INDIAN ASSOCIATION FOR THE CULTIVATION OF SCIENCE
2A&B, Raja S.C. Mullick Road, Jadavpur, Kolkata-700032, India

Seminar Notice

Speaker: Dr. Debasis Das, MIT, USA
Title: Mechanistic investigation of enzymes with potential in therapeutics and biofuel applications
Date: April 10, 2018
Time: 11:30 AM
Venue: C V Raman Hall.

Abstract: My talk will focus on an integral membrane phospho-glycosyl transferase (PGT) enzyme from Campylobacter jejuni, a serious human gastro-entero pathogen that affects millions of people worldwide. The PGT enzyme, known as PglC, catalyzes the first membrane-committed step of the N-linked protein glycosylation (pgl) pathway that is related to the pathogenicity of the organism. Therefore, PglC serves as a potential therapeutic target. Despite considerable efforts, the enzyme is poorly characterized due to difficulties associated with expression, purification and stability of integral membrane enzymes and also due to the lack of convenient biochemical methods to study the enzyme. Extensive optimization of the expression and purification of PglC was carried out to obtain the enzyme in good yield, purity and homogeneity. Employing a wide variety of biochemical and chemical methods, the chemical mechanism of PglC has been dissected. The mode of action of the enzyme is found to be fundamentally different to the mechanism of all known PGTs. To gain deeper insight, structural investigation of the enzyme was carried out. The structure reveals a novel fold and a new paradigm of membrane association that is unprecedented in the literature. The structure also uncovers the enzyme active site, located at the membrane interface to enact a challenging reaction between a membrane-embeded and a soluble substrate. These new insights that have been derived from my work will fuel small molecule inhibitor development targeted towards attenuation of the virulence of Campylobacter jejuni as well as a wide range other microbial pathogens that employ homologous enzymes.

I will also briefly highlight a newly-discovered alkane-producing enzyme in Cyanobacteria. The enzyme converts aldehydes to alkanes, once again, an extremely challenging reaction. Alkane-producing enzymes have recently gained tremendous attention due to the unusual and energetically-demanding reaction that they catalyze as well as due to the potential significance of alkane-based biofuels that can serve as a 'drop-in' renewable replacement for petroleum fuels. Extensive investigation of the enzyme was carried out that involved rigorous characterization, optimization of activity, exploration of substrate specificity and kinetic properties, and dissection of the chemical mechanism of the enzyme employing strategically designed substrate analogs. Enzymes of this class may hold important promise and potential for the production of next generation of hydrocarbon-based biofuels.

References

Ray, L. C.,‡ Das, D.,‡ Entova, S., Lukose, V., Lynch, A. J., Imperiali, B.* and Allen, K. N.* Nature Chem. Biol., 2018, In press Das, D.; Kuzmic, P; and Imperiali, B.* Proc. Natl. Acad. Sci. U.S.A., 2017, 114, 7019. Das, D.; Walvoort, M. T. C.; Lukose, V.; and Imperiali, B.* Sci. Rep., 2016, 6, 33412. Das, D.; Ellington, B.; Paul, B.; and Marsh, E. N. G.* ACS ChemBio., 2014, 9, 570. Paul, B.;‡ Das, D.;‡ Ellington, B.;‡ and Marsh, E. N. G.* J. Am. Chem. Soc., 2013, 135, 5234. Das, D.;‡ Eser, B. E.;‡ Han, J.; Sciore, A.; and Marsh, E. N. G.* Angew. Chem. Int. Ed., 2011, 50, 7148.

All are cordially invited to attend the seminar