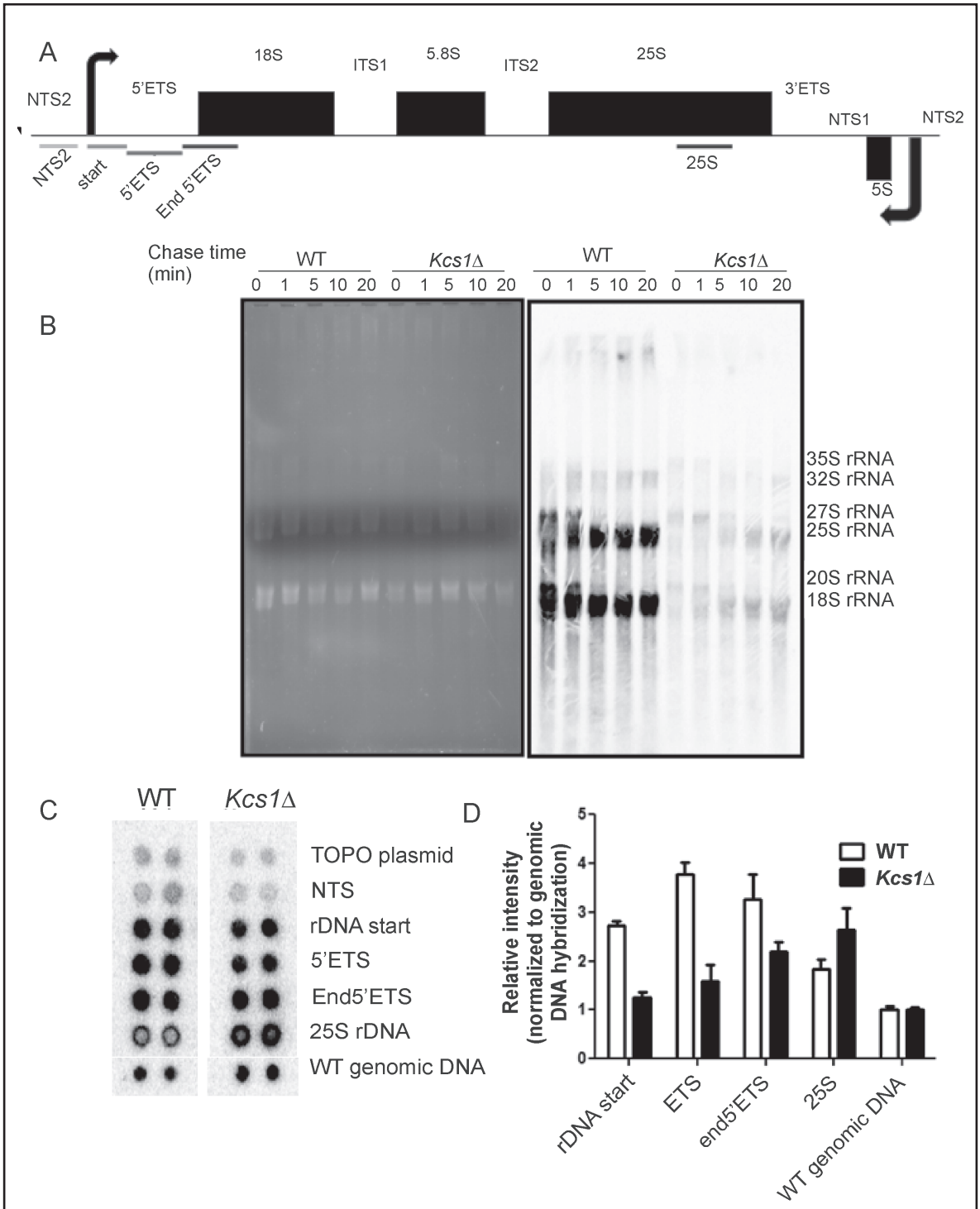


Figure 1. Loss of IP_7 leads to reduced rRNA transcription in *S. cerevisiae*. (a) Schematic description of the *S. cerevisiae* rDNA locus. Curved box-arrows mark the 35S rRNA and 5S rRNA promoters. Regions encoding mature rRNA are indicated by black boxes. Positioning of DNA fragments used for run-on transcription analysis are indicated by shaded lines. (b) Uptake of ^{14}C-labelled uracil by yeast cells was chased with unlabelled uracil for the indicated length of time. Total RNA isolated from these cells was resolved on an agarose gel, stained with ethidium bromide (left panel), transferred to a nylon membrane and imaged by a phosphorimager (right panel). (c) For run-on transcription analysis, permeabilised yeast cells were incubated with ^{32}P-labelled UTP. Total RNA from these cells was hybridized with replicate spots of DNA fragments corresponding to indicated regions on the rDNA locus (a). Radioactivity was detected by a phosphorimager. (d) The signal from each spot following run-on transcription analysis in (c) was normalised to the signal from hybridization with total genomic DNA, and the data correspond to mean ± SEM from two experiments.

compared with WT MEFs (Figure 2 a,b). We also observe a reduced number of lamellipodia and increased number of filopodia in KO MEFs compared with WT, after the cells have completely adhered to the substratum and initiated migration (Figure 2 a).

Future directions

We are attempting to identify the molecular basis for the observed role of IP_7 in regulating actin cytoskeleton dynamics during cell spreading and migration. Altered gene expression of surface integrins and defects in growth factor signalling

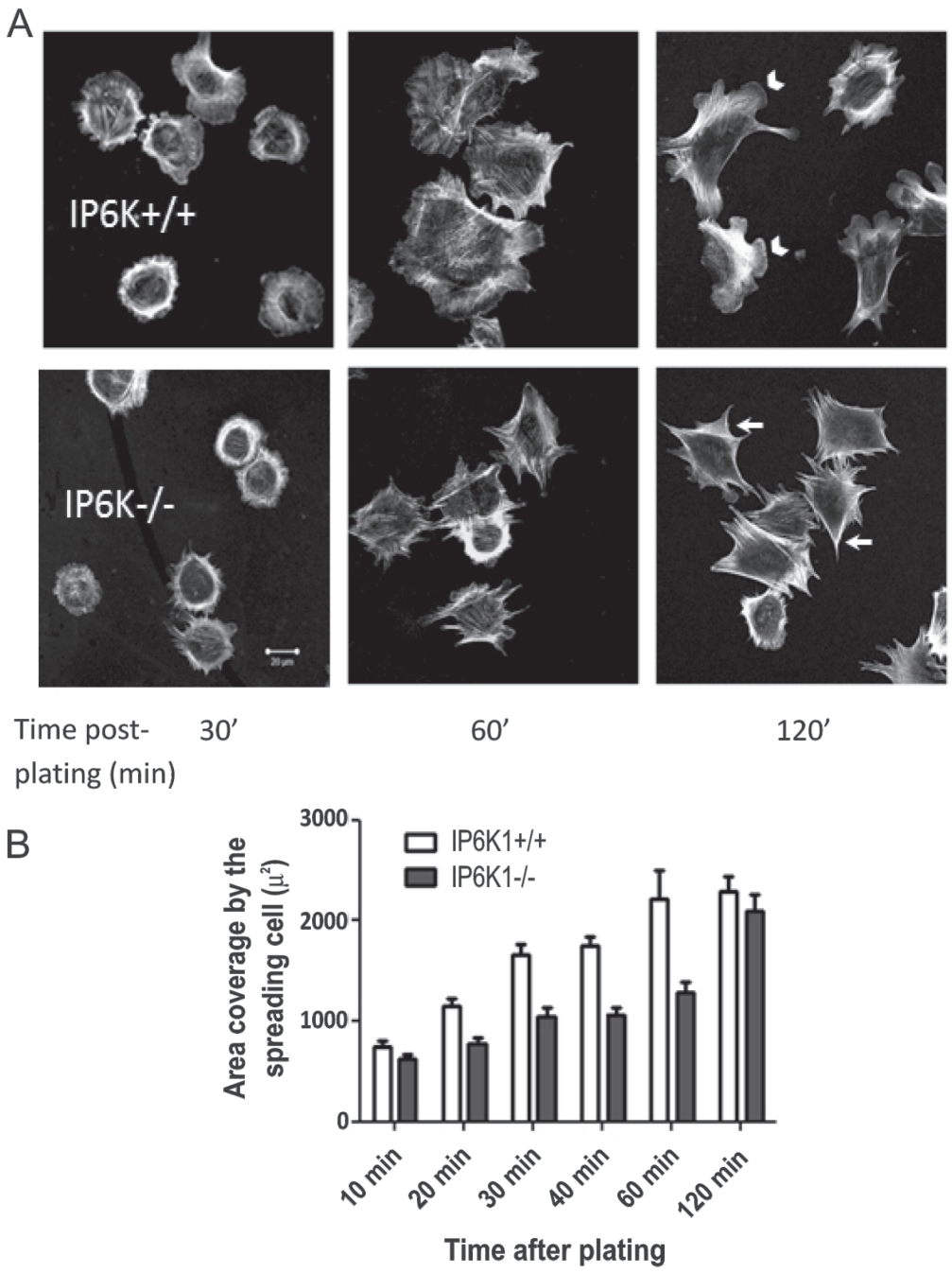


Figure 2. Delayed cell spreading in MEFs lacking IP6K1. (a) WT (IP6K1+/+) and IP6K1 knockout (IP6K1-/-) MEFs were allowed to spread on fibronectin coated cover slips for the indicated length of time, fixed, stained with rhodamine-phalloidin and imaged by confocal microscopy. Lamellipodia are indicated by arrowheads and filopodia by arrows. (b) The surface area over which each cell spread during the indicated time period was measured using ImageJ. The mean ± SEM (N=20 cells) is shown for each time point in both cell lines.

pathways may be responsible for the observed phenomena. These changes may be a direct or indirect consequence of protein pyrophosphorylation or specific binding by IP_7.

Project 3: Generation of tools to detect protein pyrophosphorylation

To screen an oligonucleotide library for DNA aptamers that specifically recognise pyrophosphoserine (ppSer) but not phosphoserine (pSer), we have standardised a procedure to couple ppSer or pSer covalently to agarose beads (Affi-Gel, BioRad Laboratories). We quantify ligand coupling to agarose beads by measuring the reactivity of TNBSA with the free amine group of uncoupled pSer or ppSer. An aliquot of the DNA library is allowed to interact with 100 fold excess immobilised ppSer, while using pSer in a negative screen. We are currently conducting several rounds of SELEX using this system and look forward to obtaining DNA aptamers that bind ppSer but not pSer.

Future directions

Once we obtain an aptamer that specifically recognises pyrophosphoserine, we will use it as a tool to identify pyrophosphorylated proteins in *S. cerevisiae* and mammalian cells.

Publication

1. Werner JK Jr, Speed T and Bhandari R (2010). Protein pyrophosphorylation by diphosphoinositol pentakisphosphate (InsP7). ***Methods in Molecular Biology*** 645: 87-102.

LABORATORY OF PLANT MICROBE INTERACTION

Understanding Virulence Mechanisms of *Xanthomonas* Plant Pathogens and Interaction with Host Plants

Principal Investigator	Subhadeep Chatterjee	Staff Scientist
PhD Students	Rikky Rai	Junior Research Fellow
	Sheo Shankar Pandey	Junior Research Fellow
	Raj Kumar Verma	Junior Research Fellow
Other Members	N Narsimha Rao	Research Associate (Since Feb. 2011)
	Binod Bihari Pradhan	Technical Officer I
	Manish Ranjan	Project Junior Research Fellow
	Sree Gowrinadh Javvadi	Project Junior Research Fellow

Objectives

1. Identification and characterization of virulence factors of *Xanthomonas*
2. Role of cell-cell communication in *Xanthomonas* colonization and virulence
3. Function of protein secretion system in *Xanthomonas* and role in virulence
4. Role of PAMP in pathogen recognition and plant defense response.

Summary of work done until the beginning of this reporting year (April 1, 2009 - March 31, 2010)

We are trying to understand the virulence mechanisms of important *Xanthomonas* pathogens like, *Xanthomonas campestris* pv. *campestris* (Xcc; a pathogen of crucifers), *Xanthomonas oryzae* pv. *oryzae* & *Xanthomonas oryzae* pv. *oryzicola* (Xoo, Xola; pathogens of rice) and *Xanthomonas axonopodis* pv. *citri* (Xac; pathogen of citrus).

Similar to *Xanthomonas,* many animal and plant pathogenic bacteria make various kinds of Quorum sensing signals (Language), which regulates diverse phenotypes including, biofilm formation, attachment, regulation of production of virulence effectors. To understand the dynamics of quorum sensing using *Xanthomonas* and *Pseudomonas syringae* as model, we have constructed GFP based biosensor which responds to the DSF and AHL family quorum molecules.

To understand the role of novel virulence factors, we have earlier screened approximately 1600 transposon induced mutants of Xoo on rice leaves and isolated a mutant (SC2), which is proficient in all virulence associated functions so far reported in *Xanthomonas* group of plant pathogens. Mapping of the mutation in SC2 revealed that it is defective in a gene, which we named as *motA* (motilityA; annotated in the genome as hypothetical protein). We have done attachment studies which indicated that *mot A* (Now we renamed *motA* as *-xadM*; *Xanthomonas adhesin M*).

Details of the progress made in the current reporting year (April 1, 2010 - March 31, 2011)

a) Extracellular cell-cell communication system in plant pathogenic bacteria

To study the dynamics of quorum sensing, we have made an Xcc biosensor in which an eGFP variant which has a short half life has been cloned downstream from a DSF responsive endoglucanase gene promoter. Since quorum sensing is a group behavior we measured GFP fluorescence intensity of Xcc stain grown in a fixed volume of culture under different time points (Figure 1A). Increase in fluorescence intensity in the wild type strain with time indicated that DSF mediated quorum sensing reached maximum threshold within 40 to 60 hours. To study the behavior of single cell in this bacterial population, we used FACS to study the dynamics of DSF mediated quorum sensing in individual cells (Figure 1A). Interestingly, even at 40 to 60 hours, only 70 to 75 percent of cells responded to quorum sensing as opposed to 100 percent, which is expected in a high density of bacterial culture at 40 to 60 hours. To investigate whether this phenomena is universal, we used a *Pseudomonas syringae* biosensor which responds to a different family of quorum sensing signaling molecule, Acyl

homoserine lactones (Figure 1B). Whole cell fluorescence assay indicated that in the wild type *P. syringae*, AHL mediated quorum sensing reached maximum threshold within 40 hours of growth in a fixed volume whereas only 65 to 70 percent of cells in that population responds to quorum. To address the question of availability and transport of quorum sensing molecules, we did experiments with exogenously added quorum sensing molecule in the Xcc and *P. syringae* biosensors which do not produce their own signal, but can respond to external quorum sensing molecules in the environment. Intriguingly, only 70% of cells (approximately) respond to quorum by the addition of very high to medium and low concentration of quorum molecules in the culture medium. Live dead

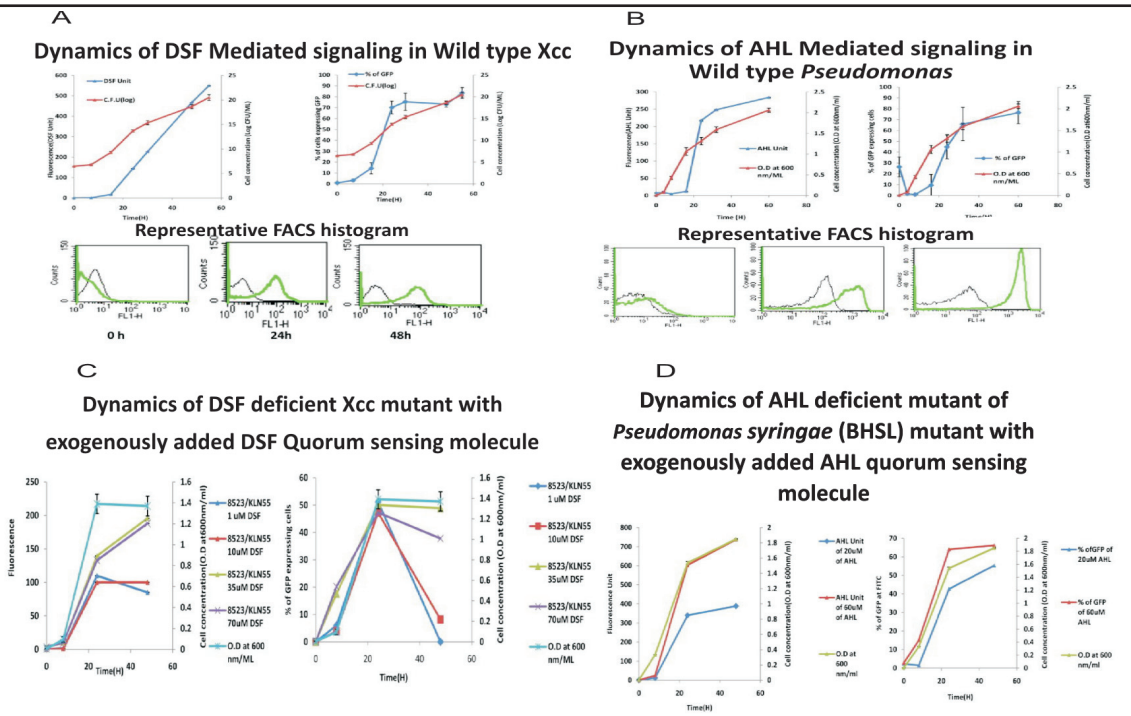


Figure 1. (A and B) Dynamics DSF and AHL sensing in Xcc and *P. syringae* wild type strain. (C and D) Induction of GFP fluorescence in response to exogenous supplementation of DSF and AHL in Xcc and *P. syringae* strains which are unable to produce quorum sensing signaling molecules, but are proficient in sensing. Average fluorescence intensity is represented in the Y-axis. Percentage of GFP expressing cells was measured by FACS with at least 10,000 events.

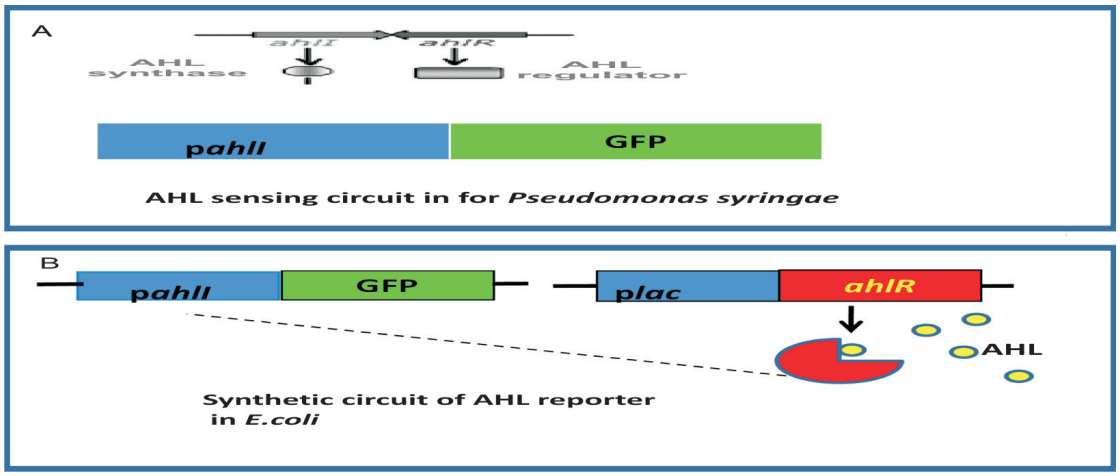


Figure 2. (A) Schematic representation of AHL production and sensing circuit in *P. syringae*. (B) *E. coli* AHL biosensor circuit which can respond to exogenous AHL.

cell analysis at different cell densities of *Xanthomonas campestris* pv. *campestris* (Xcc) and *Pseudomonas syringae* indicated that non responsiveness to quorum sensing signal is not due to presence of significant number of dead cells in the bacterial culture.

It has been indicated that bacteria utilizes quorum sensing system to synchronize group behavior like biofilm formation, motility and virulence. To investigate the behavior of quorum sensing dependent synchronization, we used an *E. coli* strain harboring the *ahlI* and *ahlR* circuit that responds to exogenously added AHL (Figure 2 A and B).

Interestingly, *E. coli* cells exhibited maximum threshold of response within 10 hours of growth and almost 100% of the cells in the population were quorum induced, which is very different from natural quorum sensing system in *Pseudomonas* and *Xanthomonas*.

As a control, approximately 95% of cells expressing GFP from a constitutive promoter in both *E. coli* as well as in *Pseudomonas syringae* exhibited synchronization in terms of GFP expression. These results indicates that although synchronization by quorum sensing can be achieved with synthetic circuits, synchronization of cell-cell signaling is quorum sensing bacteria is very dynamic in nature.

b) Role of DSF in virulence of *Xanthomonas*

Since DSF plays an important role in the virulence of *Xanthomonas oryzae* pv. *oryzae*, (Xoo), we did confocal laser scanning microscopy to investigate the biofilm formation dynamics at different time points in the air-media inter phase (Figure 3A). DSF

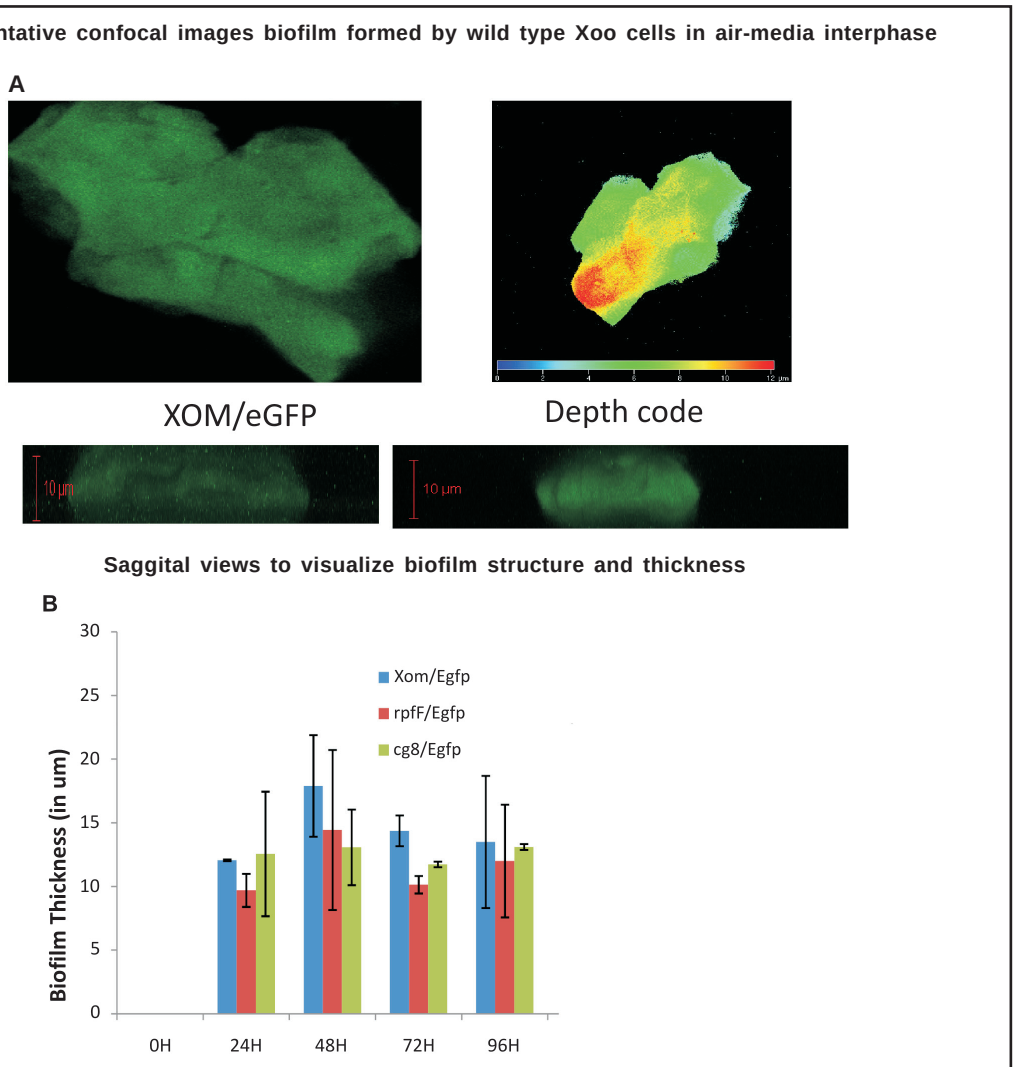


Figure 3. A. Representative confocal images of Xoo biofilm formation on air-media inter phase on a glass slide. B. Average thickness of the biofilm formed by different strains of Xoo at different time points measured by confocal microscopy.

deficient *rpfF* mutant exhibited significant reduction in the biofilm thickness as compare to the wild type and mutant with the complementing clone (Figure 3B). These results indicate that cell-cell signaling plays an important role in biofilm formation. We are presently studying in more detail the dynamics of biofilm formation in Xoo using different cell -cell signaling mutants alone or in combination to see the contribution of these in this process.

Biofilm formation is an important step in the pathogenesis, as it contributes to defense against antimicrobial agents and host defense response. We investigated whether cell-cell signaling in Xoo plays a role in defense against biocides and plant phenolic compounds which are involved in plant defense response. Interestingly the cell-cell signaling deficient *rpfF* mutant of Xoo exhibited hypersensitivity to biocides like-SDS, triton X-100 as well to plant phenolic compounds. These results indicate that cell-cell signaling mediated biofilm formation plays an important role in protection against biocides inside the host.

We have further characterized a novel virulence deficient mutant of Xoo, XadM (Xanthomonas adhesin M). XadM is involved in attachment to the EPS and adhesion to form biofilm. XadM mutants also exhibited hyper motility due to reduced stickiness. As XadM is required for virulence and for colonization, we studied the localization of XadM in Xoo using antibody against this protein. Immunofluorescence microscopy indicated that XadM is localized on the surface of the Xoo cells (Figure 4A and B). To see the regulation of expression and localization, different fractions of extracellular, whole cell lysate and outer membrane was isolated from Xoo cells grown under different conditions (Figure 4C). A 130 kDa band corresponding to the XadM protein is detected in the outer membrane and the whole cell lysate (Figure 4C). No signal was detected in the extracellular fraction indicating that XadM is primarily localized in the outer membrane of Xoo. Relative expression analysis indicated that XadM is expressed 4 fold higher in the plant growth mimicking media as compare to the rich medium, indicating that the XadM expression is influenced by conditions inside the host plant. This will be the first report of *XadM* like gene as a virulence factor,

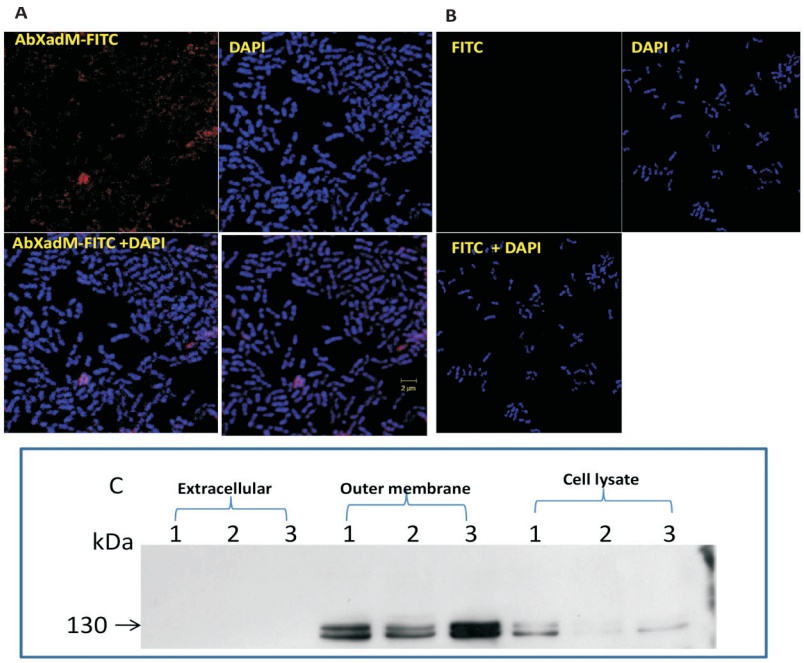


Figure 4. A and B. Immunofluorescence localization of Xad M in Xoo cells. Cells were stained with Antibody against Xad M and probed with anti rabbit FITC conjugate secondary antibody. DAPI was used to stain nucleic acid in the cells which appears blue. For control, Xoo cells were stained with DAPI and were probed with secondary antibody. C. Western blot analysis for the localization and expression of XadM protein in Xoo cells grown in 1) Minimal Media; 2) PS (rich media); 3) XOM2 media (Plant growth mimicking media)

c) Understanding the mechanism of biofilm formation and motility and virulence

which is involved in attachment and probably biofilm formation in any bacteria.

In future, we are going to study detailed biofilm assays to see, at what stage, XadM is required for the biofilm formation.

Publications

1. Chatterjee S **(**2010**)**. Fatal attraction: Bacteria exploit fungal heterokaryon incompatibility to obtain nutrients. ***Journal of Biosciences*** 35: 329-330.
2. *Chatterjee S, Killiny S, Almeida RPP and Lindow SE (2010). Role of cyclic di-GMP in *Xylella fastidiosa* biofilm formation, plant virulence and insect transmission. ***Molecular Plant-Microbe Interactions*** 23: 1356-1363.
3. Almeida RPP, Killiny N, Newman NS, Chatterjee S and Lindow SE (2011). Contribution of rpfB to cell-cell signal synthesis, virulence, and vector transmission of *Xylella fastidiosa*. ***Molecular Plant-Microbe Interactions*** (In press).
4. Li Y, Zou H, Che Y, Cui YP, Guo W, Zou L, Chatterjee S, Biddle E and Chen GA (2011). Novel regulatory role of HrpD6 in regulating *hrp-hrc-hpa* genes in *Xanthomonas oryzae* pv. *oryzicola.* ***Molecular Plant-Microbe Interactions*** (In press).

* Work done elsewhere

LABORATORY OF CELL DEATH & CELL SURVIVAL

Role of Protein Modifications in Controlling Cell Life and Death

Principal Investigator	Maddika Subba Reddy	Staff Scientist
PhD Students	Neelam Rani	Junior Research Fellow
	PV Vivek Reddy	Junior Research Fellow
	G Narmadha Reddy	Junior Research Fellow
Other Members	K Sridhar	Project Junior Research Fellow
	J Kiranmai	Project Junior Research Fellow
	Nanci Rani	Technical Assistant
Collaborators	Junjie Chen	M D Anderson, Texas, USA
	Jann N Sarkaria	Mayo Clinic, MN, USA
	Murali Bashyam	CDFD, Hyderabad

Objectives

1. Identification and characterization of novel components in the PTEN/PI3K-Akt pathway
2. Dissecting the functional interacting partners of E3 ubiquitin ligases involved in survival and proliferation of cancer cells.

Details of progress made in the current reporting year (June 15, 2010 - March 31, 2011)

Project 1: Studies on the functional interactome of PTEN phosphatase

PTEN (phosphatase and tensin homologue deleted on chromosome 10) is a lipid phosphatase, which antagonizes the cellular phosphotidylinositol-3 kinase (PI3K) signalling pathway and a well defined tumor suppressor that plays critical roles in cell survival, proliferation, and cell death. The critical role of PTEN not only during human diseases but also in multiple cellular processes such as development, hematopoietic stem cell maintenance, reproduction and angiogenesis prompted us to systematically study this vital enzyme. Tandem affinity purification using streptavadin agarose beads and S-protein agarose beads followed by mass spectrometry analysis allowed us to identify WWP2 (HECT-type E3 ubiquitin ligase) as one among several novel PTEN interacting proteins. The interaction of WWP2 and PTEN was confirmed both *in vitro* and in cultured cells by GST-pull down assay and co-immunoprecipitation experiments respectively. Our results also suggested that WWP2 interacts with the phosphatase domain of PTEN. We demonstrated that WWP2 promotes PTEN ubiquitination both *in vivo* (Figure 1A & 1C) and *in vitro*. In addition, knock down of WWP2 leads to an increase in PTEN levels (Figure 1D), which correlates with decreased Akt phosphorylation and cell survival. Interestingly, we also showed that a patient derived mutation of PTEN at tyrosine155 (Y155F) residue significantly increased the association of WWP2 with PTEN, followed by enhanced polyubiquitination and reduced PTEN protein levels (Figure 1B).

PTEN acts as tumor suppressor by negatively regulating PI3K-Akt pathway. Hence, WWP2 being an E3 ligase and a negative regulator of PTEN, might function as a proto-oncogene. By using a prostate cancer cell line model, we demonstrated that depletion of WWP2 by siRNA reduces cell proliferation (Figure 2A), fail to support the anchorage independent growth (Figure 2B) and reduces tumor growth in nude mice (Figure 2C). Over all in this study, we have identified WWP2 as a novel functional E3 ubiquitin ligase for PTEN phosphatase. Our future studies in this project are focused on characterizing the functional significance of other PTEN interacting proteins identified such as PNUTS and BCCIP.

Project 2: Systematic studies on E3 ubiquitin ligases involved in survival and proliferation of cancer cells

E3-ubiquitin ligases play a critical role in the final step of the ubiquitination process by recruiting ubiquitin charged E2s, recognizing specific substrates, and mediating, or directly catalyzing, ubiquitin transfer to the substrates. The human ubiquitin system contains nearly 500 ubiquitin

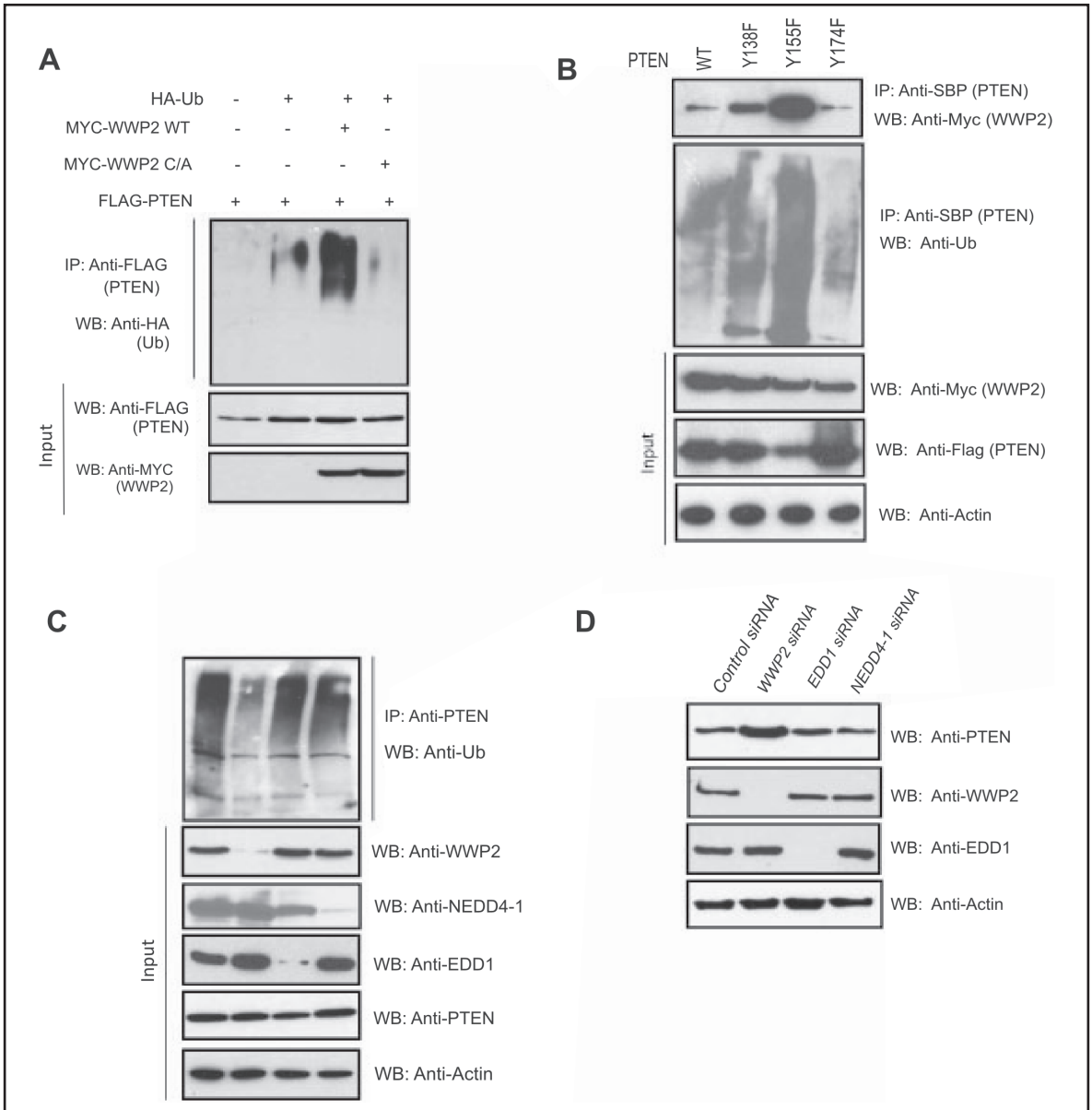


Figure 1. WWP2 regulates PTEN protein stability by polyubiquitination (A) Myc-tagged wild type or catalytically inactive C838A mutant of WWP2 were expressed in HeLa cells along with Flag-PTEN and HA-Ub. 24 hours post-transfection, cells were treated with MG132 (10 μM) for 6 hours and the levels of PTEN ubiquitination were evaluated by immunoprecipitation of PTEN using anti-FLAG antibody followed by anti-HA immunoblotting. **(B)** A triple tagged wild type PTEN and the PTEN tyrosine mutants along with Myc-WWP2 were expressed in 293T cells and the level of PTEN-WWP2 interaction was detected by immunoprecipitation and immunoblotting with the indicated antibodies. **(C)** HeLa cells were transfected with control siRNA or siRNAs against WWP2, EDD1 and NEDD4-1. The ubiquitinated PTEN was detected with anti-ubiquitin antibody after PTEN immunuprecipitation. **(D)** HeLa cells were transfected with control siRNA or siRNAs against WWP2, EDD1, and NEDD4-1. The protein levels were assessed by immunoblotting using indicated antibodies.

ligases of which several of them were classified as tumor suppressors or protooncogenes. In this project we are interested in identifying the cellular substrates and the regulators for different E3 ligases during the cancer cell survival and proliferation. As a first choice, we purified an E3 ligase WWP2. We were able to identify several novel WWP2-associated proteins, such as p73 (tumor suppressor), WDR5 (Histone methyl transferase complex protein), SMAD1 etc, which were not reported previously. The interaction of WWP2 with p73 was confirmed by immunoprecipitation. Further we also showed that WWP2 promotes p73 degradation in a proteosomal dependent pathway via its E3 ligase activity (Figure 3A & 3B). Our future studies are focused on characterizing the functional

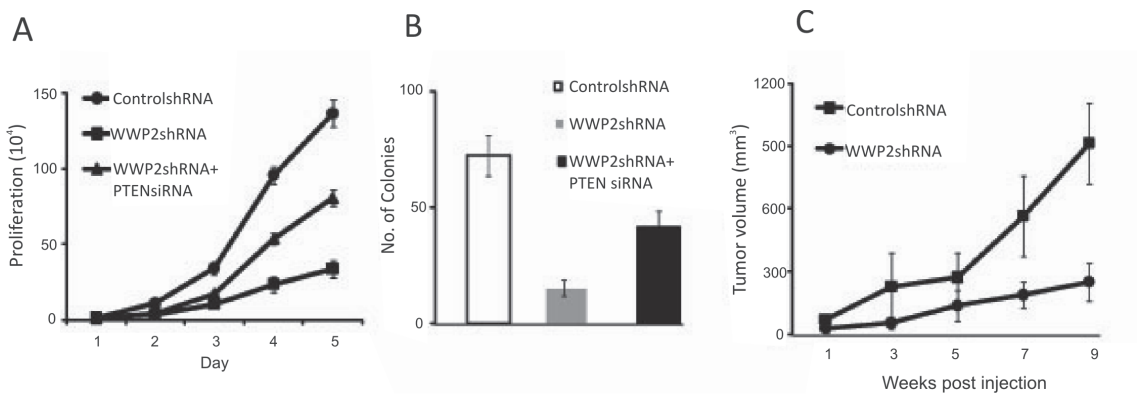


Figure2. WWP2 is required for tumorigenicity of cells. (A) DU145 stable clones either expressing control shRNA or WWP2 shRNA alone or in combination with PTEN siRNA were seeded in 100 mm dishes. Cells were trypsinized, and viable cells were counted following staining by tryphan blue exclusion method at the indicated times. The data shown is derived from four independent experiments (±s.d., $p<0.01$; student's t-test). **(B)** Control shRNA or WWP2 shRNA alone or in combination with PTEN siRNA expressing DU145 stable cell lines were tested for their anchorage independent growth in a soft agar colony assay. Viable colonies after 3 weeks were counted and the data (±s.d) was presented as summary of three independent experiments ($p<0.05$; student's t-test). **(C)** Control shRNA or WWP2 shRNA expressing DU145 stable cells (5×10^6) were subcutaneously injected into nude mice and the tumor volumes were measured three times per week (±s.d., n=5, $p<0.05$; student's t-test).

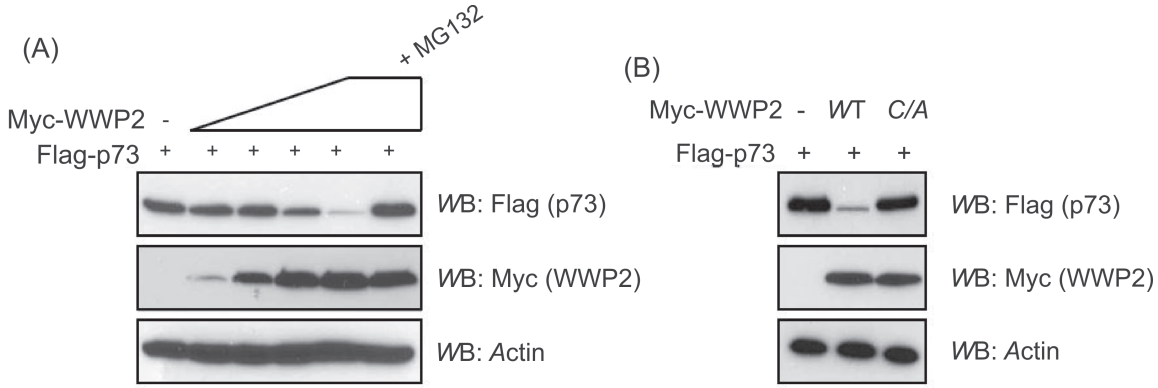


Figure 3. WWP2 regulates p73 protein stability. (A) HeLa cells were transfected with Flag tagged p73 alone or in combination with increasing concentration of Myc-WWP2. A proteosomal inhibitor (MG132) was also added to the Myc-WWP2 expressing cells (see last lane). The protein levels were assessed by immunoblotting using indicated antibodies. **(B)** HeLa cells were transfected with Flag tagged p73 alone or in combination with wild type (WT) Myc-WWP2 and catalytically inactive mutant (C/A). The protein levels were assessed by immunoblotting using indicated antibodies.

significance of WWP2-p73 interaction in regulating cell death. Several isoforms of p73 are known but full length p73 and ΔNP73 (lacking N-terminal transactivation domain) are predominantly expressed in cells. Interestingly, p73 is pro-apoptotic whereas ΔNP73 acts as a pro-survival protein. Thus, we will further test whether p73 isoforms are differentially regulated by WWP2 during cell death.

Publication

1. Maddika S, Kavela S, Rani N, Palicharla VR, Pokorny JL, Sarkaria JN and Chen J (2011). WWP2 is an E3 ubiquitin ligase for PTEN. ***Nature Cell Biology*** (In press).

LABORATORY OF DROSOPHILA NEURAL DEVELOPMENT

Understanding the Molecular Basis of the Hox Functions in *Drosophila* Central Nervous System

Principal Investigator	Rohit Joshi	Staff Scientist- Ramanujan Fellow
PhD Students	Risha Khandelwal	Junior Research Fellow (Since Feb. 2011)
Other Members	P Kalyani	Technical Officer I (Since Aug. 2010)
	V Shutha Keerthi	Project Assistant (Since Jan. 2011)

Objectives

1. Role of Hox gene *Deformed* in patterning of embryonic suboesophageal ganglia
2. Molecular basis of abdominal Hox gene function in larval central nervous system patterning in *Drosophila melanogaster.*

Details of the progress made in the current reporting year (April 1, 2010 - March 31, 2011)

The long term goal of my group is to understand the development and patterening of central nervous system (**CNS**) using model organism *Drosophila melanogaster* (fruit fly). The short life span (10 days) and the wealth of genetic tools and reagents available in *Drosophila* make it a particularly attractive model system to study this problem.

The bilaterian body plan is comprised of three axes: the anterior-posterior axis (**AP axis**), the dorsal-ventral axis and the proximal-distal axis of the limb. The specification of the AP axis by Hox genes is one of the earliest steps in the development of an organism. Hox genes are a family of highly conserved homeodomain (**HD**) containing transcription factors which are responsible for giving unique identity to the segments of the body. There are 8 Hox genes in *Drosophila* and 39 Hox genes in vertebrates (divided into 4 clusters) which makes *Drosophila* a very powerful model organism to study their role during development and patterning.

Hox proteins are known to often function with two other HD-containing transcription factors: Extradenticle (Exd in *Drosophila*; Pbx in vertebrates) and Homothorax (Hth in *Drosophila* and Meis in vertebrates).

Both in *Drosophila* and vertebrates, Hox genes are known to express in the central nervous system (**CNS**) where they play a role in AP axis determination but the molecular basis of the Hox function in CNS is not very well understood. For example, very few Hox targets genes and cofactors are known and characterized in CNS.

The key question is to address how Hox genes control proliferation and differentiation of neural stem cells (NSC) along the AP axis to pattern CNS. My specific aims focus on understanding this problem at an early embryonic stage and late larval stages of development in *Drosophila*.

1. Role of Hox gene *Deformed* in patterning of embryonic suboesophageal ganglia.

Hox genes are known to express in neural stem cells in embryonic stages of development but how does their expression patterns the embryonic nervous system is not well understood. *Deformed* is known to express in the suboesophageal ganglion of embryonic CNS, this project focuses on understanding how autoregulation of *Deformed* and how it helps in giving neural stem cells their specific positional identity.

2. Molecular Basis of abdominal Hox gene function in larval CNS patterening in *Drosophila melanogaster*.

Abdominal region of the *Drosophila* CNS has very limited number of neurons. Role of programmed cell death (PCD) in limiting the number of abdominal neurons is well known. But the precise molecular link between Hox genes and PCD of NSCs (which results in limiting the number of abdominal neurons) is not known. Characterization of this link is primary goal of this project.

Since the underlying principles of CNS patterning are conserved across species and both mammalian and *Drosophila* NSCs have very similar molecular properties (like progressive lineage restriction, mitotic quiescence and asymmetric cell division), therefore the studies done in *Drosophila* will be relevant in a wider context.

Publications

1. * Joshi R, Sun L and Mann R (2010). Understanding the functional specificity of two Hox proteins. ***Genes and Development*** 24: 1533-1545.

2. * Rohs R, Jin X, West SM, Joshi R, Honig B, and Mann RS (2010). Origins of specificity in protein-DNA recognition. ***Annual Review of Biochemistry*** 79: 233-269.

* Work done elsewhere

LABORATORY OF CELL CYCLE REGULATION

Elucidating the Role of Effector Proteins in G1 to S Phase Progression

Principal Investigator	Shweta Tyagi	Staff Scientist - Ramalingswamy Fellow
PhD Students	Aamir Ali	Junior Research Fellow
	Zaffer Ullah Zargar	Junior Research Fellow
Other Members	VN Sailaja	Technical Officer II
	G Ashwini Kumar	Project Associate

Objectives

1. Identification of new effector proteins involved in regulation of E2F-responsive promoters
2. Study of chromatin modifying proteins in cell cycle regulation.

Details of the progress in the current reporting year (June 15, 2010 - March 31, 2011)

Project I: Identification of new effector proteins involved in regulation of E2F-responsive promoters

To proliferate, eukaryotic cells have to complete an ordered series of events called the 'cell cycle', which include the faithful replication of their genome and the correct segregation of the two copies generated into two daughter cells upon cell division. A disruption of these events may lead to cell death or oncogenic transformation. The processes of cell cycle, therefore, are carefully regulated.

A key step in the eukaryotic cell cycle is the G1 to S phase transition and this step is tightly coupled to the transcriptional control of genes involved in growth and DNA replication. In mammalian cells, the E2F family of transcription factors primarily

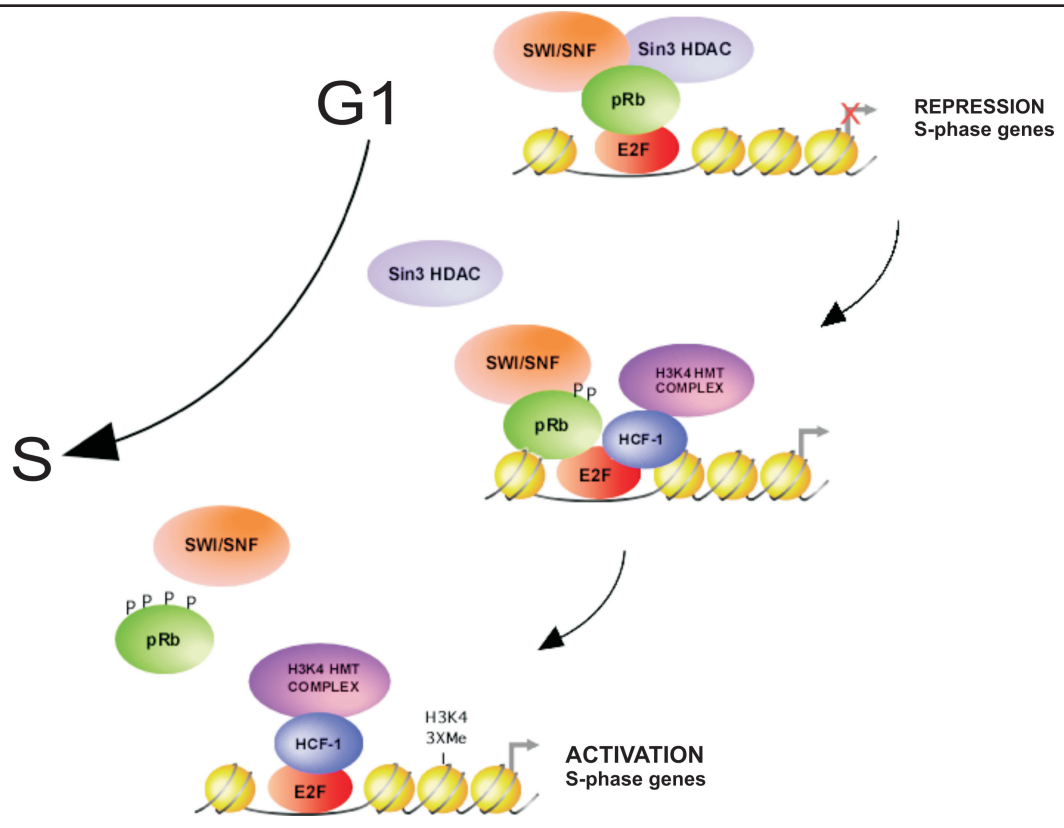


Figure 1. Proposed model for activation of S-phase promoters by E2F1. During G1/S phase transition, HCF-1 and its associated H3K4 HMTs are recruited to E2F-responsive promoters, replacing the pRb repressor complex. The E2F-HCF-H3K4HMT complex then activates transcription of S-phase genes

controls this temporal gene expression regulation. We have shown that HCF-1 is an important regulator of G1 to S-phase transition and plays a direct role in the activation of E2F-responsive promoters through the cell-cycle-specific recruitment of the MLL-family of H3K4 histone methyltransferases (Figure 1). While this work has added new effectors to G1 to S-phase transition, how E2Fs affect passage into S phase is still poorly understood. In this project we aim to identify new effector proteins involved in regulation of E2F-responsive promoters and better understand how these effectors influence transcriptional regulation during G1 to S phase progression.

Project II: Study of chromatin modifying proteins in cell cycle regulation

In multicellular organisms, semi-conservative DNA replication faithfully copies the parental nucleotide sequence into two DNA daughter strands during each cell cycle. At the same time, epigenetic marks such as DNA methylation and histone modifications are either precisely transmitted to the daughter cells or dynamically changed during cell cycle. Indeed some histone modifications are intimately linked with specific cell-cycle phases. For example, phosphorylation of Histone 3 Serine 10 is required to initiate chromosome condensation during mitosis.

Histone 3 lysine 4 trimethylation is another modification, which is linked to active gene expression, but its precise role in cell cycle regulation is recently being uncovered. We have shown that MLL-family of H3K4 histone methyltransferases is linked to cell cycle regulation by interacting with E2F1. In this project, we are looking at other roles of this chromatin-modifying complex that may influence cell cycle regulation.

अन्य वैज्ञानिक सेवाएं / सुविधाएं
Other Scientific Services /Facilities

BIOINFORMATICS

In-charge	H A Nagarajaram	Staff Scientist
Other Members	R Chandra Mohan	Technical Officer I
	Prashanthi Katta	Technical Assistant

Objectives

1. To maintain the CDFD website, to provide web based services and e-mail services
2. To maintain various servers, workstations, PCs, printers and other peripheral devices
3. To maintain Institute-wide LAN as well as the internet connectivity
4. To coordinate the procurement process of workstations, PCs, laptops, printers, other peripheral devices and softwares required
5. To secure the CDFD network from security threats
6. To integrate Institute's network into National and International grid computing networks.

Summary of work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

- Activities related to installation, administration and maintenance of servers which provide various services, databases and computational jobs were undertaken.
- A comprehensive PC Annual maintenance contract and the agreement for remote monitoring and managed services for Sun servers in the Data Center set up were renewed.
- The process of connecting CDFD network to NKN was initiated.

Details of progress made in the current reporting year (April 1, 2010 - March 31, 2011)

- Activities related to installation, administration and maintenance of servers which provide various services, databases and computational jobs were undertaken.
- E-mail, Internet, web services have been provided with enhanced functionalities.
- High-end PCs, workstations, laptops, scanners and printers were procured and installed.
- Existing PC Annual Maintenance Contract was renewed. We have also renewed the agreement for remote monitoring and managed services for Sun servers in the Data Center set up.
- Successfully migrated CDFD Network to NKN, a Gigabit network proposed by National Informatics Centre that connects various knowledgeable institutions for sharing resources. The migration was done with minimum downtime. The NKN line is an addition to an existing 4Mbps line. Configured both the lines in load balancing mode to enhance the bandwidth with no downtime. Also signed the MoU with NIC for implementing NKN.
- Signed a new MoU with CDAC for availing GARUDA-grid facility.
- Provided infrastructural facilities for the Indo-French Bioinformatics Workshop.

Instrumentation

Head	Raghavendrachar J	Staff Scientist
Other Members	R N Mishra	Technical Officer II
	S D Varalaxmi	Technical Officer I
	M Laxman	Technical Officer I
	R M K Sathyanarayana	Technical Officer I

Objectives

To maintain, repair and service all the equipment in laboratory. To provide pre-installation requirements for new instruments and to coordinate with the manufacturers/their agents in installation and warranty service of the new instruments. Also to provide the reports on the newly arrived instruments and to follow up with the suppliers for short shipped items.

Summary of work done until the beginning of this reporting year (April 1, 2009 – March 31, 2010)

We have set up the facilities for major instruments like Bruker X-Ray Diffraction system, Bruker Maldi TOF/TOF MS, BD FacsVantage SE Flowcytometer, Carl Zeiss Confocal Microscope and installed the equipment and set up standard operating procedures. We have set up the out sourcing facility, installed all the equipment like DNA Sequencers, RT-PCR, Biacore SPR System, dHPLC, HPLC, CD Spectro-polarimeter etc., Karyotyping System in Diagnostics, Genetic Analyzer, GC-MS. We have also installed various instruments like High Speed Centrifuges of Sorvall and Beckman Coulter, Ultra centrifuge of Beckman Coulter, Refrigerated Incubator Shakers, Gel Documentation Systems, set up Tissue Culture Facility and installed Laminar Flowhoods and CO_2 Incubators, set up H1N1 testing laboratory, Installed all microscopes, FPLCs, LPLCs, Nanodrop Spectrophotometers etc. We are updating with newer technologies and helping the scientists in procuring better equipment at reasonable costs.

During the year 2009-10, we have installed 94 new equipments and have also completed 312 work orders for repair & maintenance of various laboratory equipments, in addition to shifting of equipments, getting the Laboratory tables dismantled at Nacharam, installed few at first floor and got the rest stored at Gandipet.

Details of progress made in the current reporting year (April 1, 2010 – March 31, 2011)

We have set up the facilities for major instruments like ABI SOLiD 3.5 Next Generation Whole Genome DNA Sequencer, Illumina Bead Express Whole Genome Genotyping System, Becton Dickinson FACS ARIA Flowcytometer, Water's HPLC, Perkin Elmer Packard 2910 Liquid Scintillation Counter, Nikon Live Cell Imaging System, Nikon Stereomicroscope with Microinjection system and Conviron Plant Growth Chambers.

During the year 2010-11, we have installed 138 new equipments like PCR Machines, FPLC, LPLC, Nanodrop Spectrophotometers, Refrigerated Centrifuges, Orbital Shakers, Electroporators, -80^{0}C Freezer, -20^{0}C Freezers, Cold cabinets etc. and have also completed 412 work orders for repair & maintenance of various laboratory equipments. We have successfully set up the video conferencing system to communicate and presentation from CDFD to other institutions in India and abroad.

In addition, we were involved in organizing the audio and visual requirements for presentations in various seminars, lectures and workshops, Foundation Day lectures, distinguished scientist lectures held in CDFD. We were actively involved in conducting the 14th Transcription Assembly Meeting, Indo-Canada Tuberculosis Workshop and Indo-French Bioinformatics Meeting. We maintained most of the equipment with maximum uptime in the Laboratory. Most of the instruments are maintained by our Instrumentation staff, thereby saving on the expensive AMCs and with very little downtime of the equipment.

प्रकाशन
Publications

RESEARCH PAPERS

A. Publications during the year 2010

1. Agarwal S, Tamhankar PM, Kumar R and Dalal A (2010). Clinical and haematological features in a compound heterozygote (HBB:c.92+5G>C/HBB:c.93-2A>C) case of thalassaemia major. ***International Journal of Laboratory Hematology*** 32: 369-372.

2. Alam K, Ghousunnissa S, Nair S, Valluri VL and Mukhopadhyay S (2010). Glutathione-redox balance regulates c-rel-driven IL-12 production in macrophages: Possible implications in antituberculosis immunotherapy. ***Journal of Immunology*** 184: 2918-2929.

3. Angalena R, Prabitha KN, Chaudhary AK, Bashyam MD, Jain S and Dalal A (2010). A novel homozygous point mutation at codon 82 (HBB:c.247A>T) in the beta-globin gene leads to thalassemia major. ***International Journal of Laboratory Hematology*** 32: 548-549.

4. Bashyam MD, Chaudhary A, Reddy E, RamaDevi A, Savithri G, Ratheesh R, Bashyam L, Mahesh E, Sen D, Puri R, Verma I, Nampoothiri S, Vaidyanathan S, Chandrasekhar M and Kantheti P (2010). Phenylalanine hydroxylase gene mutations in phenylketonuria patients from India: Identification of novel mutations that affect PAH RNA. ***Molecular Genetics and Metabolism*** 100: 96-99.

5. Bhate R and Ramasarma T (2010). Reinstate hydrogen peroxide as the product of alternative oxidase of plant mitochondria. ***Indian Journal of Biochemistry and Biophysics*** 47: 306-310.

6. Chatterjee S **(**2010**)**. Fatal attraction: Bacteria exploit fungal heterokaryon incompatibility to obtain nutrients. ***Journal of Biosciences*** 35: 329-330.

7. *Chatterjee S, Killiny S, Almeida RPP and Lindow SE (2010). Role of cyclic di-GMP in *Xylella fastidiosa* biofilm formation, plant virulence and insect transmission. ***Molecular Plant-Microbe Interactions*** 23: 1356-1363.

8. Dalal A, Sarkar A, Priya TP and Nandineni MR (2010). Giuffrè-Tsukahara syndrome: Evidence for X-linked dominant inheritance and review. ***American Journal of Medical Genetics*** 152: 2057-2060.

9. Gangadharan C, Thoh M and Manna SK (2010). Late phase activation of nuclear transcription factor kappaB by doxorubicin is mediated by interleukin-8 and induction of apoptosis via FasL. ***Breast Cancer Research Treatment*** 120: 671-683.

10. Girisha KM, Vahab SA, Dalal A, Gopinath PM and Satyamoorthy K (2010). Compound heterozygosity for HbD Punjab and polyadenylation signal mutation causes clinically asymptomatic mild hypochromia and microcytosis. ***Annals of Hematology*** 89: 625-626.

11. *Joshi R, Sun L and Mann R (2010). Understanding the functional specificity of two Hox proteins. ***Genes and Development*** 24: 1533-1545.

12. Kalarickal NC, Ranjan A, Kalyani BS, Wal M and Sen R (2010). A bacterial transcription terminator with inefficient molecular motor action but with a robust transcription termination function. ***Journal of Molecular Biology*** 395: 966-982.

13. Khamurai S, Ranjan A, Pani B, Sen R and Sen U (2010). Crystallization and preliminary X-ray analysis of Psu, an inhibitor of bacterial transcription terminator, Rho. ***Acta Crystallographica Section F Structural Biology and Crystallization Communication*** 66: 204-206.

14. Kumar P, Joshi DC, Akif M, Akhter Y, Hasnain SE and Mande SC (2010). Mapping conformational transitions in cyclic AMP receptor protein: Crystal structure and normal-mode analysis of *Mycobacterium tuberculosis* apo-cAMP receptor protein. ***Biophysical Journal*** 98: 305-314.

15. Kumar S, Sardesai AA, Basu D, Muniyappa K and Hasnain SE (2010). DNA clasping by Mycobacterial HU: The C-terminal region of HupB mediates increased specificity of DNA binding. ***PLoS One*** 5, e12551, 1-10.

16. Manderwad GP, Gokul G, Kannabiran C, Honavar SG, Khosla S and Vemuganti G (2010). Hypomethylation of the DNMT3L

promoter in Ocular Surface Squamous Neoplasia (OSSN). ***Archives of Pathology and Laboratory Medicine*** 134: 1193-1196.

17. Manna SK, Babajan B, Raghavendra PB, Raviprakash N and Kumar CS (2010). Inhibiting TNF receptor associated factor 2-mediated activation of nuclear factor kappaB facilitates induction of activator protein-1. ***Journal of Biological Chemistry*** 285: 11617-11627.

18. Manna SK, Bose JS, Gangan V, Raviprakash N, Navneetha T, Raghavendra PB, Babajan B, Kumar CS and Jain SK (2010). Novel derivative of benzofuran induces cell death mostly by G2/M cell cycle arrest through p53-dependent pathway but partially by Inhibition of NF-κB. ***Journal of Biological Chemistry*** 285: 22318-22327.

19. Morrison NI, Koukidou M, Franz G, Miller TA, Saccone G, Simmons GS, Alphey LS, Polito LC and Nagaraju J (2010). Review: Genetic improvements to the sterile insect technique for agricultural pests. ***Asian Pacific Journal of Molecular Biology and Biotechnology*** 18: 275-295.

20. Mrinal N and Nagaraju J (2010). Dynamic repositioning of dorsal to two different *kB* motifs controls its autoregulation during immune response in *Drosophila*. ***Journal of Biological Chemistry*** 285: 24206-24216.

21. Mudunuri SB, Rao AP, Mishra P and Nagarajaram HA (2010). Comparative analysis of microsatellite detecting software: A significant variation in results and influence of parameters. ***Proceedings of International Symposium on Biocom-puting*** (ISB 2010), Kerala, February 15-17, 2010. (Link to ACM Digital Library).

22. Muteeb G and Sen R (2010). Random mutagenesis using mutator strain. ***Methods in Molecular Biology*** 634: 411-419.

23. Nagaraju J and Saccone G (2010). Preface (to special issue: How is sex determined in insects?) ***Journal of Genetics*** 89: 269-270.

24. Nagaraju J and Saccone G (2010). How is sex determined in insects? An epilogue***.*** ***Journal of Genetics*** 89: 389-390.

25. Nandineni MR, Prasad SPR, Goud ChV, Negi DS, Nagaraju J and Gowrishankar J (2010). DNA-based identification of victims of the Mangalore air crash of May 2010. ***Current Science*** 99: 341-342.

26. Priya TP, Philip N, Molho-Pessach V, Busa T, Dalal A and Zlotogorski A (2010). H syndrome: Novel and recurrent mutations in SLC29A3. ***British Journal of Dermatology*** 162: 1132-1134.

27. Purushotham G, Madhumohan K, Anwaruddin M, Nagarajaram HA, Hariram V, Narasimhan C and Bashyam MD (2010). The MYH7 p.R787H mutation causes hypertrophic cardiomyopathy in two unrelated families. ***Experimental and Clinical Cardiology*** 15: e1-e4.

28. *Rohs R, Jin X, West SM, Joshi R, Honig B, and Mann RS (2010). Origins of specificity in protein-DNA recognition. ***Annual Review of Biochemistry*** 79: 233-269.

29. Sabareesh V, Sarkar P, Sardesai AA and Chatterji D (2010). Identifying N60D mutation in ω subunit of *Escherichia coli* RNA polymerase by bottom-up proteomic approach. ***Analyst*** 135: 2723-2729.

30. Shukla JN and Nagaraju J (2010). Doublesex: A conserved downstream gene controlled by diverse upstream regulators. ***Journal of Genetics*** 89: 341-356.

31. Shukla JN and Nagaraju J (2010). Two female-specific DSX proteins are encoded by the sex-specific transcripts of *dsx*, and are required for female sexual differentiation in two wild silkmoth species, *Antheraea assama* and *Antheraea mylitta* (Lepidoptera, Saturniidae). ***Insect Biochemistry and Molecular Biology*** 40: 672-682.

32. Singh J, Singh CP, Bhavani A and Nagaraju J (2010). Discovering microRNAs from *Bombyx mori* nucleopolyhedrosis virus. ***Virology*** 407: 120-128.

33. Suresh BM, Kumar P, Rao AA, Pallamsetty S and Nagarajaram HA (2010). G-IMEx: A comprehensive software tool for detection of microsatellites from genome sequences. ***Bioinformation*** 5: 221-223.

34. Thoh M, Kumar P, Nagarajaram HA and Manna SK (2010). Azadirachtin interacts with the TNF binding domain of its receptors and inhibits TNF-induced biological responses. ***Journal of Biological Chemistry*** 285: 5888-5895.

35. Vedantham H, Silver MI, Kalpana B, Rekha C, Karuna BP, Vidyadhari K, Mrudula S, Ronnett BM, Vijayaraghavan K, Ramakrishna G, Sowjanya P, Laxmi S, Shah KV and Gravitt PE; CATCH Study Team (2010). Determinants of VIA (Visual inspection of the cervix after acetic acid application) positivity in cervical cancer screening of women in a peri-urban area in Andhra Pradesh, India. ***Cancer Epidemiology, Biomarkers and Prevention*** 19: 1373-1380.

36. Werner JK Jr, Speed T and Bhandari R (2010). Protein pyrophosphorylation by diphosphoinositol pentakisphosphate ($InsP_7$). ***Methods in Molecular Biology*** 645: 87-102.

37. Yabaluri N and Bashyam MD (2010). Hormonal regulation of gluconeogenic gene transcription in the liver. ***Journal of Biosciences*** 35: 473-484.

* Work done elsewhere

B. Publications in 2011 (Till March 31, 2011)

38. Arunkumar KP and Nagaraju J (2011). Drosophila intersex orthologue in the silkworm, *Bombyx mori* and related species. ***Genetica*** 139: 141-147.

39. Bairwa G and Kaur R (2011). A novel role for a glycosylphosphatidylinositol-anchored aspartyl protease, CgYps1, in the regulation of pH homeostasis in *Candida glabrata*. ***Molecular Microbiology*** 79: 900-913.

40. Bentur JS, Sinha DK, Padmavathy C, Revathy C, Muthulakshmi M and Nagaraju J (2011). Isolation and characterization of microsatellite loci in the asian rice gall midge (*Orseolia oryzae*) (Diptera: Cecidomyiidae). ***International Journal of Molecular Science*** 12: 755-772.

41. Bose S, Sakhuja P, Bezawada L, Agarwal AK, Kazim NS, Khan LA, Sarin SK and Ramakrishna G (2011). Hepatocellular carcinoma with persistent hepatitis B virus infection shows unusual downregulation of Ras expression and differential response to Ras mediated signaling. ***Journal of Gastroenterology and Hepatology*** 26: 135-144.

42. Chalissery J, Muteeb G, Nisha CK, Mohan S, Jisha V and Sen R (2011). Interaction surface of the transcription terminator Rho required to form a complex with the C-terminal domain of the antiterminator NusG. ***Journal of Molecular Biology*** 405: 49-64.

43. Das A and Mukhopadhyay S (2011). The evil axis of obesity, inflammation and type-2 diabetes. ***Endocrine, Metabolic and Immune Disorders - Drug Targets*** 11: 23-31.

44. Dutta UR, Rajitha P, Kumar PV and Dalal A (2011). Cytogenetic abnormalities in 1162 couples with recurrent miscarriages in southern region of India: Report and review. ***Journal of Assisted Reproduction and Genetics*** 28: 145-149.

45. Gunnarsdóttir ED, Nandineni MR, Li M, Myles S, Gil D, Pakendorf B and Stoneking M (2011). Larger mtDNA than Y-chromosome differences between matrilocal and patrilocal groups from Sumatra. ***Nature Communications*** 2: 228.

46. Kole L, Giri B, Manna SK, Pal B and Ghosh S (2011). Biochanin-A, an isoflavon, showed anti-proliferative and anti-inflammatory activities through the inhibition of iNOS expression, p38-MAPK and ATF-2 phosphorylation and blocking NF-κB nuclear translocation. ***European Journal of Pharmacology*** 653: 8-15.

47. Kumar P, Chitanya PS and Nagarajaram HA (2011). PSSRdb: A relational database of polymorphic simple sequence repeats extracted from prokaryotic genomes. ***Nucleic Acids Research*** 39: D601-D605.

48. Manna SK, Gangadharan C, Edupalli D, Raviprakash N, Navneetha T, Mahali S and Thoh M (2011). Ras puts brake on doxorubicin-mediated cell death in p53 expressing cells. ***Journal of Biological Chemistry*** 286: 7339-7347.

49. Shukla JN, Jadhav S and Nagaraju J (2011). Novel female-specific splice form of *dsx* in the silkworm, *Bombyx mori*. ***Genetica*** 139: 23-31.

50. Terenius O, …(67 authors)…, Nagaraju J, Richard H, Herrero S, Gordon K, Swevers L and Smagghe G (2011). RNA interference in

Lepidoptera: An overview of successful and unsuccessful studies and implications for experimental design. ***Journal of Insect Physiology*** 57: 231-245.

51. Thiagarajan D, Dev RR and Khosla S (2011). The DNA methyltranferase Dnmt2 participates in RNA processing during cellular stress. ***Epigenetics*** 6: 103-113.

52. Thoh M, Babajan B, Raghavendra PB, Sureshkumar C and Manna SK (2011). Azadirachtin interacts with retinoic acid receptors and inhibits retinoic acid-mediated biological responses. ***Journal of Biological Chemistry*** 286: 4690-4702.

53. Yadav AK, Desai PR, Rai MN, Kaur R, Ganesan K and Bachhawat AK (2011). Glutathione biosynthesis in the yeast pathogens *Candida glabrata* and *Candida albicans*: Essential in *C. glabrata*, and essential for virulence in *C. albicans*. ***Microbiology*** 157: 484-495.

C. Publications in Press (as on March 31, 2011)

54. Almeida RPP, Killiny N, Newman NS, Chatterjee S and Lindow SE (2011). Contribution of rpfB to cell-cell signal synthesis, virulence, and vector transmission of *Xylella fastidiosa*. ***Molecular Plant-Microbe Interactions***.

55. Arora A, Chandra NR, Das A, Gopal B, Mande SC, Prakash B, Ramachandran R, Sankaranarayanan R, Sekar K, Suguna K, Tyagi AK and Vijayan M (2011). Structural biology of *Mycobacterium tuberculosis* proteins: The Indian efforts. ***Tuberculosis***.

56. Kumar CM and Mande SC (2011). Protein chaperones and non-protein substrates: On substrate promiscuity of GroEL. ***Current Science***.

57. Li Y, Zou H, Che Y, Cui YP, Guo W, Zou L, Chatterjee S, Biddle E and Chen GA (2011). Novel regulatory role of HrpD6 in regulating *hrp-hrc-hpa* genes in *Xanthomonas oryzae* pv. *oryzicola*. ***Molecular Plant-Microbe Interactions***.

58. Maddika S, Kavela S, Rani N, Palicharla VR, Pokorny JL, Sarkaria JN and Chen J (2011). WWP2 is an E3 ubiquitin ligase for PTEN. ***Nature Cell Biology***.

59. Majumdar S, Dutta K**,** Manna SK, Basu A and Bishayi B (2011). Possible protective role of chloramphenicol in TSST-1 and coagulase positive *Staphylococcus aureus* induced septic arthritis with altered levels of inflammatory mediators. ***Inflammation***.

60. Mukhopadhyay S and Balaji KN (2011). The PE and PPE proteins of *Mycobacterium tuberculosis*. ***Tuberculosis***.

61. Nair S, Pandey AD and Mukhopadhyay S (2011). The PPE18 protein of *Mycobacterium tuberculosis* inhibits NF-κB/rel-mediated proinflammatory cytokine production by upregulating and phosphorylating SOCS3 protein. ***Journal of Immunology***.

62. Ponnala R and Dalal A (2011). Partial monosomy 7q. ***Indian Pediatrics***.

63. Priya TP and Dalal A (2011). Tuberous sclerosis: Diagnosis and prenatal diagnosis by MLPA. ***Indian Journal of Pediatrics***.

64. Sahail, Zytkowick T, Kotthuri SR, Kotthuri AL, Eaton RB and Akella RRD (2011). Neonatal screening for inborn errors of metabolism using tandem mass spectrometry: Experience of the pilot study in Andhra Pradesh, India. ***Indian Journal of Pediatrics***.

65. Shamim MT and Nagarajaram HA (2011). SVM-Based method for protein structural class prediction using secondary structural content and structural information of amino acids. ***Journal of Bioinformatics and Computational Biology***.

66. Singh NP, Madabhusi SR, Srivastava S, Senthilkumar R, Neeraja C, Khosla S and Mishra RK (2011). Epigenetic profile of the euchromatic region of human Y chromosome. ***Nucleic Acids Research***.

67. Swapna G, Chakraborty A, Kumari V, Sen R and Nagaraja V (2011). Mutations in β subunit of *E. coli* RNA polymerase perturb the activator polymerase functional interaction required for promoter clearance. ***Molecular Microbiology***.

D. Other Publications

1. Gowrishankar J (2010). Craig Venter, and the claim for 'synthetic life'. ***Current Science*** 99: 152.

2. Priya TP and Dalal A (2010). Triplet Primed PCR (TP-PCR) – A versatile method for molecular diagnosis of triplet repeat disorders. ***Newsletter of Genetics Chapter of Indian Academy of Pediatrics*** Vol 3, Issue 3 (July-Sept 2010).

3. Dalal A (2011). Annual review of genomics and human genetics, 2010. (Book Review) ***Current Science*** 100: 933-934.

4. Dalal A (2011). Genetic tests. ***API Textbook of Medicine***, 9th Edition 21-25.

5. Dutta UR, Pidugu VK and Dalal A (2011). Molecular cytogenetics illustrated: SKY and FISH. ***Newsletter of Genetics Chapter of Indian Academy of Pediatrics*** Vol 4, Issue 1 (Jan-Mar 2011).

Patents (2010-11)

I. Patents granted

1. Gowrishankar J and Nandineni MR. A microbial process for arginine production.

   (i) US Patent 7749738 B2, granted 6 July 2010.

   (ii) European Patent 1574566, granted 15 September 2010.

2. Gowrishankar J and Harinarayanan R. A method of altering levels of plasmids.

   Indian Patent 246791, granted 16 March 2011.

II. Patent application filed

1. J Nagaraju *et al.* Virus resistant transgenic silkworms. *Indian Patent* No. 332/CHE/2011 (applied on 4.2.2011).

मानव संसाधन विकास
Human Resource Development

PhD Program

For the PhD program, CDFD invites applications from highly motivated candidates willing to take up challenges in modern biology, usually in the month of March. Keeping in view the interdisciplinary nature of modern biology, the Centre especially encourages persons from different scientific disciplines to take up challenges in these areas. Those admitted as Junior Research Fellows (JRFs) are encouraged to take admission in the PhD program of Manipal Academy of Higher Education or University of Hyderabad.

The eligibility for the program is MBBS or Masters degree in any branch of Science, Technology or Agriculture from a recognized University or Institute. Candidates (other than MBBS graduates) must have cleared the CSIR/UGC/DBT/ICMR/ICAR NET for JRF or GATE or JEST. MBBS candidates are exempted from any of the eligibility tests mentioned herein. Those who have appeared for their final semester examination, but are awaiting results, are also eligible to apply. Those with independent Senior Research Fellowships (SRF) from CSIR can also apply. As the number of applicants outnumbers the seats available each year by a ratio of 1:40 or more, eligible candidates are invited for a written examination followed by interviews of short-listed candidates.

Currently the Centre has 78 Research Scholars working for their doctorates in different areas of research. In the reporting year, 9 of the Research Scholars have completed PhD and are pursuing careers in science elsewhere in India or abroad.

Post-doctoral Program

In addition to the JRF program, the Centre also carries out training at the post-doctoral level. The post-doctoral fellows are funded through the extramural grants that CDFD receives. Some post-doctoral fellows are also selected competitively by the DST fast track young scientist scheme, or the DBT post-doctoral fellowship program.

Summer Training Program

CDFD provides admissions to summer training program only to those students who are supported either by the Indian Academy of Science, Bangalore or Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore or the Kishore Vigyanik Protsahan Yojna, New Delhi. In the reporting year, 15 students received summer training at the Centre.

Training for students from BITS, Pilani

CDFD has an agreement with BITS, Pilani to provide project training to their M.Sc. students. Under this programme, the students spend 6 months to 1 year at CDFD and work on active projects being carried out here. The project work helps the students in gaining hands-on experience in modern biology. In the reporting year, 5 students were given the opportunity to avail training under this programme.

RESEARCH SCHOLARS CONFERRED PhD DEGREE DURING THE REPORTING PERIOD

Scholar	Supervisor	Date of *viva voce* examination	Title of thesis
Debashree Basu	Shekhar C Mande	07.04.2010	Structure-function studies on *Mycobacterium tuberculosis* transcription factors and stress proteins
Tabrez Anwar Shamim	H A Nagarajaram	04.05.2010	A knowledge-based approach to protein structure prediction
G Charitha	Sunil Kumar Manna	11.05.2010	Understanding the mechanism of doxorubicin mediated apoptosis and chemoresistance
Shiny Nair	Sangita Mukhopadhyay	02.07.2010	Functional characterization of *Mycobacterium tuberculosis* PPE protein RV1196 in alteration of macrophage effector responses: Approach to understand the mechanism of pathogenesis of *Mycobacterium tuberculosis*
Kaiser Alam	Sangita Mukhopadhyay	26.07.2010	Antioxidant as potential immunoadjuvant in anti-tuberculosis immunotherapy
Jisha Chalissery	Ranjan Sen	17.08.2010	Studies on the mechanism of Rho dependent transcription termination in *Escherichia coli*
Paila Uma Devi	Akash Ranjan	25.08.2010	Studies on amino acid substitutions in *Plasmodium falciparum*
Archana Rajesh Krishnan	Shekhar C Mande	31.08.2010	Site specific non-native amino acid replacement in bacteriorhdopsin for biomolecular electronics
Pankaj Kumar	H A Nagarajaram	20.10.2010	Studies on the distribution and mutation of microsatellites in pathogenic bacterial genomes

व्याख्यान, बैठक, कार्यशाला व अन्य महत्वपूर्ण कार्यक्रम

Lectures, Meetings, Workshops and Important Events

DISTINGUISHED VISITORS AND LECTURES

Visitor	Title of Lecture	Date
Dr Vishwajit Nimgaonkar, School of Medicine, University of Pittsburgh, USA	Inbreeding and risk for psychoses in Egypt	26.07.2010
Dr Raj Kandpal, Western University of Health Sciences, California, USA	Receptor tryosine kinase-mediated modulation of breast cancer invasiveness	14.09.2010
Prof Sue Lin-Chao, Institute of Molecular Biology, Academia Sinica, Taiwan	Post-transcriptional regulation of gene expression in *E. coli*: Functional roles, importance and complexity of the RNA degradation machinery	23.09.2010
Dr Antonella Ricco, MRC Laboratory of Molecular Cell Biology, University College of London, UK	Control from within: mRNA transport in developing neurons	26.10.2010
Dr Adolfo Saiardi, MRC Laboratory of Molecular Cell Biology, University College of London, UK	Inositol pyrophosphates: Linking signalling to metabolism	27.10.2010
Dr Vsevold J Makeev, State Research Centre of Genetics, Moscow, Russia	Using operons for obtaining reliable gene regulatory networks in *E. coli*	25.11.2010
Prof Rajeshwar Rao Tekmal, University of Texas Health Science Centre, USA	Role of estrogen and its receptor in breast and gynaecological cancers	26.11.2010
Prof Ananda M Chakraborty, College of Medicine, University of Illinois, USA	Microbial proteins in the potential therapy of cancer, HIV/AIDS, malaria and other diseases	30.11.2010
Dr Nishant KT, Cornell University, USA	The eukaryotic genome is remarkably stable in vegetative growth and meiosis	14.12.2010
Dr Rachna Chaba, University of California, USA	Design of stress signalling pathways in bacteria	25.01.2011
Mr Ravi Bhola, Intellectual Property Attorney, K&S Partners, Bangalore	Issues of patenting in the field of biotechnology	27.01.2011

Visitor	Title of Lecture	Date
Dr Pravin Nair, Sloan-Kettering Institute, New York, USA	Mechanistic insights to DNA ligases through biochemical and structural studies	09.02.2011
Dr Sandhya Kaushika, NCBS, Bangalore	Pre-synaptic vesicle transport: Role of motors and adapters	17.02.2011
Dr Piranit Nik Kantaputra, Chiang Mai University, Thailand	Molecular pathogenesis in craniofacial anomalies	18.02.2011
Dr Athi Narayanan Naganathan, Barcelona Supercomputing Centre, Institute for Research in Biomedicine, Spain	Characterizing experimental protein folding data using statistical models	18.02.2011
Dr Purusharth Rajyaguru, University of Arizona, USA	mRNP transitions	23.02.2011
Dr Ashok Venkitaraman, MRC Cancer Cell Unit, University of Cambridge, UK	Exploiting the mechanisms governing genome stability in new approaches for cancer therapy	15.03.2011
Dr Ayae Honda, Department of Molecular Genetics, Hosei University, Japan	Recent topics of influenza virus infection	22.03.2011

IMPORTANT EVENTS

Event	Partnering Institutions	Date
Fire drill	----------	19 May 2010
Independence Day	----------	15 August 2010
Hindi week celebration	----------	9-14 September 2010
Visit of DBT representatives to review the implementation of official language by CDFD	----------	16-19 September 2010
Discussion meeting on use of next generation whole genome sequencing	CDFD	30 September 2010
Workshop on NMR in drug discovery	CDFD	29 November 2010
Republic Day	----------	26 January 2011
14th Transcription Assembly meeting	CDFD, CCMB and HCU	20-22 January 2011
Symposium on redox status and control in tuberculosis: From basic research to drug development	CDFD, DBT and ISTP, Canada	30 January -1 February 2011
Workshop on genetic fidelity testing of tissue culture raised micropropagules employing DNA-based markers	CDFD	21-25 February 2011
MoU signing with University of Nebraska Medical Centre, Omaha, USA to foster student exchanges and promote collaborative research	CDFD and UNMC	3 March 2011
5th Indo-French Bioinformatics meeting	CDFD	23-25 March 2011
Workshop on Structural biology: Biological function and drug design	CDFD	25 March 2011

सी डी एफ डी कर्मचारियों की विदेशों में प्रतिनियुक्ति

Deputations abroad of CDFD Personnel

DEPUTATIONS ABROAD - FACULTY & STAFF

Faculty	Period	Country of Visit and Purpose
J.Gowrishankar	30.04.2010 to 14.05.2010	**France:** IFCPAR Scientific Council meeting and visit to various laboratories
	20.08.2010 to 30.08.2010	**USA:** Presentation of his group's research work at the Cold Spring Harbor Laboratory meeting and visit to various laboratories
	19.3.2011 to 24.03.2011	**Taiwan & Hong Kong:** Visit to Institute of Molecular Biology, Academia Sinica, Taipei and School of Biological Sciences, University of Hong Kong.
J Nagaraju	15.09.2010 to 26.09.2010	**Japan:** 6th International Conference on Wild Silkmoths and visit to various laboratories.
	07.11.2010 to 21.11.2010	**Japan:** Visited University of Tokyo under the Indo-Japan Cooperative Science Programme (IJCSP).
Ranjan Sen	03.11.2010 to 09.11.2010	**USA:** 15th biennial meeting on "Post Initiation Activities of RNA Polymerase" in Virginia.
MD Bashyam	08.04.2010 to 24.04.2010	**USA:** 10th Annual meeting of the American Association for Cancer Research in Washington DC.
	23.03.2011 to 09.04.2011	**USA:** 102nd Annual meeting of the American Association for Cancer Research in Orlando, FL and visit to various laboratories.
Rupinder Kaur	26.07.2010 to 30.07.2010	**Nigeria:** Workshop on DNA Fingerprinting at University of Agriculture, Abeokuta.
Ashwin B Dalal	25.05.2010 to 14.06.2010	**USA:** Workshop organized under "Tri-National Training Program for Psychiatric Genetics" and visit to laboratories in University of Pittsburgh.
	16.03.2011 to 20.03.2011	**Canada:** 20th American College of Medical Genetics Meeting in Vancouver and visit to the Medical Genetics Department, University of British Columbia.
Rashna Bhandari	02.09.2010 to 06.09.2010	**Spain:** Meeting on "Life Science Research in India" organized by EMBO Global Exchange and Wellcome Trust/DBT India Alliance.
	13.02.2011 to 21.02.2011	**USA:** Keystone Symposium on "Inositide Signalling in Pharmacology and Disease" at Keystone, Colorado.
N Madhusudan Reddy	22.04.2010 to 19.05.2010	**Germany:** Conduct research in Prof. Mark Stoneking's laboratory in Leipzig.
	07.06.2010 to 10.06.2010	**Indonesia:** Attend forensic training in West Java.
Subhadeep Chatterjee	05.06.2010 to 12.06.2010	**France:** 12th International conference on "Plant Pathogenic Bacteria".

Faculty	Period	Country of Visit and Purpose
Abhijit A Sardesai	01.03.2011 to 18.03.2011	**United Kingdom:** Department of Molecular Microbiology, School of Biosciences, University of Birmingham.
K Anupama	20.02.2011 to 22.03.2011	**Taiwan:** Institute of Molecular Biology, Academia Sinica, Taipei under the Indo-Taiwan S&T Cooperation Programme.
Muthu Lakshmi	01.09.2010 to 31.12. 2010	**Japan:** Training on "Microinjection of Silkworm Eggs to Construct Transgenic Strains" at Tsukuba, Ibaraki.
Archana Tomar	07.11.2010 to 14.11. 2010	**Japan:** Symposium on "New Silk Road: Silkworm Genome to Sustainable Agriculture" and workshop on "Silkworm Genome Annotation" at Tokyo.
V V Satyavati	08.11.2010 to 21.11.2010	**Japan:** National Institute of Agrobiological Sciences, University of Tokyo and Tsukuba & Rykyus University, Okinawa under the India-Japan Cooperative Programme.

DEPUTATIONS ABROAD - STUDENTS

Student	Period	Country of Visit and Purpose
Ratheesh R	13.04.2010 to 22.04.2010	**USA:** 101st annual meeting 2010 of the American Association for Cancer Research (AACR).
Vishal Acharya & **Vijay K Muley**	14.04.2010 to 17.04.2010	**Germany:** 4th ESF conference on "Functional Genomics and Diseases".
Pramod Kumar	18.07.2010 to 23.07.2010	**USA:** Conference on "Diffraction Methods in Structural Biology".
M Khursheed	17.08.2010 to 21.08.2010	**USA:** Conference on "Mechanism & Models of Cancer".
Shivalika Saxena & Ghazala Muteeb	24.08.2010 to 30.08.2010	**USA:** Conference on "Molecular Genetics of Bacteria and Phages".
Khalid Hussain Bhat	26.10.2010 to 01.11.2010	**USA:** Meeting on "Immunological Mechanisms of Vaccination".
Aditi Sharma	1.01.2011 to 30.06.2011	**USA:** Training program on "Research Training on Intracellular Pathogens" and visit to Dr D. Sherman's laboratory.
Chandrapal Singh	11.02.2011 to16.02.2011	**Canada:** Conference on "MicroRNA and Human Disease (J6)".
Shubhada R Hegde	22.03.2011 to 26.03.2011	**USA:** Conference on "Systems Biology: Networks".

सी डी एफ डी के
वरिष्ठ वैज्ञानिक व अधिकारी

Senior Staff and
Officers of CDFD

SCIENTIFIC GROUP LEADERS (FACULTY)

Dr J Gowrishankar

Dr J Nagaraju

Dr Shekhar C Mande

Dr Murali D Bashyam

Dr Sunil Kumar Manna

Dr H A Nagarajaram

Dr Akash Ranjan

Dr Sangita Mukhopadhyay

Dr Gayatri Ramakrishna

Dr Sanjeev Khosla

Dr Ranjan Sen

Dr Rupinder Kaur

Dr Madhusudan R Nandineni

Dr Ashwin Dalal

Dr Abhijit A Sardesai

Dr Rashna Bhandari

Dr R Harinarayanan

Dr Subhadeep Chatterjee

Dr M V Subba Reddy

Dr Shweta Tyagi

Dr Rohit Joshi

Dr K P Arun Kumar

ADJUNCT FACULTY

Dr E A Siddiq

Prof T Ramasarma

Prof Anuradha Lohia

Dr Renu Wadhwa

OTHER GROUP LEADERS

Mr J Raghavendrachar

Ms M Kavita Rao

Dr Ankkur Goel

SENIOR ADMINISTRATIVE STAFF

Mr K Ananda Rao

Mr J Sanjeev Rao

केन्द्र की समितियाँ

(31.03.2011 तक)

Committees of the Centre

(As on 31.03.2011)

MEMBERS OF CDFD SOCIETY

Shri Prithviraj Chavan Hon'ble Minister for S&T and Earth Sciences	-	President (till Nov. 2010)
Shri Kapil Sibal Hon'ble Minister for S&T and Earth Sciences	-	President (Nov. 2010-Jan. 2011)
Shri Pawan K Bansal Hon'ble Minister for S&T and Earth Sciences	-	President (From Jan. 2011)
Prof M K Bhan Secretary, DBT, New Delhi	-	Member
Dr Samir K Brahmachari Director General, CSIR, New Delhi	-	Member (Ex-officio)
Prof P Balaram Director, IISc, Bangalore	-	Member (Ex-officio)
Prof V S Chauhan Director, ICGEB, New Delhi	-	Member
Dr Siddhartha Roy Director, IICB, Kolkata	-	Member
Mr S Suresh Kumar Joint Secretary (PM) Ministry of Home Affairs, New Delhi	-	Member (Ex-officio)
Joint Secretary Ministry of Law and Justice New Delhi	-	Member (Ex-officio)
Ms Sheila Sangwan Additional Secretary & Financial Advisor DBT, New Delhi	-	Member (Ex-officio)
Mr M K Chabra Director (Modernization) Bureau of Police Research and Development New Delhi (Nominee of Director General, BPR&D)	-	Member (Ex-officio)
Dr Alka Sharma Joint Director, DBT, New Delhi	-	Member (Ex-officio)
Dr J Gowrishankar Director, CDFD	-	Member Secretary

MEMBERS OF CDFD GOVERNING COUNCIL

Prof M K Bhan Secretary, DBT, New Delhi	-	Chairperson
Dr Samir K Brahmachari Director General, CSIR, New Delhi	-	Member (Ex-officio)
Prof P Balaram Director, IISc, Bangalore	-	Member (Ex-officio)
Prof V S Chauhan Director, ICGEB, New Delhi	-	Member
Dr Siddhartha Roy Director, IICB, Kolkata	-	Member
Ms Zoya Hadke Deputy Legal Adviser Ministry of Law and Justice New Delhi (Nominee of JS, Ministry of Law & Justice)	-	Member (Ex-officio)
Mr S Suresh Kumar Joint Secretary (PM), Ministry of Home Affairs, New Delhi	-	Member (Ex-officio)
Ms Sheila Sangwan Additional Secretary & Financial Advisor DBT, New Delhi	-	Member (Ex-officio)
Ms Vanita Yadav Senior Scientific Officer Bureau of Police Research and Development, New Delhi (Nominee of DG, BPR&D)	-	Member (Ex-officio)
Dr Alka Sharma Joint Director, DBT, New Delhi	-	Member (Ex-officio)
Dr J Gowrishankar Director, CDFD	-	Member Secretary

MEMBERS OF CDFD RESEARCH AREA PANELS – SCIENTIFIC ADVISORY COMMITTEE (RAP-SAC)

Prof P Balaram Director, IISc, Bangalore	-	Chairman
Dr Siddhartha Roy Director, IICB, Kolkata	-	Member
Dr Ch Mohan Rao Director, CCMB, Hyderabad	-	Member
Dr G C Mishra Director, NCCS, Pune	-	Member
Prof H Sharat Chandra Director, CHG, Bangalore	-	Member
Dr Dinakar M Salunke Executive Director, RCB, Gurgaon	-	Member
Prof D Balasubramanian Research Director, LVPEI, Hyderabad	-	Member
Dr S S Agarwal Director (Retd.), SGPGIMS, Lucknow	-	Member
Prof Partha P Majumder ISI, Kolkata	-	Member
Prof Indira Nath National Institute of Pathology, New Delhi	-	Member
Prof Sandhya S Visweswaraiah IISc, Bangalore	-	Member
Prof Manju Bansal IISc, Bangalore	-	Member
Prof Umesh Varshney IISc, Bangalore	-	Member
Prof T D Dogra AIIMS, New Delhi	-	Member
Dr Samit Adhya Scientist, IICB, Kolkata	-	Member
Prof Anil K Tyagi University of Delhi, Delhi	-	Member
Dr Veena Parnaik Scientist, CCMB, Hyderabad (Nominee of CCMB, Hyderabad)	-	Member

Director General (or Nominee) ICMR, New Delhi	-	Member
Director General (or Nominee) ICAR, New Delhi	-	Member
Dr Alka Sharma Joint Director, DBT, New Delhi (Nominee of DBT)	-	Member
Dr S Sathyan Senior Scientific Officer, CFSL, Hyderabad (Nominee of MHA, New Delhi)	-	Member
Dr J Gowrishankar Director, CDFD	-	Member Secretary

MEMBERS OF CDFD ACADEMIC COMMITTEE

Prof A S Raghavendra Dean, School of Life Sciences University of Hyderabad, Hyderabad	-	Chairperson
Prof Anil K Tyagi University of Delhi, Delhi	-	Member
Dr K Satyamoorthy Director, Manipal Life Sciences Centre Manipal University, Manipal	-	Member
Dr D P Kasbekar Scientist, Centre for Cellular and Molecular Biology, Hyderabad	-	Member
Dr Ranjan Sen Staff Scientist, CDFD Hyderabad	-	Member
Dr Shekhar C Mande Staff Scientist and Dean (Academics) CDFD, Hyderabad	-	Member Convenor

MEMBERS OF CDFD FINANCE COMMITTEE

Dr V S Chauhan Director, ICGEB, New Delhi	-	Chairman
Ms Sheila Sangwan Addl. Secretary & Financial Adviser DBT, New Delhi	-	Member (Ex-officio)
Shri Virendra Kapoor Director, DBT, New Delhi	-	Member
Dr Siddhartha Roy Director, IICB, Kolkata	-	Member
Dr J Gowrishankar Director, CDFD, Hyderabad	-	Member
Joint Secretary & Financial Adviser Ministry of Home Affairs, New Delhi	-	Member (Ex-officio)
Shri E V Rao Head (Finance & Accounts) CDFD, Hyderabad	-	Member Secretary

MEMBERS OF CDFD BUILDING COMMITTEE

Dr V S Chauhan Director, ICGEB, New Delhi	-	Chairman
Dr J Gowrishankar Director, CDFD, Hyderabad	-	Member
Shri N S Samant Joint Secretary, DBT, New Delhi	-	Member
Shri Virendra Kapoor Director, DBT, New Delhi	-	Member
Shri B Bose Management Consultant & Former Senior Manager, NII, New Delhi	-	Member
Shri J Sanjeev Rao Head (Administration), CDFD, Hyderabad	-	Member
Shri E V Rao Head (Finance & Accounts), CDFD, Hyderabad	-	Member
Shri K Ananda Rao Staff Scientist (Engg.), CDFD, Hyderabad	-	Member Convenor

बजट एवं वित्त
Budget and Finance

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS HYDERABAD

Budget & Finance 2010 -11

Sources of Funds

The Financial resources of the Centre are the Core Plan Grant-in Aid provided by the Department of Biotechnology, Government of India as against Annual Budgetary projections made by the Institute. Other resources are in the form of Research Grants provided by various National and International agencies and also from Services rendered by CDFD. The components of the core grants are Plan (Recurring) essentially for meeting expenditures on salaries, Operating expenses etc., and Plan (Non-Recurring) for meeting expenses on account of equipments, infrastructure and furnishing etc.

Receipts during the year 2010-11

Particulars	Amount in Lakhs	Percentage %
Plan Grant in Aid	2300.00	71.68
Sponsored Projects	847.93	26.42
CDFD Services	35.45	1.01
Misc Receipts	25.59	0.80
Total	**3208.97**	**100.00**

I. Application of Funds during 2010-11 (Plan Grant in Aid)

S No	Particulars	Amount in Lakhs	Percentage %
1	**Recurring**		
	Salaries & wages	694.88	28.98
	Operating exp	1265.05	52.75
	Total	**1959.93**	**81.73**
2	**Non-Recurring**		
	Equipments, Infrastructure & furnishing	438.29	18.27
	Total	**438.29**	**18.27**
	Grand Total	**2398.22**	**100.00**

II. Application of Funds during 2010-11 (Extra Mural Projects)

S No	Particulars	Amount in Lakhs	Percentage %
1	**Recurring**		
	Salaries & wages	234.12	26.89
	Operating exp	458.73	52.70
	Total	**692.85**	**79.59**
2	**Non-Recurring**		
	Equipments	177.73	20.41
	Total	**177.73**	**20.41**
	Grand Total	**870.58**	**100.00**

लेखा परिक्षक की रिपोर्ट
Auditor's Report

BAPUJI & VENKAT

Chartered Accountants

AUDITOR'S REPORT

Date: 23-06-2011

The Director,
Centre for DNA Fingerprinting and Diagnostics,
Nampally, Hyderabad - 500 001

We have audited the attached Balance Sheet of **CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS**, Hyderabad, as at 31st March 2011 and also the Income & Expenditure Accounts for the year ended on that date annexed there to. These financial statements are the responsibility of the organization management. Our responsibility is to express an opinion on these financial statements based on our audit.

We report that:

1. We have obtained all the information and explanations, which are to the best of our knowledge and belief, were necessary for the purpose of our audit.
2. In our opinion, the organization has kept proper books of account as required by law so far, as appears from our examination of those books.
3. The Balance Sheet and Income & Expenditure account dealt with by this report are in agreement with the books of account.
4. (a) The centre has maintained accounts on cash basis.

   (b) The Centre receives extra mural grants from various National & International agencies for specific research activities. The Centre has a policy of allocating the overheads and transfer of expenditure of CDFD to different projects at the end of the financial year on adhoc basis after taking into account the amount of maximum permissible limit of overheads and also based on the approved budget estimates of the respective projects during the financial year.
5. In our opinion and to the best of our information and according to the explanations given to us, the said Balance Sheet and the Income & Expenditure account read together with the notes thereon gives the information required in the manner so required and give a true and fair view.

   a) In so far it relates to the Balance Sheet of the state of the organization as at 31st March 2011 and

   b) In so far as it relates to the Income & Expenditure account of the surplus of the organization for the year ended on 31st March 2011.

for **BAPUJI & VENKAT**
Chartered Accountants
[K VENKATACHARYULU]

Place: Hyderabad

Date: 23/06/2011

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

BALANCE SHEET AS ON 31st MARCH, 2011

(Amount - Rs.)

CORPUS/CAPITAL FUND AND LIABILITIES	Schedule	Current Year	Previous Year
Corpus / Capital Fund	1	811485570	755462253
Reserves and Surplus	2	272022338	263489419
Earmarked / Endowment Funds	3	16210479	18475777
Secured Loans & Borrowings	4	0	0
Unsecured Loans & Borrowings	5	0	0
Deffered Credit Liabilities	6	0	0
Current Liabilities and Provisions	7	89226416	72074128
TOTAL		**1188944803**	**1109501577**
ASSETS			
Fixed Assets	8	742922549	687939245
Investments - From Earmarked / Endowment Funds	9	78308000	80808000
Investments - Others	10	33724337	27346637
Current Assets, Loans, Advances, etc.	11	332084413	311502191
Miscellaneous Expenditure **Internal & External Electrification**		1905503	1905503
TOTAL		**1188944803**	**1109501577**
Significant Accounting Policies	24		
Contingent Liabilites and Notes on Accounts	25		

DIRECTOR
CDFD

for BAPUJI & VENKAT
CHARTERED ACCOUNTANTS
[K VENKATACHARYULU]
Partner

HEAD - FINANCE & ACCOUNTS
CDFD

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

INCOME AND EXPENDITURE ACCOUNT FOR THE YEAR ENDING 31st MARCH, 2011 (Amount - Rs.)

INCOME	Schedule	Current Year	Previous Year
Income from Sales/Services	12	3545801.50	58500.00
Grants/Subsidies	13	185000000.00	158700000.00
Fees/Subscriptions	14	0.00	0.00
Income from Investments	15	789164.00	4816013.00
Income from Royality, Publication, etc.	16	0.00	0.00
Interest Earned	17	2552230.00	198597.00
Other Income	18	288553.00	963872.00
Increase/(decrease) in stock of Finished goods and works-in-progress	19	0.00	0.00
TOTAL (A)		**192175748.50**	**164736982.00**
EXPENDITURE			
Establishment Expenses	20	69488171.00	63370989.00
Administrative Expenses etc.	21	114154659.00	94777202.00
Expenditure on Grants, Subsides etc.	22	0.00	0.00
Interest	23	0.00	0.00
Depreciation (Net Total at the year-end - corresponding to Schedule 8)			
TOTAL (B)		**183642830.00**	**158148191.00**
Balance being excess of Income over Expenditure (A-B)		8532918.50	6588791.00
Transfer to Special Reserve (Specify each)			
Transfer to / from General Reserve			
BALANCE BEING SURPLUS/(DEFICIT) CARRIED TO CORPUS/CAPITAL FUND			
SIGNIFICANT ACCOUNTING POLICIES	24		
CONTINGENT LIABILITIES AND NOTES ON ACCOUNTS	25		

DIRECTOR
CDFD

for BAPUJI & VENKAT
CHARTERED ACCOUNTANTS
[K VENKATACHARYULU]
Partner

HEAD - FINANCE & ACCOUNTS
CDFD

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

RECEIPTS AND PAYMENTS ACCOUNT FOR THE YEAR ENDED 31st MARCH 2011

(Amount - Rs.)

RECEIPTS	Current Year	Previous Year	PAYMENTS	Current Year	Previous Year
1. Opening Balances			**1. Expenses**		
a) Cash in hand	65550.00	43969.00	a) Establishment Expenses (corresponding to Schedule 20)	69488171.00	63370989.00
b) Bank balances			b) Administrative Expenses (corresponding to Schedule 21)	114154659.00	94777202.00
i) In current accounts	42391687.25	50672076.25	c) Schedule 22	0.00	0.00
ii) In deposit accounts	0.00	0.00			
iii) Savings accounts	6860352.72	3826152.72	**II. Payments made against funds for various projects**		
II. Grants Received			(Name of the fund or project should be shown along with the particulars of payments made for each project)		
a) From Government of India	230000000.00	243700000.00			
b) From State Government	0.00	0.00	Projects (Annexure H)	87058572.00	112224334.00
c) From other sources (details)			EMRC A/c (Stipend)	7346700.00	8374430.00
(Grants for capital & revenue			DBT A/c (Stipend)	2278102.00	2192064.00
exp.to be shown separately)			IISc A/c (Stipend)	1298574.00	968125.00
Research Associates - IISc (Stipend)	2059600.00	1613118.00	UGC A/c (Stipend)	1808382.00	1670137.00
Research Associates - UGC (Stipend)	0.00	3455015.00	DST Inspire (Stipend)	17109.00	0.00
Research Associates - DBT-JRF (Stipend)	2861218.00	213758.00	ICMR (Stipend)	1089703.00	637535.00
Research Associates - EMRC (Stipend)	7268874.00	7969829.00			
Research Associates - DBT-PDF (Stipend)	0.00	0.00	**III. Investments and deposits made**		
Research Associates - ICMR (Stipend)	954940.00	479627.00	a) Out of Earmarked/Endowment Funds	67500000.00	59500000.00
Projects (Annexure -D)	84793274.00	79320020.00	b) Out of Own Funds (Investments-others)	0.00	0.00
III. Income on Investments from			**IV. Expenditure on Fixed Assets & Capital Work-in-Progress**		
a) Earmarked/Endow. Funds	789164.00	4816013.00	a) Purchase of Fixed Assets :		
b) Own Funds (Oth. Investment)			Vehicles	0.00	56284.00
Investments cancelled	70000000.00	70000000.00	Books & Journals	853343.00	692139.00
			Equipment - Lab / Office / Furniture	30818937.00	15598161.00
IV. Interest Received			Non Consumables	0.00	0.00
a) On Bank deposits	229789.00	116256.00	b) Expenditure on Capital Work-in-progress:		
b) Loans, Advances, etc.			Building	12297977.00	17397329.00

DIRECTOR
CDFD

for BAPUJI & VENKAT
CHARTERED ACCOUNTANTS
[K VENKATACHARYULU]
Partner

HEAD - FINANCE & ACCOUNTS
CDFD

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

RECEIPTS AND PAYMENTS ACCOUNT FOR THE YEAR ENDED 31st MARCH 2011

(Amount - Rs.)

RECEIPTS	Current Year	Previous Year	PAYMENTS	Current Year	Previous Year
Interest on HBA Advances	6308.00	27927.00			
Interest earned on LC	2322441.00	82341.00			
Interest on Vehicle Advance	4628.00	0.00			
Interest on Computer Advance	521.00	0.00			
V. Refund of surplus money/Loans			**V. Refund of surplus money/Loans**		
Analysis Charges	3950970.50	0.00	a) To the Government of India	0.00	0.00
			b) To the State Government	0.00	0.00
			c) To other provides of funds	0.00	0.00
VII. Any other receipts (give details)					
I- Remittances (Annexure-A)	6585429.00	6950973.00	**VI. Finance Charges (Interest)**	0.00	0.00
TDS Recoveries (Annexure-B)	2804289.00	4510906.00			
CPF -Sub, Arrears and adv. Refund	6765955.00	5752948.00	**VII. Other Payments (Specify)**		
Sundry receipts	38031.00	744970.00	Advances (Annexure - E)	61546466.00	89613075.00
Sale of Tender forms	77500.00	61500.00	I-Remittances (Annexure - F)	6594485.00	7043784.00
Application Fees	121090.00	93700.00	TDS remitted (Annexure- G)	2708394.00	6026079.00
Guest House receipts	27900.00	23950.00	CPF A/c	6740541.00	5752974.00
Hostel receipts	12575.00	11825.00	Life Membership fees	0.00	1510.00
Loans & Advances (Recovery) - (Annexure-C)	59668099.00	33594876.00	Analysis Charges paid / refund	405169.00	0.00
Asset Transfer	6749850.00	16706823.00	CDFD Revolving Fund Expenses A/c	120000.00	60000.00
Indo-Australian Biotech Conference A/c	17832.00	8643.00	Advance for Workshop	0.00	394494.00
Sale of Vehicle	0.00	181099.00	Workshop A/c expenses	687047.00	56.00
Other receipts	0.00	600000.00	Collaboration Expenses A/c	0.00	5800056.00
Sale of Scrap	0.00	58500.00	Indo canada workshop expenses A/c	88356.00	0.00
Collaboration A/c receipts	46162.00	5827821.00	**VIII. Closing Balances**		
Workshop receipts	270000.00	3711.00	a) Cash in hand	160550.00	65550.00
Indo-Canada Workshop receipt	640000.00	0.00	b) Bank Balances		
Vehicles	10270.00	0.00	i) In current accounts	55687650.25	42391687.25
			ii) In deposit accounts	0.00	0.00
			iii) Savings accounts	7645412.22	6860352.72
TOTAL	538394299.47	541468346.97	**TOTAL**	538394299.47	541468346.97

DIRECTOR
CDFD

for BAPUJI & VENKAT
CHARTERED ACCOUNTANTS
[K VENKATACHARYULU]
Partner

HEAD - FINANCE & ACCOUNTS
CDFD

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF BALANCE SHEET AS AT 31st MARCH 2011

(Amount - Rs.)

		Current Year		Previous Year
SCHEDULE 1 - CORPUS/CAPITAL FUND :				
Balance as at the beginning of the year		755462253.00		640497431.00
Add : Contribution towards Corpus/Capital Fund				
CDFD Core - Plan (Non-Recurring)	45000000.00		85000000.00	
Capitalised portion of fixed assets of projects	11023317.00	56023317.00	29964822.00	114964822.00
Add : Balance of net income/(expenditure) transferred from the income and Expenditure Account		0.00		0.00
BALANCE AS AT THE YEAR - END		**811485570.00**		**755462253.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF BALANCE SHEET AS AT 31st MARCH 2011

(Amount - Rs.)

	Current Year		Previous Year	
SCHEDULE 2 -RESERVES AND SURPLUS :				
1.Capital Reserve :				
As per last account	263489419.00		256900628.00	
Addition during the year	8532918.50	272022337.50	6588791.00	
Less : Deductions during the year	0.00		0.00	263489419.00
2.Revalution Reserve :				
As per last account	0.00		0.00	
Addition during the year	0.00		0.00	
Less : Deductions during the year	0.00	0.00	0.00	0.00
3.Special Reserves :				
As per last account	0.00		0.00	
Addition during the year	0.00		0.00	
Less : Deductions during the year	0.00	0.00	0.00	0.00
4.General Reserve :				
As per last account	0.00		0.00	
Addition during the year	0.00		0.00	
Less : Deductions during the year	0.00	0.00	0.00	0.00
TOTAL		**272022337.50**		**263489419.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF BALANCE SHEET AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 3 - EARMARKED/ENDOWMENT FUNDS	Current Year		Previous Year	
(Refer Annexures P 03-P 102, COE I &II & A to L)				
(a) Opening balance funds :		18475777.20		51380091.20
i. Donations /grants	84793274.00		79320020.00	
ii. Income from investments made on account of funds	0.00		0.00	
iii. Other additions	0.00	84793274.00	0.00	79320020.00
TOTAL (a+b)		103269051.20		130700111.20
(c) Utilisation/Expenditure towards objective of funds				
(i) Capital Expenditure (Refer Annexures I & II)				
- Fixed Assets	11023317.00		29964822.00	
- Others	6749850.00	17773167.00	16706823.00	46671645.00
Total				
(ii) Revenue Expenditure				
- Salaries, Wages and allowances, etc.	23412168.00		18325596.00	
- Rent	0.00		0.00	
- Other Expenses	45873237.00	69285405.00	47227093.00	65552689.00
Total				
TOTAL (c)		87058572.00		112224334.00
NET BALANCE AS AT THE YEAR-END (a+b-c)		**16210479.20**		**18475777.20**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF BALANCE SHEET AS AT 31st MARCH 2011

(Amount - Rs.)

	Current Year		Previous Year	
SCHEDULE 4 - SECURED LOANS AND BORROWINGS:				
1. Central Government		0.00		0.00
2. State Government (Specify)		0.00		0.00
3. Financial Institutions				
(a) Term Loans	0.00		0.00	
(b) Interest accured and due	0.00	0.00	0.00	0.00
4. Banks:				
(a) Term Loans	0.00		0.00	
- Interest accured and due	0.00		0.00	
(b) Other Loans (specify)	0.00		0.00	
- Interest accured and due	0.00	0.00	0.00	0.00
5. Other Institutions and Agencies		0.00		0.00
6. Debentures and Bonds		0.00		0.00
7. Others (Specify)		0.00		0.00
TOTAL		**0.00**		**0.00**
Note: Amount due within one year				

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF BALANCE SHEET AS AT 31st MARCH 2011

(Amount - Rs.)

	Current Year		Previous Year	
SCHEDULE 5 - UNSECURED LOANS AND BORROWINGS:				
1. Central Government		0.00		0.00
2. State Government (Specify)		0.00		0.00
3. Financial Institutions		0.00		0.00
4. Banks:				
(a) Term Loans	0.00		0.00	
(b) Other Loans (specify)	0.00	0.00	0.00	0.00
5. Other Institutions and Agencies		0.00		0.00
6. Debentures and Bonds		0.00		0.00
7. Fixed Deposits		0.00		0.00
8. Others (Specify)		0.00		0.00
TOTAL		**0.00**		**0.00**
Note: Amounts due within one year				

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF BALANCE SHEET AS AT 31st MARCH 2011

(Amount - Rs.)

	Current Year		Previous Year	
SCHEDULE6 - DEFFERED CREDIT LIABILITIES:				
(a) Acceptances secured by hypothecation of capital equipment and other assets		0.00		0.00
(b) Others		0.00		0.00
TOTAL		0.00		0.00
Note: Amount due within one year				

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF BALANCE SHEET AS AT 31st MARCH 2011

(Amount - Rs.)

	Current Year		Previous Year	
SCHEDULE 7 - CURRENT LIABILITIES AND PROVISIONS				
A. CURRENT LIABILITIES				
1. Acceptances	0.00		0.00	
2. Sundry Creditors	0.00		0.00	
3. Advances Received	0.00		0.00	
4. Interest accured but not due on	0.00		0.00	
5. Statutory Liabilities	0.00	0.00	0.00	0.00
6. Other current Liabilities				
CDFD CP Fund A/c (Annexure - I)	33724337.32		27346637.32	
Collabaration A/c	11461906.00		11415744.00	
Workshop A/c	808763.50		808763.50	
Indo-Australian Biotech Conference A/c	520343.00		502511.00	
CDFD Revolving Fund A/c	2644290.00		2764290.00	
Asset Transfer	23456673.00		16706823.00	
BOYSCOST Fellowship	17691.00		17691.00	
Amersham Biosciences (Maintenance)	500000.00		500000.00	
Swarnajyanthi Fellowship Meeting	402040.00		402040.00	
Grant Host Meetings refundable	1033066.00		1033066.00	
T.D.S. Payable	354334.00		258439.00	
Other Loans	825.00		825.00	
CPF Subscription	34738.00		0.00	
Profession Tax	1371.00		2051.00	
HSD , LSD & TSD	932750.00		807750.00	
Security deposit/Retention money	1115975.00		1475975.00	
EMD / Margin money	5007156.00		2452934.00	
Works tax	245349.00		192044.00	
GSLI	12455.00		72535.00	

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF BALANCE SHEET AS AT 31st MARCH 2011

(Amount - Rs.)

	Current Year		Previous Year	
SCHEDULE 7 - CURRENT LIABILITIES AND PROVISIONS				
IISc, Bangalore Stipend	1586067.00		825041.00	
Vehicle Advance	95000.00		57272.00	
Income Tax	20406.00		35167.00	
Computer Advance - staff	64100.00		39900.00	
Indo - US Workshop	1166374.00		1166374.00	
DST Expert Meeting	200431.00		200431.00	
Other receipts	600000.00		600000.00	
HBA	95087.00		78820.00	
Royalties & Consultancy	2554084.00		2305004.00	
Indo Canada workshop	551644.00			
PPF	19160.00	89226415.82	6000.00	72074127.82
TOTAL (A)		89226415.82		72074127.82
B. PROVISIONS				
1. For Taxation	0.00		0.00	
2. Gratuity	0.00		0.00	
3. Superannuation/Pension	0.00		0.00	
4. Accumulated Leave Encashment	0.00		0.00	
5. Trade Warranties/Claims	0.00		0.00	
6. Others (Specify)	0.00	0.00	0.00	0.00
TOTAL (B)		0.00		0.00
TOTAL (A+B)		**89226415.82**		**72074127.82**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF BALANCE SHEET AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 8 - FIXED ASSETS	GROSS BLOCK				DEPRECIATION				NET BLOCK	
	Cost / valuation as at beginning of the year	Additions during the year	Deductions during the year	Cost / Valuation at the year end	As at the beginning of the year	On Additions during the year	On Deductions during the year	Total up to the year end	As at the Current year end	As at the Previous year end
A. FIXED ASSETS:										
1. LAND:										
a) Freehold	3900000.00	0.00	0.00	3900000.00	0.00	0.00	0.00	0.00	3900000.00	3900000.00
b) Leasehold	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2. BUILDINGS:										
a) On Freehold Land	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
b) On Leasehold Land	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
c) Ownership Flats/Premises	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
d) Superstructures on Land not belongs to the entity	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3. PLANT MACHINERY & EQUIPMENT	299740947.05	79765389.00	38200078.00	341306258.05	0.00	0.00	0.00	0.00	341306258.05	299740947.05
4. VEHICLES	4136428.00	0.00	10270.00	4126158.00	0.00	0.00	0.00	0.00	4126158.00	4136428.00
5. FURNITURE, FIXTURES	15421247.00	0.00	0.00	15421247.00	0.00	0.00	0.00	0.00	15421247.00	15421247.00
6. OFFICE EQUIPMENT	11045478.00	276943.00	0.00	11322421.00	0.00	0.00	0.00	0.00	11322421.00	11045478.00
7. COMPUTER/PERIPHERALS	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
8. ELECTRIC INSTALLATIONS	336985.00	0.00	0.00	336985.00	0.00	0.00	0.00	0.00	336985.00	336985.00
9. LIBRARY BOOKS	13043036.00	853343.00	0.00	13896379.00	0.00	0.00	0.00	0.00	13896379.00	13043036.00
10. TUBEWELLS & WATER SUPPLY	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
11. OTHER FIXED ASSETS										
Airconditioning works	5337154.00	0.00	0.00	5337154.00	0.00	0.00	0.00	0.00	5337154.00	5337154.00
Aluminium partition work	1213252.00	0.00	0.00	1213252.00	0.00	0.00	0.00	0.00	1213252.00	1213252.00
DG Set	1646305.00	0.00	0.00	1646305.00	0.00	0.00	0.00	0.00	1646305.00	1646305.00
Paintings	40000.00	0.00	0.00	40000.00	0.00	0.00	0.00	0.00	40000.00	40000.00
Typewriters	42450.00	0.00	0.00	42450.00	0.00	0.00	0.00	0.00	42450.00	42450.00
Miscellaneous non consumables	957984.50	0.00	0.00	957984.50	0.00	0.00	0.00	0.00	957984.50	957984.50
Other Assets	1018618.00	0.00	0.00	1018618.00	0.00	0.00	0.00	0.00	1018618.00	1018618.00
EMB Net	5229909.00	0.00	0.00	5229909.00	0.00	0.00	0.00	0.00	5229909.00	5229909.00
TOTAL	363109793.55	80895675.00	38210348.00	405795120.55	0.00	0.00	0.00	0.00	405795120.55	363109793.55
B. CAPITAL WORK-IN-PROGRESS	324829451.70	12297977.00	0.00	337127428.70	0.00	0.00	0.00	0.00	337127428.70	324829451.70
TOTAL	**687939245.25**	**93193652.00**	**38210348.00**	**742922549.25**	0.00	0.00	0.00	0.00	**742922549.25**	**687939245.25**

Note:- Out of the Total addition of Rs. 41842254/- the amount pertaining to Projects & Core Grants are as follows:-

Projects - Equipment	11023317.00
CDFD Core Grant	30818937.00

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF BALANCE SHEET AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 9 - INVESTMENTS FROM EARMARKED/ENDOWMENT FUNDS	Current Year	Previous Year
1. In Government Securities	0.00	0.00
2. Other approved Securities	0.00	0.00
3. Shares	0.00	0.00
4. Debentures and Bonds	0.00	0.00
5. Subsidiaries and Joint Ventures	0.00	0.00
6. Others (to be specified) - STDRs (Annexure - L)	78308000.00	80808000.00
TOTAL	**78308000.00**	**80808000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF BALANCE SHEET AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 10 - INVESTMENTS - OTHERS (Annexure - M)	Current Year	Previous Year
1. In Government Securities	0.00	0.00
2. Other approved Securities	0.00	0.00
3. Shares	0.00	0.00
4. Debentures and Bonds : UTI Bonds	936360.00	936360.00
5. Subsidiaries and Joint Ventures	0.00	0.00
6. Others (to be specified) - STDRs (CPF), CDFD CP FUND A/c	32787977.32	26410277.32
TOTAL	**33724337.32**	**27346637.32**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF BALANCE SHEET AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 11 - CURRENT ASSETS, LOANS, ADVANCES ETC.	Current Year		Previous Year	
A. CURRENT ASSETS:				
1. Inventors:				
a) Stores and Spares	0.00		0.00	
b) Loose Tools	0.00		0.00	
c) Stock-in-trade				
Finished Goods	0.00		0.00	
Work-in-progress	0.00		0.00	
Raw Materials	0.00	0.00	0.00	0.00
2. Sundry Debtors:				
a) Debts Outstanding for a period exceeding six months				
b) Others - Life Membership Fees	165935.00	165935.00	165935.00	165935.00
3. Cash balances in hand (including cheques/drafts and imprest):		160550.00		65550.00
4. Bank Balances:				
a) With Scheduled Banks:				
-On Current Accounts	55687650.25		42391687.25	
-On Deposit Accounts (includes margin money)	0.00		0.00	
-On Savings Accounts	7645412.22	63333062.47	6860352.72	49252039.97
b) With non-Scheduled Banks:				
-On Current Accounts	0.00		0.00	
-On Deposit Accounts	0.00		0.00	
-On Savings Accounts	0.00	0.00	0.00	0.00
5. Post Office-Savings Accounts				0.00
TOTAL (A)		**63659547.47**		**49483524.97**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF BALANCE SHEET AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 11 - CURRENT ASSETS, LOANS, ADVANCES, ETC.	Current Year		Previous Year	
B. LOANS, ADVANCES AND OTHER ASSETS				
1. Loans:				
a) Staff	0.00		0.00	
b) Other Entities engaged in activities/objectives similar to that of the Entity	0.00	0.00	0.00	0.00
2. Advances and other amounts recoverable in cash or in kind or for value to be received:				
a) On Capital Account (Annexure - J)	249079458.51		245684551.51	
b) Prepayments - Deposits (Annexure- K)	19345407.00		16334115.00	
c) Others	0.00	268424865.51	0.00	262018666.51
3. Income Accrued:				
a) On Investments from Earmarked/Endowment Funds	0.00		0.00	
b) On Investments - Others	0.00		0.00	
c) On Loans and Advances	0.00		0.00	
d) Others	0.00	0.00	0.00	0.00
4. Claims Receivable:				0.00
TOTAL (B)		268424865.51		262018666.51
TOTAL (A+B)		**332084412.98**		**311502191.48**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF INCOME & EXPENDITURE AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 12 - INCOME FROM SALES/SERVICES	Current Year	Previous Year
1) Income from Sales		
a) Sale of Finished Goods	0.00	0.00
b) Sale of Raw Material	0.00	0.00
c) Sale of Scraps	0.00	58500.00
2) Income from Services		
a) Labour and Processing Charges	0.00	0.00
b) Professional/Consultancy Services (Analysis Charges)	3545801.50	0.00
c) Agency Commission and Brokerage	0.00	0.00
d) Maintenance Services (Equipment/Property)	0.00	0.00
e) Others (Specify)	0.00	0.00
TOTAL	**3545801.50**	**58500.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF INCOME & EXPENDITURE AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 13 - GRANTS/SUBSIDIES	Current Year	Previous Year
(Irrevocable Grants & Subsidies Received)		
1) Central Government (DBT Plan Grant-in-Aid)	185000000.00	158700000.00
2) State Government (s)	0.00	0.00
3) Government Agencies	0.00	0.00
4) Institutions/Welfare Bodies	0.00	0.00
5) International Organisations	0.00	0.00
6) Others (Specify)	0.00	0.00
TOTAL	**185000000.00**	**158700000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF INCOME & EXPENDITURE AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 14 - FEES/SUBSCRIPTIONS	Current Year	Previous Year
1) Entrance Fees	0.00	0.00
2) Annual Fees/Subscriptions	0.00	0.00
3) Seminar/Program Fees	0.00	0.00
4) Consultancy Fees	0.00	0.00
5) Others (Specify)	0.00	0.00
	0.00	0.00
TOTAL	**0.00**	**0.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF INCOME & EXPENDITURE AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 15 - INCOME FROM INVESTMENTS	Investment from Earmarked Fund		Investments - Others	
(Income on Invest from Earmarked/Endowment Funds transferred to Funds)	Current Year	Previous Year	Current Year	Previous Year
1) Interest				
a) On Govt. Securities	0.00		0.00	
b) Other Bonds/Debentures	0.00	0.00	0.00	0.00
2) Dividends				
a) On Shares	0.00		0.00	
b) On Mutual Fund Securities	0.00	0.00	0.00	0.00
3) Rents	0.00	0.00	0.00	0.00
4) Others (Specify) STDRs	789164.00	4816013.00	0.00	0.00
TOTAL	**789164.00**	**4816013.00**	**0.00**	**0.00**
TRANSFERRED TO EARMARKED/ENDOWMENT FUNDS				

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF INCOME & EXPENDITURE AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 16 - INCOME FROM ROYALITY, PUBLICATIONS ETC.	Current Year	Previous Year
1) Income from Royality	0.00	0.00
2) Income from Publications	0.00	0.00
3) Others (Specify)	0.00	0.00
TOTAL	0.00	0.00

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF INCOME & EXPENDITURE AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 17 - INTEREST EARNED	Current Year	Previous Year
1) On Term Deposits		
a) With Scheduled Banks	2322441.00	82341.00
b) With Non-Scheduled Banks	0.00	0.00
c) With Institutions	0.00	0.00
d) Others	0.00	0.00
2) On Savings Accounts		
a) With Scheduled Banks	229789.00	116256.00
b) With Non-Scheduled Banks	0.00	0.00
c) Post Office Savings Accounts	0.00	0.00
d) Others	0.00	0.00
	0.00	0.00
3) On Loans		
a) Employees/Staff	0.00	0.00
b) Others	0.00	0.00
4) Interest on Debtors and Other Receivables	0.00	0.00
TOTAL	**2552230.00**	**198597.00**
Note - Tax deducted at source to be indicated		

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF INCOME & EXPENDITURE AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 18 - OTHER INCOME	Current Year	Previous Year
1) Profit on Sale/disposal of Assets:		
a) Owned assets	0.00	0.00
b) Assets acquired out of grants, or received free of cost	0.00	0.00
2) Export Incentives realized	0.00	0.00
3) Fees for Miscellaneous Services	0.00	0.00
4) Miscellaneous Income:		
Sundry receipts	38031.00	744970.00
Sale of tender forms	77500.00	61500.00
Guest House receipts	27900.00	23950.00
Hostel receipts	12575.00	11825.00
Application Fees	121090.00	93700.00
Interest on HBA Advance	6308.00	27927.00
Interest on Computer Advance	521.00	0.00
Interest on Vehicle Advance	4628.00	0.00
TOTAL	**288553.00**	**963872.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF INCOME & EXPENDITURE AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 19 - INCREASE/(DECREASE) IN STOCK OF FINISHED GOODS & WORK IN PROGRESS	Current Year	Previous Year
a) Closing stock		
-Finished Goods	0.00	0.00
-Work-in-progress	0.00	0.00
Total (a)	0.00	0.00
b) Less: Opening Stock		
- Finished Goods	0.00	0.00
- Work-in-progress	0.00	0.00
Total (b)	0.00	0.00
NET INCREASE/(DECREASE) [a-b]	**0.00**	**0.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF INCOME & EXPENDITURE AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 20 - ESTABLISHMENT EXPENSES	Current Year	Previous Year
a) Salaries and Wages	64482657.00	58453457.00
b) Allowances and Bonus	294502.00	240737.00
c) Contribution to Provident Fund	2584414.00	2305393.00
d) Contribution to Other Fund (Specify)	0.00	0.00
e) Staff Welfare Expenses - Medical charges	1499162.00	1389524.00
f) Expenses on Employees Retirement and Terminal Benefits	627436.00	966386.00
g) Others (specify) - Staff leased House	0.00	15492.00
TOTAL	**69488171.00**	**63370989.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF INCOME & EXPENDITURE AS AT 31st MARCH 2011

(Amount - Rs.)

	SCHEDULE 21 - OTHER ADMINISTRATIVE EXPENSES, ETC.	Current Year	Previous Year
1	Purchases (Consumables)	28907039.00	17188298.00
2	Labour and processing expenses	0.00	0.00
3	Cartage and Carriage Inwards	0.00	0.00
4	Electricity and power & Water Charges	15453669.00	10996083.00
5	Water charges	0.00	0.00
6	Insurance	0.00	0.00
7	Repairs and Maintenance	17634146.00	16227158.00
8	Excise Duty	0.00	0.00
9	Rent, Rates and Taxes	16183639.00	17343170.00
10	Vehicles Running and Maintenance	691891.00	844972.00
11	Postage, Telephone and Communication Charges	2090345.00	1597656.00
12	Printing and Stationary	1297775.00	838824.00
13	Travelling and Conveyance Expenses	7455620.00	6736314.00
14	Expenses on Seminar/Workshops	0.00	0.00
15	Subscription Expenses	34941.00	23128.00
16	Expenses on Fees (Membership Fees)	55915.00	49160.00
17	Auditors Remuneration	19854.00	19854.00
18	Hospitality Expenses (Meeting Expenses)	1042842.00	1623309.00
19	Professional Charges (Legal Expenses incl. Patent charges)	3974647.00	4811881.00
20	Provision for Doubtful Debts/Advances - Workshop	0.00	0.00
21	Irrecoverable Balances Written-off	0.00	0.00
22	Packing Charges	0.00	0.00
23	Freight and Forwarding Expenses	0.00	0.00
24	Distribution Expenses	0.00	0.00
25	Advertisement and Publicity	6176174.00	4001687.00

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF INCOME & EXPENDITURE AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 21 - OTHER ADMINISTRATIVE EXPENSES, ETC.		Current Year	Previous Year
26	Hindi / Foundation Day expenses	11580.00	44424.00
27	Bank charges	3881.00	6830.00
28	Security & Cleaning contract charges	12980676.00	10621730.00
29	Internet leased line charges	13500.00	1640095.00
30	Training Course / Symposia	126525.00	162629.00
	TOTAL	**114154659.00**	**94777202.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF INCOME & EXPENDITURE AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 22 - EXPENDITURE ON GRANTS, SUBSIDES, ETC.	Current Year	Previous Year
a) Grants given to Institutions/Organisations	0.00	0.00
b) Subsidies given to Institutions/Organisations	0.00	0.00
TOTAL	**0.00**	**0.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

SCHEDULES FORMING PART OF INCOME & EXPENDITURE AS AT 31st MARCH 2011

(Amount - Rs.)

SCHEDULE 23 - INTEREST	Current Year	Previous Year
a) On Fixed Loans	0.00	0.00
b) On Other Loans (including Bank Charges)	0.00	0.00
c) Others	0.00	0.00
TOTAL	**0.00**	**0.00**

Schedule 24: Significant Accounting Policies, and Schedule 25: Contingent Liabilities & Notes on Account for the period ended 31/03/11

1. Method of Accounting:

a. The accounting system adopted by the organization is on “Cash basis”.

b. The organization has been allocating plan grant-in-aid under the “Non-recurring” & “Recurring” heads.

2. Revenue recognition:

Income comprises of Grant-in-Aid, Internal resources through services and interest from short term deposits. Income accounted on the basis of the Cash/DD/Cheques/Cr notes received.

3. Fixed Assets:

(a) Fixed assets are stated at cost. Cost includes freight, duties, and taxes etc.

(b) Depreciation: No depreciation on the fixed assets is charged and as such no ageing of fixed assets are being done.

(c) Capital work in progress has been entered to the extent of the last running account bills paid.

(d) Realization on sale of obsolete/surplus fixed assets which is not required for the purpose of research activities are adjusted against capital cost.

4. Inventories:

All purchases of chemicals, glassware and other consumables have been charged to consumption at the time of purchase.

5. Foreign Currency transactions:

Foreign Currency transactions are recognized in the books at the exchange rates prevailing on the date of transaction.

6. Investments:

Investments in STDR’s are stated at book values.

7. Advances:

It is observed from the objection book register that advances to suppliers for consumables & equipments are to be reconciled and adjustment entries are to be passed in the books of accounts.

8. The previous year balances have been regrouped/rearranged, wherever necessary.

Director, CDFD | Head Finance & Accounts | for **Bapuji & Venkat**
Chartered Accountants
[K VENKATACHARYULU]

Place: Hyderabad
Date: 23/06/11

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

CLARIFICATION ON NOTES ON ACCOUNTS: 2010-11

- Notes on Accounts 1 to 6 & 8: Method of Accounting/ Revenue recognition/Fixed Asset/Inventories/ Foreign Currency transactions/Investments:

  These are all only informatory items.

- Notes on Accounts 7: Advances:

  The observation of the audit has been noted. The action has already been initiated to reconcile the objection book register.

E V RAO
Head, Finance & Accounts,
CDFD

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS
Details of closing balances of various Earmarked / Endowment Funds (Refer Sch-3)
for the year ended 31st March 2011

Amount in Rs.

Previous year	P No	Particulars	Current Year
-630047.00	P-03	"Transgenesis and Genetic basis of Pathogen Resistance in the Silkworm, *Bombyx Mori*	-630047.00
0.00	P-04	"Silkworm Breeding for Productivity improvement of silk	0.00
244305.00	P-09	"NMITLI Project on – Latent *M.Tuberculosis:* New targets, Drug delivery systems, Bio enhancers & Therapeutics"	244305.00
-28332.00	P-10	"Role of upstream sequence elements in Hyper activation of transcription from *Baculovirus polyhedrin* gene promoter"	-28332.00
6737.00	P-13	"Programme to delineate gene functions in the post – genomics era by a systematic two gene knockout method"	6737.00
0.00	P-15	"The Helicobacter Pylori genome programme – Genome sequencing, functional analysis and comparitive genomics of the strains obtained from Indian patients"	0.00
-687887.00	P-17	"Studies on inosital-phosphate synthesis – a novel enzyme from *Mycobacterium tuberculosis* H37RV" – Transfer from IMTECH, Chandigarh	-687887.00
-274286.00	P-18	"Mapping of receptor binding site on the Eythrocyte binding of malaria parasite"	-274286.00
0.00	P-19	"Construction of Integrated RAPD, RFLP and Microsatellite linkage map of the Silkworm, *Bombyx mori* and its corelation with the Phenotypic linkage Map"	0.00
-1888111.00	P-20	"Genomic Micro array R&D Programmes on infectious diseases and Neurological Disorders"	-1888111.00
0.00	P-21	Development of Versatile, portable software for Bio-informatics	0.00
0.50	P-22	"Biotechnology for leather – towards cleaner processing"	0.50
-34495.00	P-23	"Development of PCR base assays for detection of GMO'S"	-34495.00
-529111.00	P-25	"Functional studies of Human Immuno - deficiency Virus Type– 2 (HIV-2) Viral protien X (VPX)"	-529111.00
-79533.00	P-26	191ng cells of Escherichia coli"	-79533.00
-37624.00	P-28	*Baculovirus* resistance in transgenic silkworms	-37624.00
-310302.00	P-29	"Development of Hospital Surveillance system by advanced diagnostics method & Molecular DNA fingerprinting techniques"	-310302.00
2124902.00	P-30	"Transcription termination and anti termination in E. coli"	2045696.00
827383.00	P-31	Role of K-ras in Lung type II epithelial cells	746453.00
-234000.00	P-33	"Molecular and Epidemiological characterisation of cryptosporidium – An enteric protozoon parasite"	-234000.00
26334.00	P-34	"Molecular analysis of lepidopteran – specific immune protiens from silkmoths"	26334.00
-283883.00	P-35	"Identification, Characterization and Physical mapping of Z-Chromosome linked genes of the silk worm, *Bombyx mori*"	-283883.00
2073896.00	P-36	"Development of Artificial retina using Bacterio rhodospin and genetically engineered analogues"	2073896.00
-226058.00	P-40	"Antioxidants as a potential immuno adjuvant in anti tuberculosis immunotherapy"	-226058.00
1873605.00	P-41	"Construction, characterization and analysis of expressed sequences from silkworm"	1873605.00
-2219464.00	P-42	"Structural and functional studies on *Mycobacterium tuberculosis* heat shock proteins".	-2237285.00
754048.70	P-43	"A generalized mechanism of transcription termination in prokaryotes: a quest for mechanism based transcription inhibitors for microbial pathogens".	685906.70
-457538.00	P-44	"Understanding of role of Ras and NO / iNOS signalling in promotion of hepatocellular carcinomas with persistent HBV infection"	-457538.00
624070.00	P-45	Specialized chromatin structures as epigenetic imprints to distinguish parental alleles".	605714.00
0.00	P-46	"Effect of reactive oxygen species (ROS) on immune response : Relevance in immunosuppression and Pathogenesis"	0.00
-1586965.00	P-47	Research cum Training for DRDO Programme	-1586965.00
151826.00	P-48	'Molecular characterization of human liver stem cells for use in the treatment of hepatic diseases'.	151826.00
0.00	P-49	"The *Mycobacterium* W genome program : Complete genome sequencing and comparative genomics"	0.00
470313.00	P-49A	Grant sanctioned by International Atomic Energy	470313.00
0.00	P-50	"Cervical cancer prevention by multiple strategies in rural community in Andhra pradesh"	0.00
-284065.00	P-51	"Understanding the mechanism of doxorubicin resistance in breast cancer celline MCF-7"	-284065.00
-1231118.00	P-52	"Nucleo Cytoplasmic transport of HIV – 1 Vpr"	-1231118.00
0.00	P-53	Collaborative research project on molecular ecology and systematics	0.00
-37877.00	P-54	"Study of viability of *Mycobacterium leprae* in clinical samples and possibility of its presence in the environment using nucleic acid amplification techniques."	-37877.00
224.00	P-55	"Identification of DNA Markers for baculovirus resistance in silkworm, *Bombyx mori*"	224.00
-1231164.00	P-56	"Genetics of transcription-replication interplay and of stress adaptation in bacteria"	-1231164.00
0.00	P-57	Improved genome annotation through a combination of machine learning and experimental methods: *Plasmodium falciparum* as a case study.	0.00
0.00	P-58	"Indo-Malaysian collaboration in Bioinformatics: Development and maintenance of a web-portal hosting databases and tools of common interest"	0.00
0.00	P-58A	Functional Genomics on Rice	0.00
-2215024.00	P-59	"An integrated Approach towards understanding the biology of *Mycobacterium tuberculosis:* Genetic, biochemical, immunological and structural analyses."	-2215024.00
482124.00	P-60	"National Database of Prevalent Genetic Disorders in India: Development, Curation and Services"	482124.00
-280000.00	P-61	"Dissection of a novel phenotype of lethal accumulation of potassium in *Escherichia coli* mutants defective in thioredoxin/thioredoxin reductase and nucleoied protein H-NS"	-280000.00
-278928.00	P-62	"HIV – 1 Pathogenesis: Role of Integrate in Reverse Transciption and Nuclear Transport of Viral Genome"	-278928.00
-837574.00	P-63	"Upgradation of the existing computing infrastructure at the Bioinformatics facility at CDFD"	-837574.00

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS
Details of closing balances of various Earmarked / Endowment Funds (Refer Sch-3)
for the year ended 31st March 2011

Amount in Rs.

Previous year	P No	Particulars	Current Year
-158.00	P-64	Biotechnology for Leather: Towards cleaner processing phase-II	-158.00
-582647.00	P-65	"Molecular, genetic and functional analysis of the chromosomal plasticity region of the gastric pathogen *Helicobater pylori*"	-582647.00
7477508.00	P-65A	APEDA - CDFD Centre for Basmati DNA Analysis	16381715.00
-681246.00	P-66	Human Epigenome Variation: Analysis of CpG island methylation in chromosomes 18 and Y, and in some Hox, insulin signaling and chromatin reprogramming genes	-681246.00
-113545.00	P-67	Identification of novel Esophageal Squamous cell carcinoma (ESCC) genes by using a combination of array-based CGH and gene expression micro arrays	-113545.00
-59874.00	P-68	Identification of High risk individual with pre-cancerous states of esophageal cancer.	-59874.00
-159363.00	P-69	ICMR adhoc New Scheme 'Understanding the role of PE/PPE family of *M tuberculosis* in the activation of HIV virus type I long terminal repeat (HIV-ILTP)	0.00
-21336.00	P-70	Identification of disease causing mutations in familial hypertrophic cardiomyopathy (FHC) patients from Andhra Pradesh	-21336.00
-1615249.00	P-71	Referral Centre for Genetic fidelity testing of tissue culture raised plants	-591490.00
-1421653.00	P-72	Nuances of Non coding DNA near insulin-responsive genes	-1421653.00
-857136.00	P-73	Identification and characterization of pancreatic cancer genes located within novel localized cpy number alterations	-857136.00
0.00	P-74	Molecular basic of insect plant interactions in rice under the national fund for basic and strategic research in agriculture	0.00
-10840.00	P-75	Preparing blueprint for the macromolecular crystallography beamline at Indus-II synchrotron source	-10840.00
-50234.00	P-76	A study of Molecular Markers in childhood Autism with special references to nuclear factors - APPA B"	-50234.00
126471.00	P-77	Functional characterization of *Mycobacterium tuberculosis* PE/PPE proteins having SH3 binding domain: Understanding their role in modulating macrophage functions	124277.00
1304.00	P-78	Task Force - IMD Newborn Screening for Congenital Hypthyroidism & Congenital Adrenal Hyperplasis: A Multicentric Study"	1304.00
-2636028.00	P-79	Understanding the role of AGE proteins in inducing inflammatory responses and its regulation	-1900986.00
-28471.00	P-80	Referral Centre for Detection of Genetically Modified Foods employing DNA - based Markets	-53994.00
0.00	P-80A	Fluorescent amplified fragment length polymorphism analysis of different genomic species - development of species specific markers for the identification of Leptospirosis	0.00
10330961.00	COE-I	COE for Genetics and Genomics of silkmoths	-13198864.00
-584848.00	P-81	Reconstructing cellular Networks: Two-Component Regulatory Systems	214215.00
0.00	P-81A	Financial Assistance for award of JC Bose Fellowship to Dr J Gowrishankar	107800.00
675598.00	P-82	Functional Genomic Analysis of Candida glabrata-macrophage	423591.00
-1093034.00	P-83	Prokaryotic Transcription Termination Factor, Rho: Mechanism of Action and Biology	-1155594.00
-86075.00	P-83A	Understanding the mechanism of Azadirachtin-mediated cell signaling: role in anti-inflammation and anti-tumorigenesis	-126140.00
-1150.00	P-84	Preparing for tuberculosis vaccine efficacy trials: Baseline epidemiology, improved diagnosis, markers of protection and phase I/II trials	-1150.00
655960.00	P-84A	Human epigenetic to the rescue of Human Identification process: Entriching human DNA from DNA mixture employing antibodiesdirected against 5-methylcytosine followed by whole genome amplification	676641.00
-933501.00	P-85	IdeR associated gene regulatory network in Mycobacteria	-1118755.00
78291.00	P-86	Evaluation of *Mycobacterium* W as an immunotherapeutic against paratuberculosis (John's Disease of cattle)	0.00
-65698.00	P-87	Comparative genomic of wild silkmoths under India-Japan Co-operative Science programme (IJCSP)	-65698.00
-1454733.00	COE-II	DBT Centre of Excellence for Microbial Biology	-4591687.00
282465.00	P-88	Financial Assistance for award of TATA Innovation Fellowship to Dr J Nagaraju	740000.00
-300000.00	P-89	Characterization of *Mycobacterium tuberculosis* transcription machinery and Bacteriophage metagenomics	-300000.00
373213.00	P-90	Role of Yapsins in the Pathobiology of *Candida glabrata*	-451999.00
174154.00	P-91	DNMT3L: Epigenetic correlation with cancer	-787064.00
-73314.00	P-92	Swarnajayanti Fellowship: Designing transcription anti-terminators: a novel apprach for making. new inhibitors of gene expression	-1238545.00
817860.00	P - 93	Virtual Centre of Excellence on multidisciplinary approaches aimed at interventions against tuberculosis	-684179.00
-121469.00	P - 95	Construction of regulatory networks in prokaryotes through protein: Protein interaction predictions and transcription regulation predictions	424041.00
-1187015.00	P - 96	Molecular characterization of sporadic colorectal cancer in the young from India	-655942.00
582700.00	P - 97	Proteome-wide Analysis of serine pyrophosphorylation by inositol pyrophosphates	488524.00
812907.00	P - 98	Role of cell - cell signaling mediated by Diffusible signaling factor (DSF) in *Xanthomonas* virulence	-466554.00
1663500.00	P - 99	Role of inositol Pyrophosphates in eukaryotic cell growth, proliferation and ribosomae biogenesis	-113757.00
0.00	P - 100	Effect of reactive oxygen species on T-Cell immune response: An approach to understand the molecular mechanism of immunosuppression during tuberculosis" - National Bioscience Award	-300000.00
15288801.00	P - 101	Role of inositol pyrophosphates in cell physiology: Investigating the biochemical significance of protein pyrophosphorylation - Senior Fellowship	15688931.00
-483681.00	P - 102	Understanding the role of *Mycobacterium tuberculosis* heat shockprotein 60 as Th1/Th2 immuno modular	-445133.00
0.00	P - 103	National Bioscience Award - Regulation of mast cell signaling, apoptosis and surface receptors	0.00
0.00	P-104	Virtual Centre of Excellence on Epigenetics - Project 4: Epigenetic dynamics in cell types and its potential association with environment and disease	297613.00

Annexure - I

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS
Details of closing balances of various Earmarked / Endowment Funds (Refer Sch-3)
for the year ended 31st March 2011

0.00	P-105	Cloning, characterisation and analysis of chromosomal rearrangements in human genetic disorders	145971.00
0.00	P-106	Clinical, biochemical and molecular analysis of treatable lysosomal storagedisorders	-446056.00
0.00	P-107	IYBA Project - Mechanism and role of bacterial cell-cell signaling molecules in plant defense response	602006.00
0.00	P-108	Establishment of EBV transformed cell lines from families with rare genetic disorders	184023.00
0.00	P-109	Molecular dissection of PI3-Kinase/Akt pathway by suing proteomics based approach: A study to identify novel potential oncogenes and tumor suppressors	1476104.00
0.00	P-110	India-Japan research project title"Identification and analysis of sex determining genes in silkmoths"	24389.00
0.00	P-111	Ramalingaswami Fellowship - Refractoriness mechanism in Mosquito: cracking molecular codes at genomic scale	488631.00
0.00	P-112	Ramanujan Fellowship	803726.00
0.00	P-113	Clinical and molecular genetic analysis of squamous cell carcinoma of the tongue	550715.00
0.00	P-114	Evaluating the Calcineurin-NFAT Pathway and its regulators superoxide dismutase (SOD) AND RCAN1 (regular of Calcineurin) Down Syndrome	1532761.00
0.00	P-115	Setting up of the National Institute of Animal Biotechnology	4559305.00
0.00	P-116	DBT-India and AIST - Japan : Understanding molecular mechanisms controlling dual role of Ras, Sirtuins and CARF in relation to cellular proliferation and senescence: Novel Strategy for developing cancer therapeutics	1692817.00
0.00	P-117	Joint New Indigo Era-Net project titled "*Mycobacterium tuberculosis*:bioinformatic and structural strategies towards treatment	5251500.00
0.00	P-118	Construction of regulatory networks in *Mycobacterium tuberculosis* through analysis of gene expression data and transcription regulation predictions. (MOU with Russian Foundation)	1115770.00
0.00	P-119	Analysis of DNA copy number alterations in esophaeal cancer	560342.00
0.00	P-120	Effect of reactive oxygen species on macrophage signalosome: impact on antigen presentation functions and T Cell priming responses	617000.00
0.00	P-121	Identification and characterization of PTEN regulators	37096.00
18475777.20		**Total**	**16210479.20**

Annexure - II

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS
Details of Fixed Assets Fund (Capitalised portion of Project Grants)
for the year ended 31st March 2011

Amount in Rs.

Previous year	P No	Particulars	Current Year
600000.00	P-03	"Transgenesis and Genetic basis of Pathogen Resistance in the Silkworm, *Bombyx mori*	600000.00
329289.00	P-07	"Collection of well characterised clinical samples and strains of *Mycobacterium tuberculosis* and development of molecular techniques for detection of drug resistant strains – Multi Centric Project"	329289.00
588400.00	P-09	"NMITLI Project on – Latent M.tuberculosis: New targets, Drug delivery systems, Bio enhancers & Therapeutics"	588400.00
47400.00	P-10	"Role of upstream sequence elements in Hyper activation of transcription from Baculovirus *polyhedrin* gene promoter"	47400.00
529750.00	P-12	Molecular genetics and Functional genomics of *M.tuberculosis* patient isolates in India	529750.00
1334600.00	P-13	"Programme to delineate gene functions in the post – genomics era by a systematic two gene knockout method"	1334600.00
5163243.00	P-14	"Comparitive and functional genomics approaches for the identification and characterization of genes responsible for multi drug resistance of *Mycobacterium tuberculosis"*	5163243.00
6000000.00	P-15	"The *Helicobacter pylori* genome programme – Genome sequencing, functional analysis and comparitive genomics of the strains obtained from Indian patients"	6000000.00
1814901.00	P-16	NMITLI Project on – Latent *M.tuberculosis:* New targets, Drug delivery systems, Bio enhancers & Therapeutics	1814901.00
244400.00	P-17	"Studies on inosital-phosphate synthesis – a novel enzyme from Mycobacterium tuberculosis H37RV" – Transfer from IMTECH, Chandigarh	244400.00
344020.00	P-18	"Mapping of receptor binding site on the Eythrocyte binding of malaria parasyte"	344020.00
7246511.00	P-19	"Construction of Integrated RAPD, RFLP and Microsatellite linkage map of the Silkworm, *Bombyx mori* and its corelation with the Phenotypic linkage Map"	7246511.00
27331134.00	P-20	"Genomic Micro array R&D Programmes on infectious diseases and Neurological Disorders"	27331134.00
5300000.00	P-21	Development of Versatile, portable software for Bio-informatics	5300000.00
603747.00	P-22	"Biotechnology for leather – towards cleaner processing"	603747.00
375999.00	P-23	"Development of PCR base assays for detection of GMO'S"	375999.00
600000.00	P-25	"Functional studies of Human Immuno - deficiency Virus Type– 2 (HIV-2) Viral protien X (VPX)"	600000.00
500000.00	P-26	Occurrence of Mutations in Non dividing cells of *Escherichia coli"*	500000.00
260367.00	P-29	"Development of Hospital Surveillance system by advanced diagnostics method & molecular DNA fingerprinting techniques"	260367.00
3746538.00	P-30	"Transcription termination and anti termination in *E. coli"*	3746538.00
3131006.00	P-31	Role of K-ras in Lung type II epithelial cells	3131006.00
4857938.00	P-36	"Development of Artificial retina using Bacterio rhodospin and genetically engineered analogues "	4857938.00
358470.00	P-39	"Computational analysis and functional characterization of mycobacterial protien(s) interacting with macrophase effector – APC functions – an approach to understand the molecular basis of pathogenesis of *M. tuberculosis"*	358470.00
49738.00	P-40	"Antioxidants as a potential immuno adjuvant in anti tuberculosis immunotherapy"	49738.00
3894086.00	P-41	"Construction, characterization and analysis of expressed sequences from silkworm "	3894086.00
9500000.00	P-42	"Structural and functional studies on *Mycobacterium tuberculosis* heat shock proteins".	9500000.00
11970000.00	P-43	"A generalized mechanism of transcription termination in prokaryotes: a quest for mechanism based transcription inhibitors for microbial pathogens".	11970000.00
3313021.00	P-45	Specialized chromatin structures as epigenetic imprints to distinguish parental alleles".	3331377.00
416137.00	P-46	"Effect of reactive oxygen species (ROS) on immune response : Relevance in immunosuppression and Pathogenesis"	416137.00
377567.00	P-47	Research cum Training for DRDO Programme	377567.00
1413292.00	P-48	'Molecular characterization of human liver stem cells for use in the treatment of hepatic diseases'.	1413292.00
198095.00	P-50	"Cervical cancer prevention by multiple strategies in rural community in Andhra pradesh"	198095.00
401738.00	P-51	"Understanding the mechanism of doxorubicin resistance in breast cancer celline MCF-7"	401738.00
1359129.00	P-52	"Nucleo Cytoplasmic transport of HIV – 1 Vpr"	1359129.00
1114495.00	P-53	Collaborative research project on molecular ecology and systematics	1114495.00
1163764.00	P-56	"Genetics of transcription-replication interplay and of stress adaptation in bacteria"	1163764.00
2131403.00	P-57	Improved genome annotation through a combination of machine learning and experimental methods: *Plasmodium falciparum* as a case study.	2131403.00
63000.00	P-58	"Indo-Malaysian collaboration in Bioinformatics: Development and maintenance of a web-portal hosting databases and tools of common interest"	63000.00
32974662.00	P-59	"An integrated Approach towards understanding the biology of Mycobacterium tuberculosis: Genetic, biochemical, immunological and structural analyses."	32974662.00
5720800.00	P-60	"National Database of Prevalent Genetic Disorders in India: Development, Curation and Services"	5720800.00
4308314.00	P-62	"HIV – 1 Pathogenesis: Role of Integrate in Reverse Transciption and Nuclear Transport of Viral Genome"	4308314.00
9637574.00	P-63	"Upgradation of the existing computing infrastructure at the Bioinformatics facility at CDFD"	9637574.00
600585.00	P-64	Biotechnology for Leather: Towards cleaner processing phase-II	600585.00
260000.00	P-65	"Molecular, genetic and functional analysis of the chromosomal plasticity region of the gastric pathogen Helicobater pylori"	260000.00
16909024.00	P-65A	APEDA - CDFD Centre for Basmati DNA Analysis	16921476.00
264430.00	P-66	Human Epigenome Variation: Analysis of CpG island methylation in chromosomes 18 and Y, and in some Hox, insulin signaling and chromatin reprogramming genes	264430.00

Annexure - II

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS
Details of Fixed Assets Fund (Capitalised portion of Project Grants)
for the year ended 31st March 2011

Amount in Rs.

Previous year	P No	Particulars	Current Year
622747.00	P-67	Identification of novel Esophageal Squamous cell carcinoma (ESCC) genes by using a combination of array-based CGH and gene expression micro arrays	622747.00
235593.00	P-69	ICMR adhoc New Scheme 'Understanding the role of PE/PPE family of *M tuberculosis* in the activation of HIV virus type I long terminal repeat (HIV-ILTP)	235593.00
1012807.00	P-70	Identification of disease causing mutations in familial hypertrophic cardiomyopathy (FHC) patients from Andhra Pradesh	1012807.00
1573795.00	P-71	Referral Centre for Genetic fidelity testing of tissue culture raised plants	1573795.00
45653.00	P-72	Nuances of Non coding DNA near insulin-responsive genes	45653.00
1000000.00	P-74	Molecular basic of insect plant interactions in rice under the national fund for basic and strategic research in agriculture	1000000.00
33672.00	P-75	Preparing blueprint for the macromolecular crystallography beamline at Indus-II synchrotron source	33672.00
245266.00	P-76	A study of Molecular Markers in childhood Autism with special references to nuclear factors - APPA B"	245266.00
1541411.00	P-77	Functional characterization of *Mycobacterium tuberculosis* PE/PPE proteins having SH3 binding domain: Understanding their role in modulating macrophage functions	1543605.00
496826.00	P-79	Understanding the role of AGE proteins in inducing inflammatory responses and its regulation	496826.00
4192480.00	P-80	Referral Centre for Detection of Genetically Modified Foods employing DNA - based Markets	4192480.00
77690.00	P-81A	Financial Assistance for award of JC Bose Fellowship to Dr J Gowrishankar	195728.00
1137050.00	P-82	Functional Genomic Analysis of Candida glabrata-macrophage	1387806.00
912255.00	P-83	Prokaryotic Transcription Termination Factor, Rho: Mechanism of Action and Biology	912255.00
388583.00	P-83A	Understanding the mechanism of Azadirachtin-mediated cell signaling: role in anti-inflammation and anti-tumorigenesis	388583.00
44854.00	P-84	Preparing for tuberculosis vaccine efficacy trials: Baseline epidemiology, improved diagnosis, markers of protection and phase I/II trials	44854.00
1139040.00	P-84A	Human epigenetic to the rescue of Human Identification process: Entriching human DNA from DNA mixture employing antibodiesdirected against 5-methylcytosine followed by whole genome amplification	1256286.00
371200.00	P-89	Characterization of *Mycobacterium tuberculosis* transcription machinery and Bacteriophage metagenomics	374630.00
1003190.00	P-90	Role of Yapsins in the Pathobiology of *Candida glabrata*	1054715.00
924523.00	P-91	DNMT3L: Epigenetic correlation with cancer	932151.00
6505192.00	P-92	Swarnajayanti Fellowship: Designing transcription anti-terminators: a novel apprach for making new inhibitors of gene expression	8128158.00
2104275.00	P - 93	Virtual Centre of Excellence on multidisciplinary approaches aimed at interventions against tuberculosis	2389387.00
246320.00	P - 95	Construction of regulatory networks in prokaryotes through protein: Protein interaction predictions and transcription regulation predictions.	246320.00
581900.00	P- 97	Proteome-wide Analysis of Serine pyrophosphorylation by inositol pyrophosphates	597647.00
2159680.00	P- 98	Role of cell - cell signaling mediated by Diffusible signaling factor (DSF) in *Xanthomonas* virulence	2624610.00
1648300.00	P- 99	Role of inositol Pyrophosphates in eukaryotic cell growth, proliferation and ribosomae biogenesis	2272340.00
17784.00	P - 100	Effect of reactive oxygen species on T-Cell immune response: An approach to understand the molecular mechanism of immunosuppression during tuberculosis" - National Bioscience Award	17784.00
1425442.00	P-101	Role of inositol pyrophosphates in cell physiology: Investigating the biochemical significance of protein pyrophosphorylation - Senior Fellowship	3391337.00
450000.00	P-102	Understanding the role of *Mycobacterium tuberculosis* heat shockprotein 60 as Th1/Th2 immuno modular	658171.00
0.00	P-107	IYBA Project - Mechanism and role of bacterial cell-cell signaling molecules in plant defense response	529925.00
0.00	P - 113	Clinical and molecular genetic analysis of squamous cell carcinoma of the tongue	268914.00
8722699.00	COE-I	COE for Genetics and Genomics of silkmoths	11713327.00
8534636.00	COE-II	DBT Centre of Excellence for Microbial Biology	10000000.00
228743430.00		**Total**	**239766747.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS

FOR THE YEAR ENDED 31st MARCH 2011

Annexure: A Forming part of Receipts & Payment a/c

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	I-Remittances	
265031.00	GSLI	342116.00
4403709.00	Income tax	3545182.00
662389.00	LIC	892851.00
388447.00	Professional tax	440959.00
447534.00	Works Tax	371342.00
188478.00	Service Tax	211659.00
595385.00	PPF	781320.00
0.00	Donations	0.00
6950973.00		**6585429.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS

FOR THE YEAR ENDED 31st MARCH 2011

Annexure: B Forming part of Receipts & Payment a/c

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	T.D.S.Recoveries	
673378.00	TDS on professional service	380647.00
2891099.00	TDS on Rent	1544357.00
946429.00	TDS on works / Contractors	872899.00
0.00	TDS on deposits	6386.00
4510906.00		**2804289.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS

FOR THE YEAR ENDED 31st MARCH 2011

Annexure: C Forming part of Receipts & Payment a/c

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	Advance refunds/recovery/Adjst.	
3506494.00	Advances for Consumables	733288.00
7755111.00	Advances for Equipment	29703699.00
265561.00	Advances to staff for L.P	202181.00
6044413.00	Deposits - Customs duty	0.00
736700.00	EMD / Margin money	23092222.00
79350.00	Festival Advances recovery	92400.00
477703.00	H B A	16267.00
161500.00	HSD, LSD & TSD	204000.00
694219.00	LTC Advances	1311816.00
684642.00	Other Advances	73100.00
173590.00	Revolving Advances	154519.00
3422034.00	TA/DA Advances	3682761.00
35268.00	Vehicle / Conveyance A dvance	37728.00
7250000.00	Royalties & Consultancy	249080.00
195937.00	Security Deposit / Retension Money	50000.00
25200.00	Computer Advance - staff	24200.00
2087154.00	Rent Advance	0.00
0.00	Computer Advance - Research Fellows	40838.00
33594876.00		**59668099.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS
FOR THE YEAR ENDED 31st MARCH 2011

Annexure: D Forming part of Receipts & Payment a/c

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	Projects - Receipts	
327500.00	P - 22	0.00
1904000.00	P - 53	0.00
679000.00	P - 64	0.00
17028704.00	P - 65A	9566000.00
845840.00	P - 69	159363.00
628000.00	P - 70	0.00
0.00	P - 71	1808000.00
666200.00	P - 74	0.00
2709000.00	P- 77	0.00
0.00	P- 79	751300.00
300000.00	P- 80	0.00
0.00	P- 81	951800.00
800000.00	P- 81A	1455000.00
1480000.00	P- 82	596000.00
1170400.00	P- 83	0.00
550000.00	P- 83A	0.00
1298850.00	P- 84	0.00
1480000.00	P- 84A	714000.00
400000.00	P- 85	0.00
740000.00	P - 88	1480000.00
0.00	P - 89	300000.00
626000.00	P - 90	0.00
760000.00	P - 91	0.00
0.00	P - 92	3132400.00
0.00	P - 93	657000.00
1006020.00	P - 95	700000.00
1737438.00	P - 96	1251970.00
2027000.00	P - 97	835000.00
3947000.00	P - 98	290000.00
4225000.00	P - 99	0.00
300000.00	P - 100	0.00
18792749.00	P - 101	6784587.00
481319.00	P - 102	1181319.00
0.00	P - 103	300000.00
0.00	P - 104	1437000.00
0.00	P - 105	827000.00
0.00	P - 106	238302.00
0.00	P - 107	2027000.00

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS
FOR THE YEAR ENDED 31st MARCH 2011

Annexure: D Forming part of Receipts & Payment a/c

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	Projects - Receipts	
0.00	P - 108	487000.00
0.00	P - 109	2027000.00
0.00	P - 110	170000.00
0.00	P - 111	1400000.00
0.00	P - 112	1460000.00
0.00	P - 113	1139487.00
0.00	P - 114	2070000.00
0.00	P - 115	5000000.00
0.00	P - 116	2037200.00
0.00	P - 117	5593000.00
0.00	P - 118	1400770.00
0.00	P - 119	800000.00
0.00	P - 120	827000.00
0.00	P - 121	345776.00
7821000.00	COE- I	8913000.00
4589000.00	COE- II	13680000.00
79320020.00		**84793274.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS

FOR THE YEAR ENDED 31st MARCH 2011

Annexure: E Forming part of Receipts & Payment a/c

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	Advances	
238420.00	Advance to staff for local purchases	394883.00
13360502.00	Advances for Consumables	9093263.00
63536388.00	Advances for Equipment	22723544.00
4044415.00	Deposits for Custom duty etc.	3011292.00
2088414.00	EMD / Margin money	20538000.00
93000.00	Festival advances paid	99000.00
60000.00	LSD , HSD & TSD	79000.00
1182112.00	LTC Advance	928731.00
1343177.00	Other Advances	181729.00
151000.00	Revolving Advance	182500.00
2563966.00	TA / DA Advance	3659524.00
0.00	Royalties & Consultancy	0.00
943323.00	Security Deposit / Retension Money	410000.00
7758.00	HBA	0.00
0.00	Computer Advance - Research Fellows	245000.00
89612475.00		**61546466.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS

FOR THE YEAR ENDED 31st MARCH 2011

Annexure: F Forming part of Receipts & Payment a/c

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	I-Remittances paid	
202410.00	GSLI	402196.00
4386020.00	Income tax	3559943.00
662389.00	LIC	892851.00
387697.00	Professional tax	441639.00
621405.00	Works Tax	318037.00
188478.00	Service Tax	211659.00
595385.00	PPF	768160.00
7043784.00		**6594485.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS

FOR THE YEAR ENDED 31st MARCH 2011

Annexure: G Forming part of Receipts & Payment a/c

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	TDS remitted in Central Govt. a/c	
812934.00	TDS on professional service	327736.00
4202516.00	TDS on Rent	1539198.00
1010629.00	TDS on works / Contractors	835074.00
0.00	TDS on deposits	6386.00
6026079.00		**2708394.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS

FOR THE YEAR ENDED 31st MARCH 2011

Annexure: H Forming part of Receipts & Payment a/c

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	Projects - Expenditure	
1000000.00	P - 4	0.00
327420.00	P - 22	0.00
0.00	P - 30	79206.00
0.00	P - 31	80930.00
1359078.00	P - 42	17821.00
338663.00	P - 43	68142.00
0.00	P - 45	18356.00
339070.00	P - 46	0.00
0.00	P - 47	0.00
0.00	P - 49	0.00
157056.00	P - 49A	0.00
57663.00	P - 50	0.00
1195711.00	P - 53	0.00
3394100.00	P - 57	0.00
267773.00	P - 58	0.00
200000.00	P - 58A	0.00
59540.00	P - 59	0.00
15485.00	P - 60	0.00
659403.00	P - 64	0.00
1271672.00	P - 65A	661793.00
-3476.00	P - 66	0.00
9058.00	P - 67	0.00
98395.00	P - 69	0.00
151467.00	P - 70	0.00
2036094.00	P - 71	784241.00
291935.00	P - 72	0.00
315249.00	P - 73	0.00
497421.00	P - 74	0.00
-8033.00	P - 76	0.00
1954959.00	P - 77	2194.00
913651.00	P - 79	16258.00
1436927.00	P - 80	25523.00
443800.00	P - 81	152737.00
800000.00	P - 81A	1347200.00
1599413.00	P - 82	848007.00
1490258.00	P - 83	62560.00
585692.00	P - 83A	40065.00
1857502.00	P - 84A	693319.00

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS

FOR THE YEAR ENDED 31st MARCH 2011

Annexure: H Forming part of Receipts & Payment a/c

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	Projects - Expenditure	
1058096.00	P - 85	185254.00
256095.00	P - 86	78291.00
597535.00	P - 88	1022465.00
300000.00	P - 89	300000.00
1310327.00	P - 90	825212.00
2008725.00	P - 91	961218.00
9337864.00	P - 92	4297631.00
4033440.00	P - 93	2159039.00
874580.00	P - 95	154490.00
1454003.00	P - 96	720897.00
1444300.00	P - 97	929176.00
3134093.00	P - 98	1569461.00
2561500.00	P - 99	1777257.00
300000.00	P - 100	300000.00
3503948.00	P - 101	6384457.00
965000.00	P - 102	1142771.00
0.00	P - 103	300000.00
0.00	P - 104	1139387.00
0.00	P - 105	681029.00
0.00	P - 106	684358.00
0.00	P - 107	1424994.00
0.00	P - 108	302977.00
0.00	P - 109	550896.00
0.00	P - 110	145611.00
0.00	P - 111	911369.00
0.00	P - 112	656274.00
0.00	P - 113	588772.00
0.00	P - 114	537239.00
0.00	P - 115	440695.00
0.00	P - 116	344383.00
0.00	P - 117	341500.00
0.00	P - 118	285000.00
0.00	P - 119	239658.00
0.00	P - 120	210000.00
0.00	P - 121	308680.00
36127668.00	COE - I	37209825.00
17844214.00	COE - II	12049954.00
112224334.00		**87058572.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS

FOR THE YEAR ENDED 31st MARCH 2011

Annexure: I Forming part of Balance Sheet

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	CDFD C.P. FUND ACCOUNT	
23241865.32	Opening Balance	27346637.32
	Add:	
5812355.00	Employees subscription / refunds	6786724.00
	Transfer from other departments	769851.00
2765162.00	Institute contribution (incl. Projects staff)	3123315.00
133561.00	Interest received	68411.00
31952943.32		38094938.32
4606306.00	Less: Advances/withdrawals/Transfer/ Adjst	4370601.00
27346637.32		**33724337.32**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS

FOR THE YEAR ENDED 31st MARCH 2011

Annexure: J Forming part of Balance sheet

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	LOANS AND ADVANCES	
62468714.00	Advances for Consumables	70828689.00
154118442.45	Advances for Equipment	147138287.45
234580.50	Advances to staff for L.P	427282.50
25512.00	DBT PDF (Stipend receivable)	25512.00
58800.00	Festival Advance	65400.00
4310.00	G.S.L.I Recovery	4310.00
907246.00	Grant receivable - Host meetings	907246.00
582372.00	LTC Advance	199287.00
4931474.00	Other Advances	5040103.00
240569.00	Rent Advance	240569.00
133665.00	Revolving Advances	161646.00
635231.56	TA/DA Advance & Recoupments	611994.56
3000000.00	CDFD Staff Reserve Fund	3000000.00
1979945.00	DBT JRF A/c (Stipend receivable)	1396829.00
4788357.00	EMRC A/c (Stipend receivable)	4866183.00
249141.00	ICMR A/c (Stipend receivable)	383904.00
681501.00	Indo - Japan Workshop	681501.00
10000000.00	NIMS - Advance	10000000.00
72.00	Service Tax	72.00
250099.00	UGC (Stipend receivable)	2058481.00
394494.00	Advance for workshop	394494.00
26.00	CPF Subscription	0.00
0.00	Computer advance - Research Fellows	204162.00
0.00	CPF Advance Recovery	9350.00
0.00	DST Inspire	17109.00
0.00	Transcription Assembly Meeting	417047.00
245684551.51		**249079458.51**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS

FOR THE YEAR ENDED 31st MARCH 2011

Annexure: K Forming part of Balance sheet

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	DEPOSITS	
4317957.00	A.P.Transco	4317957.00
11713171.00	Balmer Lawrie - Customs duty	14713171.00
35900.00	Gas agencies	35900.00
15000.00	Internet	15000.00
185000.00	Telephones	185000.00
47680.00	APSRTC	47680.00
12000.00	University Filling Station	12000.00
7407.00	Others	18699.00
16334115.00		**19345407.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS

FOR THE YEAR ENDED 31st MARCH 2011

Annexure: L Forming part of Balance sheet

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	INVESTMENT A/C	
12270000.00	Internal resources / Core	12270000.00
57238000.00	Project Funds	54738000.00
10600000.00	Collaboration Funds	10600000.00
700000.00	Workshop Funds	700000.00
80808000.00		**78308000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS
FOR THE YEAR ENDED 31st MARCH 2011

Annexure: M Forming part of Balance sheet

Previous Year Amount Rs.	Particulars	Current Year Amount Rs.
	CDFD C.P.FUND INVESTMENT A/C	
660170.00	60229.549 Units of UTI BOND FUND	660170.00
276190.00	21616.5080 Units of UTI BOND FUND	276190.00
22202519.00	Fixed deposits	28702519.00
4207758.32	CDFD C.P. FUND a/c	4085458.32
27346637.32		**33724337.32**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-03 : D.B.T Project on "TRANSGENESIS & GENETIC BASIS OF PATHOGEN RESISTANCE IN THE SILKWORM, *Bombyxmori*"

P.I: Dr J NAGARAJU

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			630047.00	Opening Balance	630047.00
0.00	Opening Balance	0.00	0.00	Equipment	0.00
0.00	Grant in aid	0.00	0.00	Salaries - Manpower	0.00
			0.00	Consumables	0.00
			0.00	Travel	0.00
			0.00	Contingencies	0.00
0.00		0.00	630047.00		630047.00
630047.00	Excess of expenditure over income	630047.00			
630047.00		**630047.00**	**630047.00**		**630047.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-09 - "CSIR, NMITLI Project on - Latent M.Tuberculosis: New targets, Drug delivery systems, Bio enhancers & Therapeutics"

P.I.: Dr SEYED E HASNAIN

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2001 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
244305.00	**Opening Balance**	244305.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
244305.00		244305.00	0.00		0.00
			244305.00	Closing Balance	244305.00
244305.00		**244305.00**	**244305.00**		**244305.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-10 : DST Project on "ROLE OF UPSTREAM SEQUENCE ELEMENTS IN HYPERACTIVATION OF TRANSCRIPTION FROM *BACULOVIRUS POLYHEDRIN* GENE PROMOTER" -

P.I : Dr M D BASHYAM

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	28332.00	Opening Balance	28332.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	28332.00		28332.00
28332.00	Excess of expenditure over income	28332.00			
28332.00		**28332.00**	**28332.00**		**28332.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-13 : DBT Project on "PROGRAMME TO DELINATE GENE FUNCTIONS IN THE POST - GENOMICS ERA BY A SYSTEMATIC TWO GENE KNOCKOUT METHOD"

P.I : Dr J GOWRISHANKAR

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
6737.00	**Opening Balance**	6737.00	0.00	Salaries- Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
6737.00		6737.00	0.00		0.00
			6737.00	Closing balance	6737.00
6737.00		**6737.00**	**6737.00**		**6737.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-17 : DST Project on "STUDIES ON INOSITAL - PHOSPHATE SYNTHESIS - A NOVEL ENZYME FROM *MYCOBACTERIUM TUBERCULOSIS* - H37RV"

P.I : Dr SHEKHAR C MANDE

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			687887.00	Opening Balance	687887.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Over heads	0.00
			0.00	Equipment	0.00
0.00		0.00	687887.00		687887.00
687887.00	Excess of expenditure over income	687887.00			
687887.00		**687887.00**	**687887.00**		**687887.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-18 : DST Project on "MAPPING OF RECEPTOR BINDING SITE ON THE EYTHROCYTE BINDING OF MALARIA PARASITE"

P.I : Dr AKASH RANJAN

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	274286.00	Opening balance	274286.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	274286.00		274286.00
274286.00	Excess of expenditure over income	274286.00			
274286.00		**274286.00**	**274286.00**		**274286.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P - 20 : DBT Project on "Genomic Micro array R&D programmes on infectious diseases and Neurological Disorders"
P.I: Dr M D BASHYAM
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			1888111.00	Opening balance	1888111.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	1888111.00		1888111.00
1888111.00	Excess of expenditure over income	1888111.00	0.00	Closing balance	0.00
1888111.00		**1888111.00**	**1888111.00**		**1888111.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-22 : CSIR Project on "Biotechnology for Leather towards cleaner processing"
P.I : Dr J GOWRISHANKAR
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year.	Payments	Current Year
			79.50	Opening balance	0.00
	Opening Balance	0.50	0.00	Salaries- Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
327500.00	Cheque cancelled	0.00	0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Equipment	0.00
			327420.00	Project funds refund	0.00
327500.00		0.50	327499.50		0.50
0.00	Excess of expenditure over income	0.00	0.50	Closing balance	0.50
327500.00		**0.50**	**327500.00**		**0.50**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-23: DBT Project on "Development of PCR base assays for detection of GMO'S"
P.I : Dr J NAGARAJU
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			34495.00	Opening balance	34495.00
0.00	**Opening Balance**	0.00	0.00	Salaries- Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	34495.00		34495.00
34495.00	Excess of expenditure over income	34495.00	0.00	Closing balance	0.00
34495.00		**34495.00**	**34495.00**		**34495.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-25 : DBT Project on "Functional studies of Human Immuno deficiency virus type-2(HIV-2), Viral protein X(VPX)"
P.I : Dr S MAHALINGAM
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			529111.00	Opening balance	529111.00
0.00	**Opening Balance**	0.00	0.00	Salaries- Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	529111.00		529111.00
529111.00	Excess of expenditure over income	529111.00			
529111.00		**529111.00**	**529111.00**		**529111.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-26 : IFCPAR Project on "Occurrence of Mutations in Non-dividing cells of *Escherichia coli*"
P.I: Dr J GOWRISHANKAR
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			79533.00	Opening balance	79533.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	79533.00		79533.00
79533.00	Excess of expenditure over income	79533.00			
79533.00		**79533.00**	**79533.00**		**79533.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-28 : IFCPAR Project on "Baculovirus - Resistance in transgenic silkworms"
P.I : Dr J NAGARAJU
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			37624.00	Opening balance	37624.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	37624.00		37624.00
37624.00	Excess of expenditure over income	37624.00			
37624.00		**37624.00**	**37624.00**		**37624.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-29 : DST Project on "Development of Hospital infection surveillance system by advanced diagnostics method & Molecular DNA fingerprinting techniques"
P.I : Dr K PRASHANTH
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			310302.00	Opening balance	310302.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	310302.00		310302.00
310302.00	Excess of expenditure over income	310302.00			
310302.00		**310302.00**	**310302.00**		**310302.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-30 : NIH Project on "Transcription termination and anti termination in *E. coli*"
P.I : Dr RANJAN SEN
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount	Payments	Current Year
2124902.00	**Opening Balance**	2124902.00	0.00	Salaries - Manpower	79206.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
2124902.00		2124902.00	0.00		79206.00
			2124902.00	Closing balance	2045696.00
2124902.00		**2124902.00**	**2124902.00**		**2124902.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-31 : NIH Project on "Functioning of K-ras in lung type II epithelial cells"
P.I : Dr GAYATRI RAMAKRISHNA
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
827383.00	**Opening Balance**	827383.00	0.00	Salaries - Manpower	80930.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
827383.00		827383.00	0.00		80930.00
			827383.00	Closing balance	746453.00
827383.00		**827383.00**	**827383.00**		**827383.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-33: DBT Project on "Molecular and Epidemiological characterisation of cryptosporidium - An enteric protozoon parasite"
P.I. : Dr A RADHA RAMA DEVI
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			234000.00	Opening balance	234000.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	234000.00		234000.00
234000.00	Excess of expenditure over income	234000.00			
234000.00		**234000.00**	**234000.00**		**234000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-34 : DBT Project on "Molecular analysis of lepidopteran - specific immune protiens from silkmoths"
P.I: Dr J NAGARAJU
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
26334.00	**Opening Balance**	26334.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
26334.00		26334.00	0.00		0.00
			26334.00	Closing balance	26334.00
26334.00		**26334.00**	**26334.00**		**26334.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-35 : DST Project on "Identification, Characterization and physical mapping of Z-chromosome linked genes of the silkworm, *Bombyx mori*"
P.I : Dr J NAGARAJU
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			283883.00	Opening balance	283883.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	0.00		0.00
283883.00	Excess of expenditure over income	283883.00			
283883.00		**283883.00**	**283883.00**		**283883.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-36 : DBT Multicentric project on "Development of artificial retina using Bacteriorhodospin and genetically engineered analogues" at CDFD & MRC
P.I : Dr SHEKAR C MANDE
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
2073896.00	**Opening Balance**	2073896.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
2073896.00		2073896.00	0.00		0.00
			2073896.00	Closing balance	2073896.00
2073896.00		**2073896.00**	**2073896.00**		**2073896.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-40 : DST Project on "Antioxidants as a potential immuno-adjuvant in anti-tuberculosis immunotherapy"
P.I : Dr SANGITA MUKHOPADHYAY
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			226058.00	Opening balance	226058.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	226058.00		226058.00
226058.00	Excess of expenditure over income	226058.00			
226058.00		**226058.00**	**226058.00**		**226058.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-41 : DBT Project on "Construction and characterization and analysis of expressed sequences from silkworm"
P.I : Dr J NAGARAJU
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			0.00	Opening balance	0.00
1873605.00	**Opening Balance**	1873605.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
1873605.00		1873605.00	0.00		0.00
0.00	Excess of expenditure over income	0.00	1873605.00	Closing balance	1873605.00
1873605.00		**1873605.00**	**1873605.00**		**1873605.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-42 : The Wellcome Trust, UK Project on "Structural and functional studies on *Mycobacterium tuberculosis* heat shock proteins"
P.I : Dr SHEKAR C MANDE
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			860386.00	Opening balance	2219464.00
0.00	**Opening Balance**	0.00	60228.00	Salaries - Manpower	17821.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
			1298850.00	Funds transferred to P-84	0.00
0.00		0.00	2219464.00		2237285.00
2219464.00	Excess of expenditure over income	2237285.00	0.00	Closing balance	0.00
2219464.00		**2237285.00**	**2219464.00**		**2237285.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-43 : The Wellcome Trust, UK Project on "A generalised mechanism of transcription termination in prokaryotes: A quest for mechanism based transcription inhibitors for microbial pathogens"

P.I: Dr RANJAN SEN

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
1092711.70	**Opening Balance**	754048.70	12860.00	Salaries - Manpower	68142.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			325803.00	Equipment	0.00
1092711.70		754048.70	338663.00		68142.00
			754048.70	Closing balance	685906.70
1092711.70		**754048.70**	**1092711.70**		**754048.70**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-44 : DBT Project on "Understanding the role of Ras and NO /iNOS signalling in promotion of hepatocellular carcinomas with persistent HBV infection"

P.I : Dr GAYATRI RAMAKRISHNA

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			457538.00	Opening balance	457538.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	457538.00		457538.00
457538.00	Excess of expenditure over income	457538.00			
457538.00		**457538.00**	**457538.00**		**457538.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-45 : The Wellcome Trust, UK Project on "Specialised chromatin structures as epigenetic imprints to distinguish parental alleles"
P.I: Dr SANJEEV KHOSLA
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			0.00	Opening balance	0.00
624070.00	**Opening Balance**	624070.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	18356.00
624070.00		624070.00	0.00		18356.00
	Excess of expenditure over income		624070.00	Closing Balance	605714.00
624070.00		**624070.00**	**624070.00**		**624070.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-47 DRDO - DBT Project on " Research Cum Training for DRDO Programme"
P.I : Dr J GOWRISHANKAR, Dr S MAHALINGAM, Dr SHEKAR C MANDE, Dr J NAGARAJU & Dr NIYAZ AHMED
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			1586965.00	Opening balance	1586965.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	1586965.00		1586965.00
1586965.00	Excess of expenditure over income	1586965.00			
1586965.00		**1586965.00**	**1586965.00**		**1586965.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-48 DBT Project on " Molecular Characterization of human liver stem cells for use in the treatment of hepatic diseases"
P.I: Dr SANJEEV KHOSLA
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
151826.00	**Opening Balance**	151826.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
151826.00		151826.00	0.00		0.00
			151826.00	Closing balance	151826.00
151826.00		**151826.00**	**151826.00**		**151826.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P - 49 A: "Grant sanctioned by International Atomic Energy" - P.I : Dr J NAGARAJU
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
627369.00	**Opening Balance**	470313.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			157056.00	Travel	0.00
		0.00		Overheads	0.00
			0.00	Equipment	0.00
627369.00		470313.00	157056.00		0.00
			470313.00	Closing balance	470313.00
627369.00		**470313.00**	**627369.00**		**470313.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-51: DST Project on " Understanding the mechanism of doxorubicin resistance in breast cancer celline MCF - 7

P.I : Dr SUNIL KUMAR MANNA

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			284065.00	Opening Balance	284065.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	284065.00		284065.00
284065.00	Excess of expenditure over income	284065.00			
284065.00		**284065.00**	**284065.00**		**284065.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-52: DBT Project on "Nucleo Cytoplasmic transport of HIV - 1 Vpr"

P.I. Dr S MAHALINGAM & Dr SUNIL KUMAR MANNA

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			1231118.00	Opening Balance	1231118.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	1231118.00		1231118.00
1231118.00	Excess of expenditure over income	1231118.00	0.00	Closing balance	0.00
1231118.00		**1231118.00**	**1231118.00**		**1231118.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-54: ICMR Project on "Study of viability of *Mycobacterium leprae* in Clinical Samples and possibility of its presence in the Environment using Nucleic acid amplification techniques"

P.I. Dr NIYAZ AHMED

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			37877.00	Opening balance	37877.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
		0.00		Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	37877.00		37877.00
37877.00	Excess of expenditure over income	37877.00	0.00	Closing Balance	0.00
37877.00		**37877.00**	**37877.00**		**37877.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-55: DBT Project on " Identification of DNA Markers for baculovirus resistance in silkworm, *Bombyx mori*"

P.I. Dr J NAGARAJU

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
224.00	**Opening Balance**	224.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
224.00		224.00	0.00		0.00
			224.00	Closing Balance	224.00
224.00		**224.00**	**224.00**		**224.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-56: DBT Project on " Genetics of transcription - replication interplay and of stress adaptation in bacteria"

P.I: Dr J GOWRISHANKAR

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			1231164.00	Opening Balance	1231164.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	1231164.00		1231164.00
1231164.00	Excess of expenditure over income	1231164.00	0.00	Closing Balance	0.00
1231164.00		**1231164.00**	**1231164.00**		**1231164.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-59: DBT Project on "An integrated Approach towards understanding the biology of *Mycobacterium tuberculosis:* Genetic, biochemical, immunological and structural analyses"

P.I. - Dr S E HASNAIN, Dr J GOWRISHANKAR, Dr SHEKHAR C MANDE & Dr RANJAN SEN

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			2155484.00	Opening Balance	2215024.00
0.00	**Opening Balance**	0.00	8911.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			50629.00	Equipment	0.00
0.00		0.00	2215024.00		2215024.00
2215024.00	Excess of expenditure over income	2215024.00	0.00	Closing Balance	0.00
2215024.00		**2215024.00**	**2215024.00**		**2215024.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-60: DBT Project on "National Database of Prevalent Genetic Disorders in India: Development, Curation and Services"
P.I: Dr H A NAGARAJARAM
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
497609.00	**Opening Balance**	482124.00	15485.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
497609.00		482124.00	15485.00		0.00
			482124.00	Closing Balance	482124.00
497609.00		**482124.00**	**497609.00**		**482124.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-61: DST Project on "Dissection of a novel phenotype of lethal accumulation of potassium in *Escherichia coli* mutants defective in thioredoxin / thioredoxin reductase and nucleoied protein H-NS"
P.I: ABHIJIT A SARDESAI
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			280000.00	Opening balance	280000.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	280000.00		280000.00
280000.00	Excess of expenditure over income	280000.00			
280000.00		**280000.00**	**280000.00**		**280000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-62: DBT Project on "HIV-1 Pathogenesis: Role of Integrate in Reverse Transcription and Nuclear Transport of Viral Genome"

P.I: Dr S MAHALINGAM

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			278928.00	Opening Balance	278928.00
0.00	**Opening Balace**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	278928.00		278928.00
278928.00	Excess of expenditure over income	278928.00	0.00	Closing Balance	0.00
278928.00		**278928.00**	**278928.00**		**278928.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-63: DBT Project on "Upgradation of the existing computing infrastructure at the Bioinformatics facility at CDFD"

P.I: Dr SEYED E HASNAIN

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			837574.00	Opening balance	837574.00
0.00	**Opening Balance**	0.00	0.00	Salaries -Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	837574.00		837574.00
837574.00	Excess of expenditure over income	837574.00			
837574.00		**837574.00**	**837574.00**		**837574.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-64: NMITLI Project on "Biotechnology for Leather: Towards cleaner processing phase - II"

P.I: Dr J GOWRISHANKAR

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			19755.00	Opening Balance	158.00
0.00	**Opening Balance**	0.00	171000.00	Salaries - Manpower	0.00
679000.00	Grant in aid	0.00	300000.00	Consumables	0.00
			50000.00	Contingencies	0.00
			26403.00	Travel	0.00
			112000.00	Overheads	0.00
			0.00	Equipment	0.00
679000.00		0.00	679158.00		158.00
158.00	Excess of expenditure over income	158.00			
679158.00		**158.00**	**679158.00**		**158.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-65: DST Project on "Molecular, genetic and functional analysis of the chromosomal plasticity region of the gastric pathogen Helicobacter pylori"

P.I. Dr AYESHA ALVI

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			42264.00	Opening balance	582647.00
0.00	**Opening Balance**	0.00	248226.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			10000.00	Contingencies	0.00
			2157.00	Travel	0.00
			20000.00	Overheads	0.00
			260000.00	Equipment	0.00
0.00		0.00	582647.00		582647.00
582647.00	Excess of expenditure over income	582647.00	0.00	Closing balance	0.00
582647.00		**582647.00**	**582647.00**		**582647.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-65A: APEDA-CDFD Centre for Basmati DNA Analysis

P.I. Dr J NAGARAJU

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			8279524.00	Opening Balance	0.00
0.00	**Opening Balance**	7477508.00	687372.00	Salaries - Manpower	521891.00
15110300.00	Grant in aid	0.00	0.00	Consumables	100000.00
1918404.00	Basmati Analysis Charges	1566000.00	9800.00	Contingencies	27450.00
	AMC amount received	8000000.00	0.00	Travel	0.00
			0.00	Overheads	0.00
			450000.00	Consultancy & Knowledge fee	0.00
			0.00	Vehicle	0.00
			124500.00	Equipment	12452.00
17028704.00		17043508.00	9551196.00		661793.00
	Excess of expenditure over income		7477508.00	Closing Balance	16381715.00
17028704.00		**17043508.00**	**17028704.00**		**17043508.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-66: DBT Project on "Human Epigenome Variation: Analysis of CpG island methylation in chromosomes 18 and Y, and in some Hox, Insulin signaling and chromatin reprogramming genes"

P.I: Dr SANJEEV KHOSLA

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			684722.00	Opening Balance	681246.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			-3476.00	Equipment	0.00
0.00		0.00	681246.00		681246.00
681246.00	Excess of expenditure over income	681246.00	0.00	Closing Balance	0.00
681246.00		**681246.00**	**681246.00**		**681246.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-67: DBT Project on "Identification of novel Esophageal Squamous Cell Carcinoma (ESCC) genes by using a combination of array-based CGH and gene expression microarrays"
P.I: Dr M D BASHYAM
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			104487.00	Opening Balance	113545.00
0.00	**Opening Balance**	0.00	9058.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	113545.00		113545.00
113545.00	Excess of expenditure over income	113545.00			
113545.00		**113545.00**	**113545.00**		**113545.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-68: DST Project on "Identification of High Risk Individual with Precancerous States of Esophagal Cancer"
P.I: Dr GAYATRI RAMAKRISHNA
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			0.00	Opening Balance	59874.00
116000.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	100000.00	Consumables	0.00
			20000.00	Contingencies	0.00
			7874.00	Travel	0.00
			48000.00	Overheads	0.00
			0.00	Equipment	0.00
116000.00		0.00	175874.00		59874.00
59874.00	Excess of expenditure over income	59874.00	0.00	Closing Balance	0.00
175874.00		**59874.00**	**175874.00**		**59874.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-69: ICMR Project on "Understanding the role of PE/PPE family of *M.tuberculosis* in the activation of HIV Virus type I long terminal repeat (HIV-ILTP)"

P.I. Dr SANGITA MUKHOPADHYAY

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			906808.00	Opening Balance	159363.00
0.00	**Opening Balance**	0.00	98395.00	Salaries - Manpower	0.00
845840.00	Grant in aid	159363.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
845840.00		159363.00	1005203.00		159363.00
159363.00	Excess of expenditure over income	0.00	0.00	Closing Balance	0.00
1005203.00		**159363.00**	**1005203.00**		**159363.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-70: DBT Project on "Identification of disease causing mutations in familial Hypertrophic Cardiomyopathy (FHC) patients from Andhra Pradesh" -

P.I : Dr M D BASHYAM

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			497869.00	Opening Balance	21336.00
0.00	**Opening Balance**	0.00	51467.00	Salaries - Manpower	0.00
628000.00	Grant in aid	0.00	100000.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
628000.00		0.00	649336.00		21336.00
21336.00	Excess of expenditure over income	21336.00	0.00	Closing Balance	0.00
649336.00		**21336.00**	**649336.00**		**21336.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-71: DBT Project on "Referral Centre for Genetic Fidelity Testing of Tissue Culture Raised Plants"

P.I: Dr N MADHUSUDAN REDDY

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
				Opening Balance	1615249.00
420845.00	**Opening Balance**	1808000.00	294400.00	Salaries - Manpower	308942.00
0.00	Grant in aid	0.00	1400000.00	Consumables	400000.00
			75000.00	Contingencies	50000.00
			28574.00	Travel	25299.00
			0.00	Overheads	0.00
			238120.00	Equipment	0.00
420845.00		1808000.00	2036094.00		2399490.00
1615249.00	Excess of expenditure over income	591490.00	0.00	Closing Balance	0.00
2036094.00		**2399490.00**	**2036094.00**		**2399490.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-72: DST Project on "Nuances of Non-coding DNA near insulin-responsive genes"

P.I. Dr NIRMALA YABALURI

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			1129718.00	Opening balance	1421653.00
0.00	**Opening Balance**	0.00	141935.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	34000.00	Consumables	0.00
			20000.00	Contingencies	0.00
			0.00	Travel	0.00
			96000.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	1421653.00		1421653.00
1421653.00	Excess of expenditure over income	1421653.00			
1421653.00		**1421653.00**	**1421653.00**		**1421653.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-73: DST Project on "Identification and characterization of pancreatic cancer genes located within novel localized cpy number alternations"

P.I: Dr M D BASHYAM

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			541887.00	Opening Balance	857136.00
	Opening Balance		67600.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	200000.00	Consumables	0.00
			0.00	Contingencies	0.00
			47649.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	857136.00		857136.00
857136.00	Excess of expenditure over income	857136.00			
857136.00		**857136.00**	**857136.00**		**857136.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-75: DST Project on "Preparing blueprint for the macromolecular crystallography beamline at Indus-II synchrotron source"

P.I: Dr SHEKAR C MANDE

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			0.00	Opening Balance	10840.00
243171.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	50000.00	Consumables	0.00
			20000.00	Contingencies	0.00
			104011.00	Travel	0.00
			80000.00	Overheads	0.00
			0.00	Equipment	0.00
243171.00		0.00	254011.00		10840.00
10840.00	Excess of expenditure over income	10840.00	0.00	Closing Balance	0.00
254011.00		**10840.00**	**254011.00**		**10840.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-76: DBT project on "A study of Molecular Markers in childhood Autism with special references to nuclear factors - KAPPA B"

P.I: Dr SUNIL KUMAR MANNA

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			58267.00	Opening Balance	50234.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			-8033.00	Equipment	0.00
0.00		0.00	50234.00		50234.00
50234.00	Excess of expenditure over income	50234.00	0.00	Closing Balance	0.00
50234.00		**50234.00**	**50234.00**		**50234.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-77 : DBT project on "Functional characterization of Mycobacterium tuberculosis PE/PPE proteins having SH3 binding domain: Understanding their role in modulating macrophage functions"

P.I: Dr SANGITA MUKHOPADHYAY

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			627570.00	Opening Balance	0.00
0.00	**Opening Balance**	126471.00	442779.00	Salaries - Manpower	0.00
2709000.00	Grant in aid	0.00	1300000.00	Consumables	0.00
			30000.00	Contingencies	0.00
			28070.00	Travel	0.00
			0.00	Overheads	0.00
			154110.00	Equipment	2194.00
2709000.00		126471.00	2582529.00		2194.00
0.00	Excess of expenditure over income	0.00	126471.00	Closing Balance	124277.00
2709000.00		**126471.00**	**2709000.00**		**126471.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-78: ICMR project on "Task Force - IMD Newborn Screening for Congenital Hypthyroidism & Congenital Adrenal Hyperplasis: A Multicentric Study"

P.I: Dr A RADHA RAMA DEVI

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			0.00	Opeaning Blance	0.00
1304.00	**Opening Balance**	1304.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
			0.00	Project funds refund	0.00
1304.00		1304.00	0.00		0.00
			1304.00	Closing Balance	1304.00
1304.00		**1304.00**	**1304.00**		**1304.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-79: DRDO project on "Understanding the role of AGE proteins in inducing inflammatory responses and its regulation"

P.I.: Dr SUNIL KUMAR MANNA

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			1722377.00	Opening Balance	2636028.00
0.00	**Opening Balance**	0.00	202422.00	Salaries - Manpower	16258.00
0.00	Grant in aid	751300.00	450000.00	Consumables	0.00
			25000.00	Contingencies	0.00
			25444.00	Travel	0.00
			70287.00	Overheads	0.00
			140498.00	Equipment	0.00
0.00		751300.00	2636028.00		2652286.00
2636028.00	Excess of expenditure over income	1900986.00	0.00	Closing Balance	0.00
2636028.00		**2652286.00**	**2636028.00**		**2652286.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-80: DBT Project on "Referral Centre for Detection of Genetically Modified Foods employing DNA - based Markets"

P.I. Dr N MADHUSUDAN REDDY

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			0.00	Opening Balance	28471.00
1108456.00	**Opening Balance**	0.00	401120.00	Salaries - Manpower	25523.00
300000.00	Grant in aid	0.00	900000.00	Consumables	0.00
			0.00	Contingencies	0.00
			23902.00	Travel	0.00
			0.00	Overheads	0.00
			111905.00	Equipment	0.00
1408456.00		0.00	1436927.00		53994.00
28471.00	Excess of expenditure over income	53994.00	0.00	Closing Balance	0.00
1436927.00		**53994.00**	**1436927.00**		**53994.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-81: DBT project on "Reconstructing cellular Networks: Two Component Regulatory Systems"

P.I.: Dr SHEKAR C MANDE

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			141048.00	Opening Balance	584848.00
0.00	**Opening Balance**	0.00	293800.00	Salaries - Manpower	152737.00
0.00	Grant in aid	951800.00	150000.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		951800.00	584848.00		737585.00
584848.00	Excess of expenditure over income		0.00	Closing Balance	214215.00
584848.00		**951800.00**	**584848.00**		**951800.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-81A: Financial Assistance for award of JC Bose Fellowship to

Dr J GOWRISHANKAR

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
200000.00	**Opening Balance**	0.00	240000.00	Salaries - Manpower	280000.00
600000.00	Grant in aid	1455000.00	138225.00	Consumables	630841.00
			0.00	Contingencies	0.00
			284085.00	Travel	258321.00
			60000.00	Overheads	60000.00
			77690.00	Equipment	118038.00
800000.00		1455000.00	800000.00		1347200.00
			0.00	Closing Balance	107800.00
800000.00		**1455000.00**	**800000.00**		**1455000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-82: DBT project on "Functional Genomic Analysis of Candida glabrata-macrophage"

P.I.: Dr RUPINDER KAUR

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
795011.00	**Opening Balance**	675598.00	66929.00	Salaries - Manpower	186642.00
1480000.00	Grant in aid	596000.00	650000.00	Consumables	300000.00
			0.00	Contingencies	0.00
			13434.00	Travel	0.00
			200000.00	Overheads	110609.00
			669050.00	Equipment	250756.00
2275011.00		1271598.00	1599413.00		848007.00
0.00	Excess of expenditure over income	0.00	675598.00	Closing Balance	423591.00
2275011.00		**1271598.00**	**2275011.00**		**1271598.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-83: DBT project on "Prokaryotic Transcription Termination Factor, Rho: Mechanism of Action and Biology"

P.I.: Dr RANJAN SEN

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			773176.00	Opening Balance	1093034.00
0.00	**Opening Balance**	0.00	100893.00	Salaries - Manpower	62560.00
1170400.00	Grant in aid	0.00	1300000.00	Consumables	0.00
			30000.00	Contingencies	0.00
			59365.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
1170400.00		0.00	2263434.00		1155594.00
1093034.00	Excess of expenditure over income	1155594.00	0.00	Closing Balance	
2263434.00		**1155594.00**	**2263434.00**		**1155594.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-83A: DST project on "Understanding the mechanism of Azadirachtin-mediated cell signaling: role in anti-inflammation and anti-tumorigenesis"

P.I.: Dr SUNIL KUMAR MANNA

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			50383.00	Opening Balance	86075.00
0.00	**Opening Balance**	0.00	110400.00	Salaries - Manpower	40065.00
550000.00	Grant in aid	0.00	335000.00	Consumables	0.00
			29000.00	Contingencies	0.00
			11292.00	Travel	0.00
			100000.00	Overheads	0.00
			0.00	Equipment	0.00
550000.00		0.00	636075.00		126140.00
86075.00	Excess of expenditure over income	126140.00	0.00	Closing Balance	0.00
636075.00		**126140.00**	**636075.00**		**126140.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-84: Norway project on "Preparing for tuberculosis vaccine efficacy trials: Baseline epidemiology, improved diagnosis, markers of protection and phase I/II trials"
P.I : Dr NIYAZ AHMED
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			1300000.00	Opening Balance	1150.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
1298850.00	Grant in aid (Transfer from P-42)	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
1298850.00		0.00	1300000.00		1150.00
1150.00	Excess of expenditure over income	1150.00	0.00	Closing Balance	0.00
1300000.00		**1150.00**	**1300000.00**		**1150.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-84A: DBT project on "Human epigenetic to the rescue of Human Identification process: Entriching human DNA from DNA mixture employing antibodies directed against 5-methylcytosine followed by whole genome amplification"
P.I. : Dr MADHUSUDAN REDDY
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
1033462.00	**Opening Balance**	655960.00	0.00	Salaries - Manpower	185640.00
1480000.00	Grant in aid	714000.00	950000.00	Consumables	300000.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			200000.00	Overheads	90433.00
			707502.00	Equipment	117246.00
2513462.00		1369960.00	1857502.00		693319.00
0.00	Excess of expenditure over income	0.00	655960.00	Closing Balance	676641.00
2513462.00		**1369960.00**	**2513462.00**		**1369960.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-85: DBT project on "IdeR associated gene regulatory network in Mycobacteria"

P.I. : Dr AKASH RANJAN

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	348699.00	Salaries - Manpower	185254.00
400000.00	Grant in aid	0.00	600000.00	Consumables	0.00
			30000.00	Contingencies	0.00
			79397.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
400000.00		0.00	1333501.00		1118755.00
933501.00	Excess of expenditure over income	1118755.00	0.00	Closing Balance	0.00
1333501.00		**1118755.00**	**1333501.00**		**1118755.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-86: DBT project on "Evaluation of Mycobacterium W as an immunotherapeutic against paratuberculosis (John's Disease of cattle)"

P.I.: Dr NIYAZ AHMED

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
334386.00	**Opening Balance**	78291.00	0.00	Salaries - Manpower	18580.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
		0.00		Overheads	0.00
			0.00	Equipment	0.00
			256095.00	Project funds refund	59711.00
334386.00		78291.00	256095.00		78291.00
0.00	Excess of expenditure over income	0.00	78291.00	Closing Balance	0.00
334386.00		**78291.00**	**334386.00**		**78291.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-87: DST project on "Comparative genomic of wild silkmoths under India-Japan Co-operative Science programme (IJCSP)"

P.I.: Dr J NAGARAJU & Dr TORU SHIMADA

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			65698.00	Opening Balance	65698.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	0.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
		0.00		Overheads	0.00
			0.00	Equipment	0.00
0.00		0.00	65698.00		65698.00
65698.00	Excess of expenditure over income	65698.00	0.00	Closing Balance	0.00
65698.00		**65698.00**	**65698.00**		**65698.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P - 88: DBT Project on "Financial Assistance for award of TATA Innovation Fellowship"

P.I.: Dr J NAGARAJU

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
140000.00	**Opening Balance**	282465.00	240000.00	Salaries - Manpower	240000.00
740000.00	Grant in aid	1480000.00	0.00	Consumables	640318.00
			0.00	Contingencies	0.00
			357535.00	Travel	142147.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
880000.00		1762465.00	597535.00		1022465.00
0.00	Excess of expenditure over income	0.00	282465.00	Closing Balance	740000.00
880000.00		**1762465.00**	**880000.00**		**1762465.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-89: DBT Project on "Characterization of *Mycobacterium tuberculosis* transcription machinery and Bacteriophage metagenomics"

P.I.: Dr RANJAN SEN

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs.	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			0.00	Opening Balance	300000.00
0.00	**Opening Balance**	0.00	38400.00	Salaries - Manpower	62240.00
0.00	Grant in aid	300000.00	190400.00	Consumables	234330.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			71200.00	Equipment	3430.00
0.00		300000.00	300000.00		600000.00
300000.00	Excess of expenditure over income	300000.00	0.00	Closing Balance	0.00
300000.00		**600000.00**	**300000.00**		**600000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-90: DBT Project on "Role of Yapsins in the Pathobiology of Candida Glabrata"

P.I.: Dr RUPINDER KAUR

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
1057540.00	**Opening Balance**	373213.00	204844.00	Salaries - Manpower	217783.00
626000.00	Grant in aid	0.00	800000.00	Consumables	500000.00
			30000.00	Contingencies	20000.00
			6380.00	Travel	35904.00
			0.00	Overheads	0.00
			269103.00	Equipment	51525.00
1683540.00		373213.00	1310327.00		825212.00
0.00	Excess of expenditure over income	451999.00	373213.00	Closing Balance	
1683540.00		**825212.00**	**1683540.00**		**825212.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-91: DBT Project on "DNMT3L: Epigenetic correlation with cancer"

P.I.: Dr SANJEEV KHOSLA & Dr GAYATRI RAMAKRISHNA

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2009 TO 31.03.2010

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
1422879.00	**Opening Balance**	174154.00	216000.00	Salaries - Manpower	187839.00
760000.00	Grant in aid	0.00	900000.00	Consumables	700000.00
			50000.00	Contingencies	30000.00
			29802.00	Travel	35751.00
			0.00	Overheads	0.00
			812923.00	Equipment	7628.00
2182879.00		174154.00	2008725.00		961218.00
0.00	Excess of expenditure over income	787064.00	174154.00	Closing Balance	
2182879.00		**961218.00**	**2182879.00**		**961218.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-92 : DST project on "Swarnajayanti Fellowship: Designing transcription anti-terminators: A novel apprach for making new inhibitors of gene expression"

P.I.: Dr RANJAN SEN

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			0.00	Opening Balance	73314.00
9264550.00	**Opening Balance**	0.00	675348.00	Salaries - Manpower	675382.00
0.00	Grant in aid	3132400.00	2500000.00	Consumables	1800000.00
			30000.00	Contingencies	20000.00
			13574.00	Travel	99283.00
			100000.00	Overheads	80000.00
			6018942.00	Equipment	1622966.00
9264550.00		3132400.00	9337864.00		4370945.00
73314.00	Excess of expenditure over income	1238545.00	0.00	Closing Balance	0.00
9337864.00		**4370945.00**	**9337864.00**		**4370945.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-93: DBT Project on "Virtual Centre of Excellence on multidisciplinary approaches aimed at interventions against tuberculosis"

P.I.: Dr SHEKAR C MANDE & Dr SANGITA MUKHOPADHYAY

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
4851300.00	**Opening Balance**	817860.00	212693.00	Salaries - Manpower	869521.00
0.00	Grant in aid	657000.00	1600000.00	Consumables	900000.00
			160000.00	Contingencies	90000.00
			42772.00	Travel	14406.00
			0.00	Overheads	0.00
			2017975.00	Equipment	285112.00
4851300.00		1474860.00	4033440.00		2159039.00
0.00	Excess of expenditure over income	684179.00	817860.00	Closing Balance	
4851300.00		**2159039.00**	**4851300.00**		**2159039.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-95: DST Project on "Construction of regulatory networks in prokaryotes through protein: Protein interaction predictions and transcription regulation predictions."

P.I.: Dr SHEKAR C MANDE

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			252909.00	Opening balance	121469.00
0.00	**Opening Balance**	0.00	151975.00	Salaries - Manpower	154490.00
1006020.00	Grant in aid	700000.00	400000.00	Consumables	0.00
			40000.00	Contingencies	0.00
			81815.00	Travel	0.00
			77379.00	Overheads	0.00
			123411.00	Equipment	0.00
1006020.00		700000.00	1127489.00		275959.00
121469.00	Excess of expenditure over income	0.00	0.00	Closing Balance	424041.00
1127489.00		**700000.00**	**1127489.00**		**700000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-96 : NIH / FIRCA Project on "Molecular Characterization of sporadic colorectal cancer in the young from India"
P.I.: Dr M D BASHYAM
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			1470450.00	Opening Balance	1187015.00
0.00	**Opening Balance**	0.00	257400.00	Salaries - Manpower	404743.00
1737438.00	Grant in aid	1251970.00	823636.00	Consumables	0.00
			120497.00	Contingencies	0.00
			130317.00	Travel	316154.00
			122153.00	Overheads	0.00
			0.00	Equipment	0.00
1737438.00		1251970.00	2924453.00		1907912.00
1187015.00	Excess of expenditure over income	655942.00	0.00	Closing Balance	0.00
2924453.00		**1907912.00**	**2924453.00**		**1907912.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-97 : DBT Project on "Proteome-wide Analysis of Serine pyrophosphorylation by inositol pyrophosphates"
P.I.: Dr RASHNA BHANDARI
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	582700.00	62400.00	Salaries - Manpower	192232.00
2027000.00	Grant in aid	835000.00	591256.00	Consumables	600000.00
			0.00	Contingencies	0.00
			8744.00	Travel	0.00
			200000.00	Overheads	121197.00
			581900.00	Equipment	15747.00
2027000.00		1417700.00	1444300.00		929176.00
			582700.00	Closing Balance	488524.00
2027000.00		**1417700.00**	**2027000.00**		**1417700.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-98 : DBT Project on "Role of cell - cell signaling mediated by Diffusible signaling factor (DSF) in Xanthomonas virulence"

P.I.: Dr SUBHADEEP CHATTERJEE

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	812907.00	64413.00	Salaries - Manpower	187200.00
3947000.00	Grant in aid	290000.00	900000.00	Consumables	900000.00
			10000.00	Contingencies	10000.00
			0.00	Travel	7331.00
			0.00	Overheads	0.00
			2159680.00	Equipment	464930.00
3947000.00		1102907.00	3134093.00		1569461.00
0.00	Excess of expenditure over income	466554.00	812907.00	Closing Balance	0.00
3947000.00		**1569461.00**	**3947000.00**		**1569461.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-99 : DBT Project on "Role of inositol Pyrophosphates in eukaryotic cell growth, proliferation and ribosomae biogenesis"

P.I.: Dr RASHNA BHANDARI

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	1663500.00	83200.00	Salaries - Manpower	269496.00
4225000.00	Grant in aid	0.00	800000.00	Consumables	800000.00
			30000.00	Contingencies	50000.00
			0.00	Travel	33721.00
			0.00	Overheads	0.00
			1648300.00	Equipment	624040.00
4225000.00		1663500.00	2561500.00		1777257.00
0.00	Excess of expenditure over income	113757.00	1663500.00	Closing Balance	
4225000.00		**1777257.00**	**4225000.00**		**1777257.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-100: DBT Project on "Effect of reactive oxygen species on T-Cell immune response: An approach to understand the molecular mechanism of immunosuppression during tuberculosis" - National Bioscience Award

P.I.: Dr SANGITA MUKHOPADHAYAY

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	72950.00	Salaries - Manpower	203350.00
300000.00	Grant in aid	0.00	209266.00	Consumables	96650.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			17784.00	Equipment	0.00
300000.00		0.00	300000.00		300000.00
0.00	Excess of expenditure over income	300000.00	0.00	Closing Balance	0.00
300000.00		**300000.00**	**300000.00**		**300000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-101 : WT-DBT Alliance Project on "Role of inositol pyrophosphates in cell physiology: Investigating the biochemical significance of protein pyrophosphorylation - Senior Fellowship"

P.I.: Dr RASHNA BHANDARI

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	15288801.00	459965.00	Salaries - Manpower	1878334.00
18792749.00	Grant in aid	6784587.00	1300000.00	Consumables	1800000.00
			0.00	Contingencies	0.00
			0.00	Travel	159823.00
			318541.00	Overheads	580405.00
			1425442.00	Equipment	1965895.00
18792749.00		22073388.00	3503948.00		6384457.00
			15288801.00	Closing Balance	15688931.00
18792749.00		**22073388.00**	**18792749.00**		**22073388.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-102 : ICMR Project on "Understanding the role of *Mycobacterium tuberculosis* heat shockprotein 60 as Th1/Th2 immuno modular"

P.I.: Dr SANGITA MUKHOPADHYAY

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
			0.00	Opening Balance	483681.00
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	234600.00
481319.00	Grant in aid	1181319.00	500000.00	Consumables	700000.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			15000.00	Overheads	0.00
			450000.00	Equipment	208171.00
481319.00		1181319.00	965000.00		1626452.00
483681.00	Excess of expenditure over income	445133.00	0.00	Closing Balance	0.00
965000.00		**1626452.00**	**965000.00**		**1626452.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-103: DBT Project on "National Bioscience Award - Regulation of mast cell signaling, apoptosis and surface receptors"

P.I.: Dr SUNIL KUMAR MANNA

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	300000.00	0.00	Consumables	300000.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		300000.00	0.00		300000.00
0.00	Excess of expenditure over income	0.00	0.00	Closing Balance	0.00
0.00		**300000.00**	**0.00**		**300000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-104: DBT Project on "Virtual Centre of Excellence on Epigenetics - Project 4: Epigenetic dynamics in cell types and its potential association with environment and disease"
P.I.: Dr SANJEEV KHOSLA
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	398371.00
0.00	Grant in aid	1437000.00	0.00	Consumables	700000.00
			0.00	Contingencies	30000.00
			0.00	Travel	11016.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		1437000.00	0.00		1139387.00
			0.00	Closing Balance	297613.00
0.00		**1437000.00**	**0.00**		**1437000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-105 : DBT Project on "Cloning, characterisation and analysis of chromosomal rearrangements in human genetic disorders"
P.I.: Dr ASHWIN DALAL
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	157040.00
0.00	Grant in aid	827000.00	0.00	Consumables	500000.00
			0.00	Contingencies	20000.00
			0.00	Travel	3989.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		827000.00	0.00		681029.00
			0.00	Closing Balance	145971.00
0.00		**827000.00**	**0.00**		**827000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-106 : ICMR Project on "Clinical, biochemical and molecular analysis of treatable lysosomal storage disorders"

P.I.: Dr ASHWIN DALAL

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	214425.00
0.00	Grant in aid	238302.00	0.00	Consumables	450000.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	19933.00
			0.00	Equipment	0.00
0.00		238302.00	0.00		684358.00
	Excess of expenditure over income	446056.00	0.00	Closing Balance	0.00
0.00		**684358.00**	**0.00**		**684358.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-107: DBT IYBA Project on "Mechanism and role of bacterial cell-cell signaling molecules in plant defense response"

P.I.: Dr SUBHADEEP CHATTERJEE

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries- Manpower	109200.00
0.00	Grant in aid	2027000.00	0.00	Consumables	600000.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	185869.00
			0.00	Equipment	529925.00
0.00		2027000.00	0.00		1424994.00
			0.00	Closing Balance	602006.00
0.00		**2027000.00**	**0.00**		**2027000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-108 : DBT Project on "Establishment of EBV transformed cell lines from families with rare genetic disorders"

P.I.: Dr ASHWIN DALAL

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	112220.00
0.00	Grant in aid	487000.00	0.00	Consumables	150000.00
			0.00	Contingencies	20000.00
			0.00	Travel	20757.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		487000.00	0.00		302977.00
	Excess of expenditure over income		0.00	Closing Balance	184023.00
0.00		**487000.00**	**0.00**		**487000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-109: DBT IYBA Project on "Molecular dissection of PI3-Kinase/Akt pathway by suing proteomics based approach: A study to identify novel potential oncogenes and tumor suppressors"

P.I.: Dr M SUBBA REDDY

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	79040.00
0.00	Grant in aid	2027000.00	0.00	Consumables	400000.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	71856.00
			0.00	Equipment	0.00
0.00		2027000.00	0.00		550896.00
			0.00	Closing Balance	1476104.00
0.00		**2027000.00**	**0.00**		**2027000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-110: DST Project on "India-Japan research project title"Identification and analysis of sex determining genes in silkmoths"

P.I.: Dr J NAGARAJU

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	170000.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	145611.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		170000.00	0.00		145611.00
			0.00	Closing Balance	24389.00
0.00		**170000.00**	**0.00**		**170000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-111: DBT Ramalingaswami Fellowship "Refractoriness mechanism in mosquito: cracking molecular codes at genomic scale"

P.I.: Dr SHEWTA TYAGI

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	610028.00
0.00	Grant in aid	1400000.00	0.00	Consumables	300000.00
			0.00	Contingencies	0.00
			0.00	Travel	1341.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		1400000.00	0.00		911369.00
			0.00	Closing Balance	488631.00
0.00		**1400000.00**	**0.00**		**1400000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-112: DBT Ramanujan Fellowship
P.I.: Dr ROHIT JOSHI
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	404691.00
0.00	Grant in aid	1460000.00	0.00	Consumables	200000.00
			0.00	Contingencies	0.00
			0.00	Travel	11583.00
			0.00	Overheads	40000.00
			0.00	Equipment	0.00
0.00		1460000.00	0.00		656274.00
			0.00	Closing Balance	803726.00
0.00		**1460000.00**	**0.00**		**1460000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-113: ICMR Project on "Clinical and molecular genetic analysis of squamous cell carcinoma of the tongue"
P.I.: Dr M D BASHYAM
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	110542.00
0.00	Grant in aid	1139487.00	0.00	Consumables	200000.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	9316.00
			0.00	Equipment	268914.00
0.00		1139487.00	0.00		588772.00
			0.00	Closing Balance	550715.00
0.00		**1139487.00**	**0.00**		**1139487.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-114: DBT Project on "Evaluating the Calcineurin-NFAT Pathway and its regulators superoxide dismutase (SOD) AND RCAN1 (regular of Calcineurin) Down Syndrome"
P.I.: Dr GAYATRI RAMAKRISHNA
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	37239.00
0.00	Grant in aid	2070000.00	0.00	Consumables	500000.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		2070000.00	0.00		537239.00
			0.00	Closing Balance	1532761.00
0.00		**2070000.00**	**0.00**		**2070000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-115: Setting up the National Institute of Animal Biotechnology at Hyderabad
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	291680.00
0.00	Grant in aid	5000000.00	0.00	Consumables	0.00
			0.00	Contingencies	0.00
			0.00	Travel	0.00
			0.00	Overheads	149015.00
			0.00	Equipment	0.00
0.00		5000000.00	0.00		440695.00
			0.00	Closing Balance	4559305.00
0.00		**5000000.00**	**0.00**		**5000000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-116: DBT-India and AIST - Japan : Understanding molecular mechanisms controlling dual role of Ras, Sirtuins and CARF in relation to cellular proliferation and senescence: Novel Strategy for developing cancer therapeutics

P.I.: Dr GAYATRI RAMAKRISHNA

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	32709.00
0.00	Grant in aid	2037200.00	0.00	Consumables	300000.00
			0.00	Contingencies	0.00
			0.00	Travel	11674.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		2037200.00	0.00		344383.00
			0.00	Closing Balance	1692817.00
0.00		**2037200.00**	**0.00**		**2037200.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-117: DBT Project on "Joint New Indigo Era-Net project titled "*Mycobacterium tuberculosis* : bioinformatic and structural strategies towards treatment"

P.I.: Dr SHEKHAR C MANDE

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	5593000.00	0.00	Consumables	200000.00
			0.00	Contingencies	25000.00
			0.00	Travel	66500.00
			0.00	Overheads	50000.00
			0.00	Equipment	0.00
0.00		5593000.00	0.00		341500.00
			0.00	Closing Balance	5251500.00
0.00		**5593000.00**	**0.00**		**5593000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-118: DST Project on "Construction of regulatory networks in *Mycobacterium tuberculosis* through analysis of gene expression data and transcription regulation predictions. (MOU with Russian Foundation)"

P.I.: Dr SHEKHAR C MANDE

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	0.00
0.00	Grant in aid	1400770.00	0.00	Consumables	200000.00
			0.00	Contingencies	15000.00
			0.00	Travel	20000.00
			0.00	Overheads	50000.00
			0.00	Equipment	0.00
0.00		1400770.00	0.00		285000.00
			0.00	Closing Balance	1115770.00
0.00		**1400770.00**	**0.00**		**1400770.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD

P-119: DBT Project on "Analysis of DNA copy number alterations in esophaeal cancer"

P.I.: Dr M D BASHYAM

RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries- Manpower	24658.00
0.00	Grant in aid	800000.00	0.00	Consumables	200000.00
			0.00	Contingencies	15000.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		800000.00	0.00		239658.00
			0.00	Closing Balance	560342.00
0.00		**800000.00**	**0.00**		**800000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-120: DBT Project on "Effect of reactive oxygen species on macrophage signalosome: Impact on antigen presentation functions and T Cell priming rsponses"
P.I.: Dr SANGITA MUKHOPADHAYAY
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries- Manpower	0.00
0.00	Grant in aid	827000.00	0.00	Consumables	200000.00
			0.00	Contingencies	10000.00
			0.00	Travel	0.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		827000.00	0.00		210000.00
			0.00	Closing Balance	617000.00
0.00		**827000.00**	**0.00**		**827000.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
P-121: DBT Project on "Identification and characterization of PTEN regulators"
P.I.: Dr M SUBBA REDDY
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
0.00	**Opening Balance**	0.00	0.00	Salaries - Manpower	120774.00
0.00	Grant in aid	345776.00	0.00	Consumables	158350.00
			0.00	Contingencies	23600.00
			0.00	Travel	5956.00
			0.00	Overheads	0.00
			0.00	Equipment	0.00
0.00		345776.00	0.00		308680.00
			0.00	Closing Balance	37096.00
0.00		**345776.00**	**0.00**		**345776.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
COE on Genetics and Genomic of Silkworms
P.I. Dr J NAGARAJU
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
38637629.00	**Opening Balance**	10330961.00	5621624.00	Salaries - Manpower	6002999.00
7821000.00	Grant in aid	13680000.00	7000000.00	Consumables	5000000.00
			280000.00	Contingencies	560000.00
			398317.00	Travel	862106.00
			0.00	Workshop / Training	2900000.00
			0.00	Equipment Maintenance	12000000.00
			0.00	Books & Journals	144242.00
			0.00	Overheads	0.00
			22827727.00	Equipment	9740478.00
46458629.00		24010961.00	36127668.00		37209825.00
0.00	Excess of expenditure over income	13198864.00	10330961.00	Closing Balance	0.00
46458629.00		**37209825.00**	**46458629.00**		**37209825.00**

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS, HYDERABAD
COE - II : DBT Project on "Centre of Excellence for Microbial Biology"
P.I: Dr J GOWRISHANKAR, Dr K ANUPAMA, Dr ABHIJIT A SARDESAI, Dr RANJAN SEN AND Dr SHEKAR C MANDE
RECEIPTS AND PAYMENTS ACCOUNT FROM 01.04.2010 TO 31.03.2011

Previous Year Amount Rs	Receipts	Current Year Amount Rs.	Previous Year. Amount Rs	Payments	Current Year Amount Rs
11800481.00	**Opening Balance**	0.00	5256529.00	Salaries - Manpower	6699151.00
4589000.00	Grant in aid	8913000.00	5900000.00	Consumables	3000000.00
			710000.00	Contingencies	520000.00
			318725.00	Travel	365439.00
			0.00	Overheads	0.00
			5658960.00	Equipment	1465364.00
16389481.00		8913000.00	17844214.00		13504687.00
1454733.00	Excess of expenditure over income	4591687.00	0.00	Closing Balance	0.00
17844214.00		**13504687.00**	**17844214.00**		**13504687.00**

फोटो गैलरी
Photo Gallery

गणतंत्र दिवस के अवसर पर श्रोतागण को संबोधित करते हुए सी डी एफ डी के निदेशक डा. ज. गौरीशंकर

Dr J Gowrishankar, Director, CDFD addressing the audience on Independence Day, 2010

हिन्दी दिवस समारोह (सितंबर 14, 2010)

Hindi Day Celebrations (September 14, 2010)

14वी ट्रान्स्क्रीपशन एसेम्बली मिटींग (20-22 जनवरी 2011)
14th Transcription Assembly Meeting (20-22 January 2011).

"रेडॉक्स परिस्थिती एवं क्षय रोग पर नियंत्रण: मूलभूत अनुसंधान से औषधी निर्माण तक" संगोष्ठी
(जनवरी 30 - फरवरी 2011)

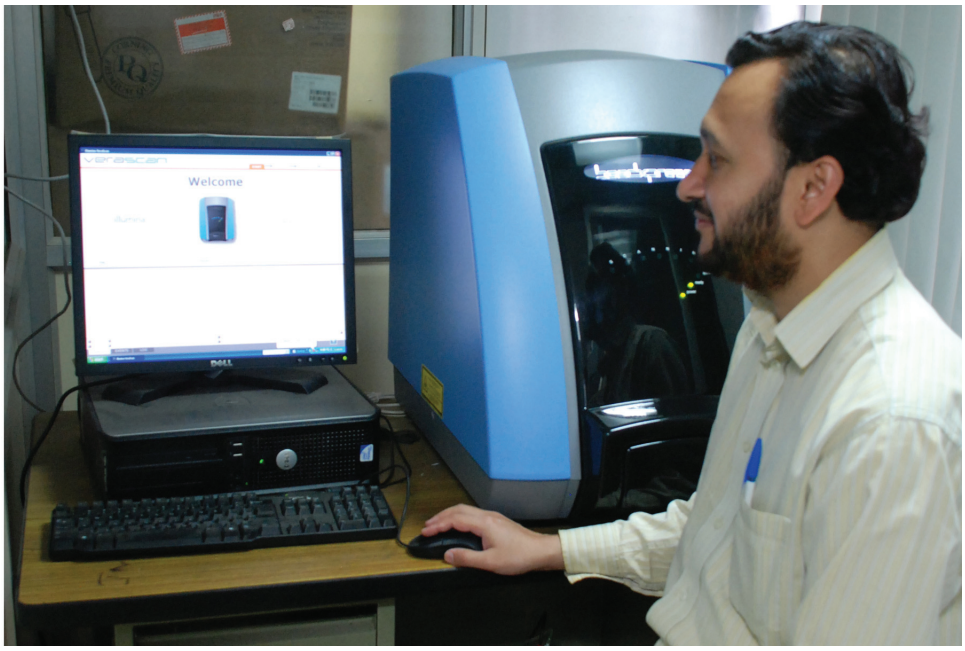
Symposium on "Redox Status and Control in Tuberculosis: From Basic Research to Drug Development"
(January 30 - February 1, 2011)

सी डी एफ डी एवं नेब्रास्का मेडीकल सेन्टर विश्वविद्यालय, ओमाहा के बीच समझौते पर हस्ताक्षर करते हुए
(3 मार्च 2011)

Signing of MoU between CDFD and the University of Nebraska Medical Centre, Omaha, USA
(3 March 2011)

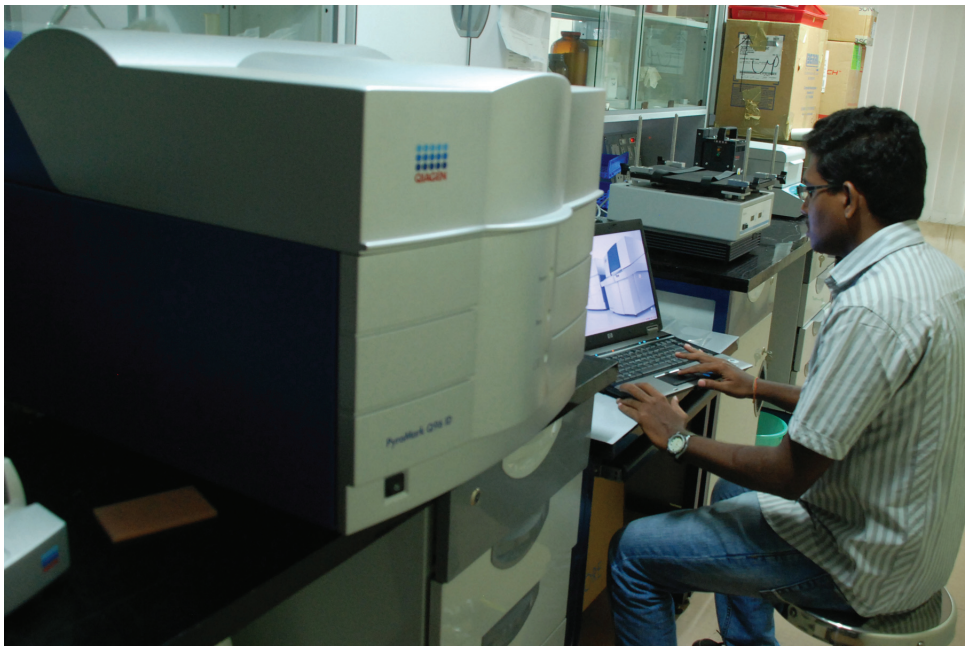
5 वी इन्डो-फ्रेंच बायोइन्फॉमेटिक्स मीटींग (23-25 मार्च 2011)
5th Indo-French Bioinformatics Meeting (23-25 March 2011)

हमारी प्रयोगशालाओं में स्थापित कुछ नये उपकरण
NEW INSTALLATIONS AT OUR LABORATORIES

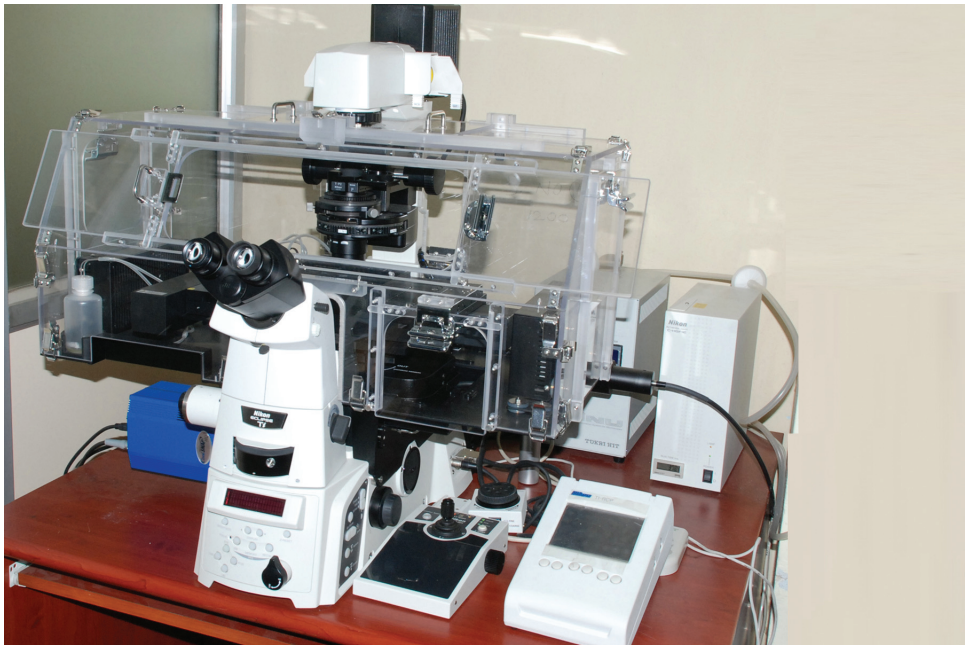


इलूमिना बीड एक्स्प्रेस जीनोम जीनोटाइपिंग सिस्टम
Illumina Bead Express Whole Genome Genotyping System

परकिन एल्मर पैकार्ड 2910 लिक्विड सीन्टीलेशन काउन्टर
Perkin Elmer Packard 2910 Liquid Scintillation Counter



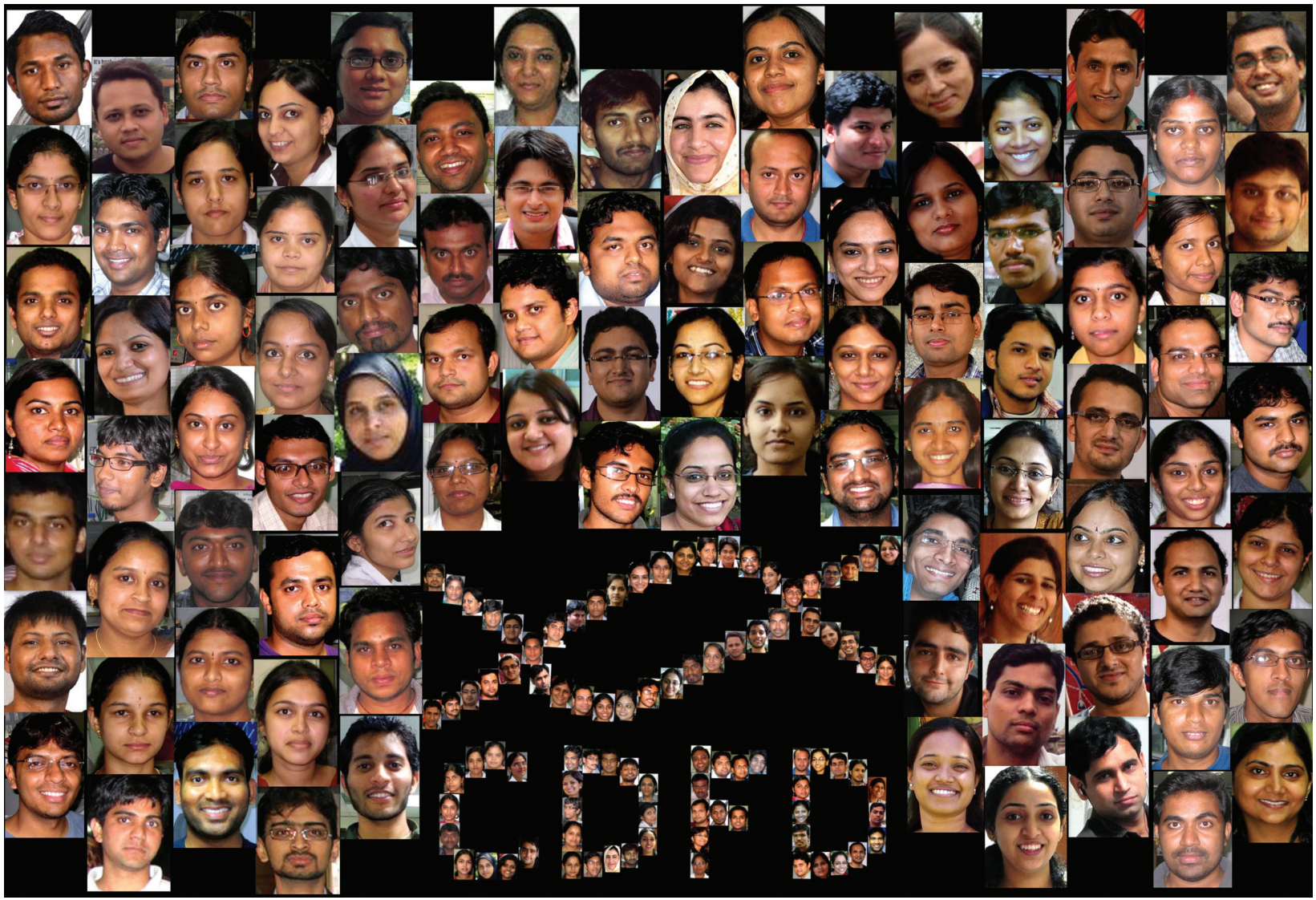
क्विआजेन पाइरोसिक्वेन्सर
Qiagen Pyrosequencer



निकॉन लाइव सेल इमेजींग सिस्टम
Nikon Live Cell Imaging System

कनवाइरॉन प्लान्ट ग्रोथ चेम्बर
Conviron Plant Growth Chamber

ए बी आई 3.5 नेक्स्ट जन्रेशन होल जीनोम डी एन ए सीक्वेन्सर
ABI SOLiD 3.5 Next Generation Whole Genome DNA Sequencer



सी डी एफ डी के अध्येता एवं परियोजना कर्मचारियों का समूह

A section of the CDFD Scholars and Project Staff

NOTES / REMARKS

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