



R&D Newsletter

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INDIAN INSTITUTE OF TECHNOLOGY KANPUR

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Structural and Biochemical Investigations on *M. tuberculosis* N-acetyl Glucosamine-1-Phosphate Uridyltransferase (GlmU) - a Novel Substrate of PknB

PI: Prof. Balaji Prakash, Dept. of Biological Sciences & Bioengineering
Collaborator: Dr. Vinay Kumar Nandicoori, National Institute of Immunology New Delhi
Sponsor: Department of Biotechnology

Specific Objectives of the Project

- Crystallographic snapshots of uridyltransferase reaction in GlmU from *M. tuberculosis*.
- Structural and Biochemical characterization of C-terminal extension in GlmU from *M. tuberculosis*.
- Generation of conditional knock out mutants of GlmU in *M. tuberculosis* H37Rv.

Technical Results Obtained

Using biochemical and crystallographic studies, two-metal ion mechanism in *Mycobacterium tuberculosis* GlmU (GlmU^{Mtb}) has been identified. Further, attempts to delineate the roles of the metal ions in substrate stabilization, nucleophile activation and transition-state stabilization are presented. The snapshots following the uridyltransfer reaction depict that the product 'pyrophosphate' exits the active site through a tunnel, in complex with a Mg²⁺ ion. Accelerated molecular

dynamics simulations affirm the above observation. The snapshots also depict differing coordination states for Mg²⁺ during exit, and based on these, a probable Mg²⁺ facilitated product release mechanism is proposed. Additionally, acetyl-CoA bound crystal structure of GlmU provides an insight into substrate recognition, catalytic mechanism for acetyl transfer and features unique to GlmU^{Mtb}, which may be exploited for the development of inhibitors specific to GlmU.

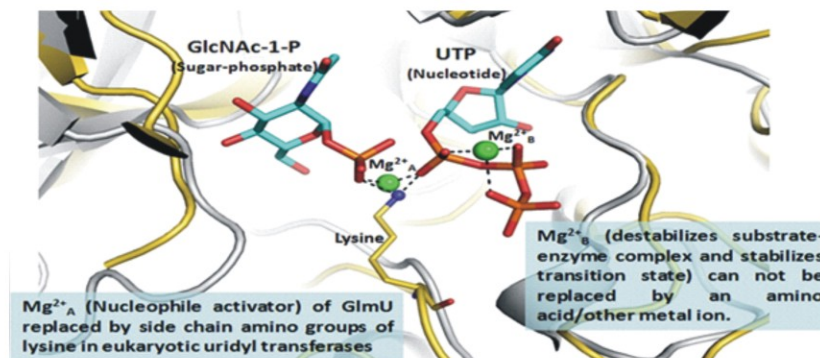


Figure: The comparison of 'one-metal ion' catalytic mechanism with 'two-metal ion' catalytic mechanism in SNTs

Some Major Publications

□ Pravin Kumar Ankush Jagtap, Sunil Kumar Verma, Neha Vithani, Vaibhav Singh Bais and Balaji Prakash, Crystal structures identify an atypical two-metal ion mechanism for uridyl transfer in GlmU: Its significance to sugar nucleotidyl transferases. **Journal of Molecular Biology**, (2013), 425, 1745 -1759.

□ Pravin Kumar Ankush Jagtap, Vijay Soni, Neha Vithani, Gagan Deep Jhingan, Vaibhav Singh Bais, Vinay Kumar Nandicoori, and Balaji Prakash, Substrate bound crystal structures reveal features unique to *Mycobacterium tuberculosis* N-acetyl-glucosamine-1-phosphate uridyltransferase and a catalytic mechanism for acetyl transfer, **Journal of Biological Chemistry** (2012), 287, 39524-37.

Unravelling The Role of Human Non Coding Satellite-III Transcripts in Cellular Stress Response

PI: Prof. S Ganesh, Dept. of Biological Sciences & Bioengineering

Sponsor: Department of Biotechnology

Specific Objectives of the Project

Non-coding RNAs are a class of messengers that do not code for proteins and whose cellular functions are yet to be fully understood. The aim of this project was to understand the cellular functions of the Satellite-III non-coding transcripts (SatIII) in human.

Technical Results Obtained

Non-coding RNAs are known to play critical regulatory roles in cellular physiology and aberrant functions in some of these RNAs are thought to underlie various pathophysiological processes. One such non-coding RNAs known to express in response to cellular stress is SatIII, and its expression is believed to be a stress-adaptive response of the cell. SatIII transcripts form sub-nuclear compartments known as nuclear stress bodies and these structures sequester transcription factors and splicing factors that are critical regulators of gene expression. We discovered that the SatIII-dependent sequestration of these factors is important for the cell to mount a stress adaptive response, and that the SatIII transcripts are essential for the stress-dependent reprogramming of transcriptional processes. Our results have also indicated a causative role for SatIII in neurodegenerative disorders. We propose that the physiological stress in neurodegenerative disorders, such as Huntington's disease, could trigger the expression of SatIII and the SatIII-mediated transcriptional

reprogramming. Thus, suppressing SatIII-mediated functions could be a potential therapeutic option in such conditions.

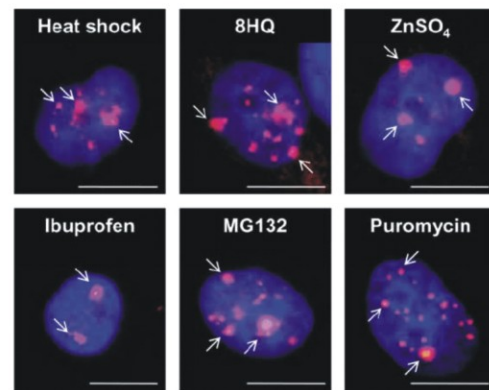


Figure: The expression pattern of SatIII transcripts (pink color speckles) in the nucleus (blue color) of a human cell line upon exposure to heat shock or other forms of physiological stressors as indicated. Note the difference in the number of speckles for each stress, suggesting the stress-specific expression for the SatIII in the human chromosomes.



Recently Registered Projects

Numerical Characterization of Strut-ramp Injector for Supersonic Combustion Using Large Eddy Simulation (LES)

PI: Prof. Ashoke De, Dept. of Aerospace Engineering

Co-PI: Dr. Dileep, Vikram Sarabhai Space Centre

Sponsor: ISRO-IITK Space Technology Cell

The primary aim of this project is to investigate the flow and mixing characteristic in strut-ramp injector configuration in oncoming supersonic flow using Large Eddy Simulation (LES) methodology. Thorough understanding of the effect of strut-ramp injector would enlighten the understanding of mixing behavior and

complex flow physics, which would offer deeper insight into the flame stabilization mechanism. It is anticipated that variation in injector configuration would interact with the complex flow field, dominated by shock waves would provide better understanding towards flame stabilization and mixing phenomenon.





Paleo-Seismic and Paleo-Tsunami Investigations along South-Middle Andaman & Car Nicobar Islands towards Earthquake and Tsunami Hazard Assessment of A&N Islands

PI: Prof. Javed N Malik, Dept. of Civil Engineering

Co-PI: Dr. T. Srinivasa Kumar, Indian National Centre for Ocean Information Services (INCOIS), Hyderabad.

Sponsor: Indian National Centre For Ocean Information Services

Tsunami word has been known since decades in Japanese literature (tsunami – the harbour wave). It is well established from various studies that such giant waves are generated by sudden disturbance of sea water column particularly by large magnitude subduction or seafloor earthquakes, submarine landslides, underwater volcanic eruption etc. Out of these causes mentioned above, the earthquake-induced tsunami has widespread affects. The most recent giant tsunamis were generated by 2004 Sumatra Andaman (Mw 9.3) and 2011 Tohoku (Mw 9.1) earthquakes. The region of Andaman and Nicobar Island (A&N) has a great potential to trigger mega-earthquakes similar to one experienced during 2004. These mega-earthquakes not only generate tsunamis, but also results into land-level change in the coastal areas (Figure 1 A& B). Till date a very little is known about the past earthquakes and associated tsunamis those occurred during recent historic past in A&N region.

This major project has been sanctioned to undertake Earthquake and Tsunami studies in A&N Islands as a part of XII-five year plan (2012-2017) emphasized on R&D in Tsunami and Tectonic related studies in the Indian Ocean Region,

Main Focus:

- (1) Identification of paleo-tsunami and paleo-earthquake (land-level change) signatures preserved in the shallow sub-surface sediment succession –to reconstruct the chronology of the historic/prehistoric tsunami events and to understand the recurrence of tsunamis/ large magnitude earthquakes in Andaman & Nicobar Islands.
- (2) Identification, mapping and dating of uplifted coastal terraces –for reconstructing the active tectonic history along Andaman Islands.
- (3) Earthquake hazard and risk assessment using above generated information and by tsunami modeling for A & N Islands and area adjoining the coastline in Indian Mainland.

This information will be extremely helpful:

(a) in having a complete data base of paleo-earthquake and associated paleo-tsunami events resulted by near field

(occurring along A&N arc) and far field (occurring in Sumatra region) sources, (b) to understand their recurrence interval and nature of events, (c) towards evaluating the hazard and risk posed not only to the vulnerable coastlines of A&N Islands but also to the coastline encircling the Indian Mainland as well as coastline of adjacent countries, and (d) estimating the threat posed to existing nuclear power station and also to the upcoming stations if any in near future. Attempt will be made to show-case the ancient tsunami record at IITK.

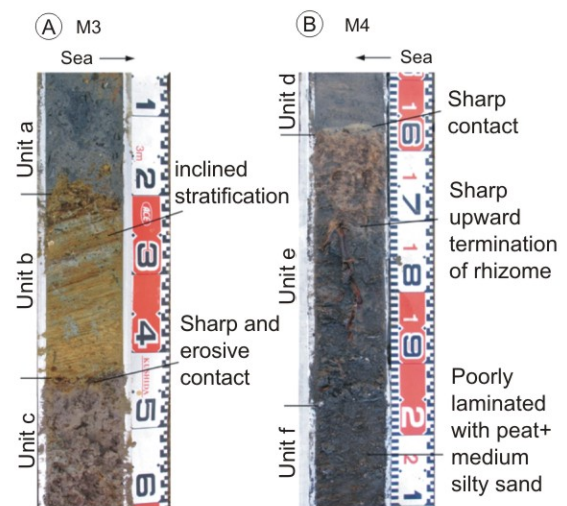


Figure 1: (A) Geoslicer section shows inclined stratification toward land and sharp to erosive contact with unit c. Unit b is interpreted as tsunami deposit of AD 1700, (B) Geoslicer peel sample showing prominent change in sedimentary facies – from massive clay (unit d) and underlying peaty soil (unit e). This sharp contact between units d and e, sharp termination of rhizome in unit e – is indicative of sudden land-level change caused by large magnitude earthquake during AD 1600.

Investigate Potential Mechanism Involved in AGTR1 Mediated Oncogenic Effects: A Pharmaceutical Intervention for Treatment of AGTR1 Positive Breast Cancer

PI: Prof. Bushra Ateeq, Dept. of Biological Sciences & Bioengineering

Sponsor: Science and Engineering Research Board



The use of biomarkers, such as estrogen receptor (ER) and HER2, for breast cancer treatment selection are well established; yet even with these markers; there are deficiencies in the methodologies due to numerous subtypes within these groups that may affect their application. We have nominated AGTR1, the angiotensin receptor, a target of hypertension medications as a second ranked meta-outlier employing Meta-COPA analyses (Meta-Analysis and Cancer Outlier Profile Analysis) and it has also been validated as one of the most highly over-expressed genes in 10-20% of breast tumors

across several independent patient cohorts. We are investigating the mechanism of AGTR1 over-expression and performing functional characterization to provide a strong rationale for the use of AGTR1 antagonists or small molecule inhibitors in AGTR1-positive subset of breast cancer patients. Moreover, the cell signaling pathways linked to AGTR1-Ang II dependent cell invasion and metastases in AGTR1-positive subset of breast cancer patients are also being explored.

Clinical Collaborator: GSVM Medical College, Kanpur

Shape-based Fluorescence Optical Tomography for Grading of Dysplasia in Cervical Cancer Progression

PI: Prof. Naren Naik, Dept. of Electrical Engineering

Co-PI: Prof. Asima Pradhan, Centre for Laser Technology/Dept. of Physics

Sponsor: Department of Atomic Energy



Tumor detection in various parts of the body by optical tomographic methods is often a limited data problem with only back-scattered light available for analysis of the subsurface. The reconstruction challenge is to obtain reconstructions for small tumors (characteristic of early cancer stages), while facing problems of clutter in the tissue environment in addition to data SNR issues and the inherent ill-posedness of the reconstruction. This prompts the approximate-tomographic reconstruction of the shape and typical optical parameters of the affected tissue rather than a full pointwise estimate.

For the reconstruction problem in cervical cancer detection, we propose an alternative level set based reconstruction approach to obtain the optical-property profile of the subsurface tissue from above-surface measurements of the back-scattered light, while keeping the number of reconstruction unknowns small. For this problem, we investigate the suitability of the diffusion model of propagation with respect to that based on the radiative

transfer equation. A spatially resolved fluorescence set up in frequency domain and DC modes will be developed. The fluorescence spectra at various positions will be used to reconstruct a layered inhomogeneity in solid layered phantoms as well as cervical tissue, subsequent to working with a homogeneous liquid phantoms to verify the model used.





Development of Metal Monolith Catalysts for Steam Reforming of Methane

PI: Prof. Deepak Kunzru, Dept. of Chemical Engineering

Co-PI: Prof. Goutam Deo, Dept. of Chemical Engineering

Sponsor: Science and Engineering Research Board

Steam reforming of methane on supported nickel catalyst pellets in fixed bed reactors is a well-established commercial process for producing CO and H₂ but suffers from the disadvantage of poor catalyst utilization and heat transfer limitations. A potentially attractive alternative to overcome these limitations is to use metal monoliths coated with noble metal promoted nickel catalysts. In this study, steam reforming of methane will be investigated on metal monoliths coated with Rh or

Pt promoted Ni/MgAl₂O₄ and the results compared with the data obtained on powdered catalysts in fixed bed reactors. The promoted catalysts will be thoroughly characterized to explain the promotional effect. For the most active and stable catalyst, the intrinsic kinetics will be determined and incorporated in a model for the monolith reactor. This reactor model will be used to determine the best heat integration strategy for carrying out this reaction on monoliths.

Effect of Iron in Supported & Unsupported Nickel-Iron & Cobalt-Iron Bimetallic Catalysts

PI: Prof. Goutam Deo, Dept. of Chemical Engineering

Sponsor: Council of Scientific and Industrial Research

Supported nickel and cobalt systems are important catalysts used for several industrial processes. Promotion of these catalysts will give rise to more efficient processes. One such promoter is iron. Development of structure-reactivity relationships for showing the effect of iron addition to supported nickel and cobalt catalysts will involve the synthesis of several supported and unsupported nickel and cobalt catalysts with and without iron. These catalysts will be characterized

under ambient, in situ and reaction conditions. The CO₂ hydrogenation reaction will be considered as a probe for studying the reactivity of the supported and supported catalysts in the presence and absence of iron. Information obtained from the characterization and reactivity studies will enable development of appropriate structure-reactivity relationships. Optimum composition (Ni:Fe/Co:Fe ratios and total metal loading) of some catalysts will also be determined.



Microwave Imaging and Remote Sensing of Concealed Objects

PI: Prof. M Jaleel Akhtar, Dept. of Electrical Engineering

Sponsor: Science and Engineering Research Board

This project mainly focuses on the development of a viable prototype system for the imaging of concealed objects using microwaves. The basic aim of the project is to explore the use of an alternative technique based on the microwave technology for the imaging of concealed objects at airport and other important public locations. The conventional X-ray systems

presently being used at such places are usually not considered to be much safer because of their ionizing nature, and they are not able to fully detect plastic explosives. This project would also concentrate on detection of anti-personal plastic mines in case of remote sensing, which can otherwise not be detected using the conventional metal detectors.

Planar High Gain Antennas Based on Electromagnetic Band Gap Concept

PI: Prof. Animesh Biswas, Dept. of Electrical Engineering

Collaborator: Prof. Karu Esselle, Macquarie University, Australia

Sponsor: Department of Science & Technology under Indo-Australia Partnership



This is an Indo-Australia joint partnership project. The main aim of this project is to develop a novel, versatile class of low-profile (thin) high-gain antennas with steerable antenna beams, for current and emerging microwave (MW) and millimetre-wave (MMW) wireless communication systems. Innovative antennas with high performance will be designed, prototyped and tested to enhance the quality of wireless services in rural areas, homes, hospitals, schools, offices and other work places. These antennas will have thin flat shapes and can be attached to any flat surface such as an outdoor or indoor wall, ceiling or cabinet. Due to reduced

losses of the antennas and enhanced radiation characteristics, wireless systems based on these antennas will consume significantly less electricity. They will also dramatically reduce the level of radio-frequency exposure to non-users in the wireless environment.

Decision Support System to Enhance Safety of Railway Track Workers

PI: Prof. B V Phani, Dept. of Industrial & Management Engineering

Prof. Deepu Philip, Dept. of Industrial & Management Engineering

Sponsor: Department of Science and Technology



Ever since creation of rail transportation, inspection of railway tracks has been a hazardous job due to lack of appropriate warning systems for approaching trains. The project aims to exploit advances in various technologies like wireless, communication networks, sensors and information management to develop a fail-safe robust decision support system to enhance safety of track workers and bring global benefits to

tune of \$1 billion. The project is a joint initiative of IIT Kanpur, McMaster University Canada and Bombardier Canada and funded by ISTP Canada – GITA India. The TrackSafe DSS developed by the team won Innovation Awards, 2012."





Development of Higher Conductive Co-doped $\text{Sc}_2\text{O}_3\text{-ZrO}_2$ Based Electrolyte for Solid Oxide Fuel Cell

PI: Prof. Shobit Omar, Dept. of Materials Sc. & Engineering

Co-PI: Prof. Kantesh Balani, Dept. of Materials Sc. & Engineering

Sponsor: Department of Science and Technology



The aim of the project is to rationally design materials with higher oxygen ion conductivity for the electrolyte application in solid oxide fuel cells. This will allow lowering the operational temperature of the device from 1000°C to $500\text{-}700^\circ\text{C}$, which can significantly reduce the cost and extend its domain to portable power market sectors. In this work, structure-conductivity relationships will be investigated in Sc_2O_3 stabilized ZrO_2 based materials as they exhibit high ionic conductivity and minimal electronic conduction. In addition, conductivity ageing studies will be performed (over 1000 h) at high temperatures. For this work, an impedance analyzer (Solartron 1260) will be procured that can measure impedances ($>100\text{ M}\Omega$) in applied frequency range from 32 MHz to $10\mu\text{MHz}$. A setup will also be developed for conductivity measurement at high temperatures.

R&D News

6th National Power Electronics Conference (NPEC 2013)

The National Power Electronics Conference 2013 was organized by the department of Electrical Engineering in IIT Kanpur during December 20-22, 2013. It was the sixth biennial conference of the Power Electronics community in India focusing on the ongoing research in this area and seeking to find potential users of the laboratory-scale developments in industry. The objectives of this conference were to provide a forum to promote and accelerate high quality research inviting professional interactions for the advancement and indigenization of Power Electronics in India. The conference was organized under the convenorship of Prof. Partha Sensharma, Prof. S.P. Das and Prof. Santanu Mishra.



Feedback/Suggestions

dord@iitk.ac.in
chitrab@iitk.ac.in

Address for Correspondence

Dean, Research & Development
Indian Institute of Technology Kanpur
Kanpur 208016
dord@iitk.ac.in
Phone: +91-512-259 7578
www.iitk.ac.in/dord/