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Enhancing Ligation Efficiency of Peptide Asparaginyl Ligase via Alteration of Substrate Residues Using Phage Display

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Host: Dr Deepak Choudhury

Seminar Abstract

Peptide asparaginyl ligases (PALs) represent a class of enzymes that facilitates head-to-tail cyclization or intermolecular ligation of proteins/peptides by connecting their N-terminus to a C-terminus containing a tripeptide recognition motif. As highly efficient transpeptidases with specificity for only Asn or Asp residue in the P1 position of C-terminus, PALs are versatile tools in a wide range of biotechnological applications such as protein labelling, and precision biomanufacturing of biotherapeutics such as antibody-drug conjugate. Success in genetic engineering has yielded PALs with significantly improved catalytic efficiency, though site-directed mutagenesis remains an indispensable laborious and time-consuming rational approach. In the recent years, several studies have reported the enhancement of ligation efficiency by targeting its substrates instead of the ligases. In my study, I sought to explore the potential of incoming nucleophiles of peptide substrate with the aid of phage display, peptide synthesis, and mass spectrometry to enhance ligation efficiency.

About the Speaker

Lim Ching Koon obtained a BSc (microbiology) and M.Biot from the University of Queensland. He then took up a research officer position at the Singapore Immunology Netowrk (SIgN) before pursuing a PhD under the supervision of Prof. James P. Tam at the NTU School of Biological Sciences, where he explored the specificity of substrates for peptide asparaginyl ligases (PALs) and the potential of substrate alteration for enhancing ligation efficiency using a combination of peptide chemistry, analytical chemistry, mass spectrometry, and high-throughput screening approaches.

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