NANYANG TECHNOLOGICAL UNIVERSITY

School of Biological Sciences

Reg. No. 200604393R

Research Theme: De-novo Protein Design

Research Project Title: Designing Functional Mini-proteins

Principal Investigator/Supervisor: A/P Surajit Bhattacharyya

Co-supervisor/ Collaborator(s) (if any):

Project Description

a) Background:

One of goals in synthetic biology is to design proteins that can mimic function of naturally occurring proteins or possess unique functions and structures. Recently, we have designed heme coordinating synthetic b-sheet mini-proteins. Heme as a protein cofactor serves a number of biological activities e.g. enzymatic, electron transfer and energy conservation; therefore, designing hemeproteins have gained considerable attention in the past and recent years. Most naturally occurring proteins bind heme with helical structures; heme binding b-sheet proteins are less frequent. Therefore, a majority of the de novo designed heme-proteins are based on helices. By contrast, assemblies of b-sheets frequently resulted in insoluble aggregations or stabilization of heterogeneous amyloid like b-structures. Consequently, de novo designing of discretely folded b-sheet proteins are often found to be challenging. The all b-sheet protein designing success remain limited to miniaturized, water soluble, b-sheet proteins containing three to four antiparallel b-strands. However, engineering biological functions or ligand binding into the miniaturized b-sheet proteins have met only limited success. In particular, b-sheet proteins demonstrating high affinity heme binding remained obscure.

b) Proposed work:

Utilizing non-coded amino acids and creating heme binding pockets, we have successfully designed mini protein sequences (<40 amino acids) that fold into desired multi-stranded β-sheet topologies and able to coordinate single heme or di-heme inside the heme binding pockets (refs: Angew Chem Int Ed Engl 2013, Chemical Science, 2016, Angew Chem Int Ed Engl 2017). In more recent on-going works (unpublished) we created β-sheet proteins that can accommodate multiple (four to eight) heme molecules. Capturing multiple heme molecules would generate novel protein based materials with enormously important applications e.g. fast enzymes, biosensors, light harvesting systems etc. In future works, we plan to develop synthetic proteins or nano-materials (conjugated with nano-particles) with heme or metal-ions based functionalities.

Supervisor contact:

If you have questions regarding this project, please email the Principal Investigator: surajit@ntu.edu.sg

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