Tata Institute of Fundamental Research
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Internal Seminar

Chemical Protein Synthesis: Developing small D-protein inhibitors against malaria

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Widespread resistance of Plasmodium falciparum, a deadly malaria parasite, against front line antimalarials warrants immediate alternatives for containing its outbreak. Two proteins, Apical Membrane Antigen 1 (AMA1) and Rhoptry Neck protein (RON2), are known to be crucial for erythrocyte invasion of blood stage parasite, the merozoites. Disrupting AMA1-RON2 interaction alone can inhibit merozoite invasion of red blood cells. Even though many L-protein/peptide-based inhibitors are already known to disrupt AMA1-RON2 binding, their low serum stability and high immunogenicity limit them to be used as therapeutic agents. Unnatural D-peptide/protein based inhibitors have huge potential as therapeutics due to their high protease resistance and low immunogenicity. However, it is tricky to develop a successful D-peptide/protein inhibitor due to their inverse stereochemistry. We are utilizing a unique combination of chemical protein synthesis and 'Mirror-Image Phage Display', to find a suitable D-protein inhibitor for both pfAMA1 and pfRON2. The key step here is the total chemical protein synthesis of D-isomers of functional domains of malaria proteins (pfAMA1-Domain-I and pfRON2L). In this talk, I will describe challenges associated with chemical protein synthesis of both L and D isomers of malaria proteins and how we are tackling them.

In the second part of my talk I will describe the utility of protein chemistry in electrochemical research. Water electrolysis has been considered to be one of the clean and viable energy resources to replace fossil fuels. We found that functionalizing carbon nanotubes (CNT) by protein does significantly enhance CNT's activity in electrochemical hydrogen evolution reaction (HER). In this talk I will brief about how protein functionalization increases HER-activity, and how we can improve it further.

Thursday, Oct 11th 2018

2:30 PM (Tea/Coffee at 2:00 PM)

Seminar Hall, TIFR-H