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THE HONG KONG UNIVERSITY OF SCIENCE & TECHNOLOGY
Division of Life Science

Seminar Notice

"Rewriting Natural Decoding Rules by *de novo* Genome Synthesis"

by

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Abstract

Unnatural amino acids could be incorporated to expand the chemical, physical and biological properties of proteins to expand the function of life itself. There are two conceptual possibilities to achieve this goal: i). creation of an orthogonal translation system in which the orthogonal decoding rules run independently to the wildtype decoding rules to incorporate unnatural amino acids; and ii). *de novo* synthesis of a new genome in which synthetic decoding rules can be artificially redefined to expand natural decoding capacities to include unnatural amino acids.

To explore the first possibility of the orthogonal translation system, the decoding property of the orthogonal ribosome was evolved to firstly efficiently decode the conventional UAG amber stop codon as a new sense codon (riboX), then to decode quadruplet codons (riboQ). Subsequently, a set of four tRNAs derived from Pyl $tRNA_{CUA}$ were evolved to efficiently decode their cognate quadruplet codons on an orthogonal mRNAs by riboQ for incorporation of multiple distinct unnatural amino acids. These experiments established the possibility to co-evolve the ribosome and the tRNAs to drastically enhance the efficiency of unnatural amino acid incorporation in response to a synthetic orthogonal quadruplet codes, creating maximally 4^4=256 new quadruplet codons for unnatural amino acid incorporation.

The second possibility requires the development of strategies to build a synthetic genome with re-programmed synthetic decoding rules to fully harness the potential of unnatural amino acid incorporation and synthetic quadruplet codes to re-build a synthetic life that fundamentally go beyond the limits of the basic 20 natural amino acid side chains. To pave the foundation to reach for this goal, an efficient, specific, and iterative method in *E. coli* to replace defined genomic fragment with synthetic sequence (replicon excision enhanced recombination, REXER) has been developed; together with a feasible, modular, and scalable route for *de novo* genome synthesis (genome stepwise interchange synthesis, GENESIS) based on iteration of REXER. Given the length independence of REXER and the ability of *E. coli* to readily accept 300-kb BACs, the entire 4.6-mb *E. coli* genome can be replaced with synthetic DNA in around 15 steps or less by GENESIS.

Date : 27 March 2017 (Monday)
Time : 3:30 p.m.
Venue : Room 2304 (Lifts 17-18)
The Hong Kong University of Science & Technology
Clear Water Bay, Kowloon

(Host faculty: Prof. Randy Poon/Prof. Bik Tye)

ALL ARE WELCOME!!