

SINERGY SEMINAR SERIES

NUS Synthetic Biology for Clinical and Technological Innovation (NUS SynCTI)
Member of Singapore Consortium for Synthetic Biology (Sinergy)



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Functional Metagenomics: Gene Function Discovery in Uncultivated Bacteria

How do we develop a more thorough understanding of the vast majority of microbes on Earth that have never been successfully cultured? Many of these microbes are known from their DNA sequences, but not well understood. Metagenomics is a DNA sequence-based technology that facilitates the study of uncultured organisms in microbial communities at the genetic level. It relies on extraction of DNA directly from environmental samples. Whereas sequence-based metagenomics involves comparison to databases of known genes, function-based metagenomics aims to identify novel sequence / function relationships. Phenotypic screening of cloned and expressed environmental DNA has the potential to contribute to the discovery of novel sequences for biochemical activities, while enhancing the overall knowledge of the relationship between sequence and function. It has already been demonstrated that this approach leads to discovery of genes that would not have been associated with given functions by sequence analysis alone. This knowledge should improve the quality of sequence database annotations that are fundamental to sequence-based metagenomics, microbial systems biology, synthetic biology, and genome engineering.

A challenge in functional metagenomics is that the host background often limits the diversity of genes isolated, due to differential requirements for gene expression. To address this challenge, we have emphasized the development of tools for screening in multiple host backgrounds. We construct large insert cosmid libraries that are able to replicate in a variety of different hosts, and design screens that often involve complementation of mutant phenotypes. We maintain

*Trevor C. Charles, Ph.D. is a bacterial geneticist with a research program in plant-microbe interactions, functional metagenomics, and bacterial genome engineering for bioproducts. Following B.Sc. Microbiology at University of British Columbia, he obtained his Ph.D. in Turlough Finan's lab at McMaster University (symbiotic nitrogen fixation) and did postdoctoral work in Gene Nester's lab at University of Washington (Agrobacterium). He held a faculty position at McGill University before moving to his current position at University of Waterloo in 1998, where he is now Professor, and Director of Waterloo Centre for Microbial Research. He has developed, with his team, a wide-ranging research program with current activity in the following areas: 1. Transcriptional regulation control in *Sinorhizobium meliloti*, the bacterial nitrogen fixing symbiont, with a focus on a regulatory system that is required for root nodule development. 2. Genome engineering of methanotrophic bacteria. 3. Bacterial production of novel bioplastics. 4. Beneficial endophytic bacteria in controlled environment agriculture. 5. Bacterial degradation of the herbicide glyphosate. He is also co-founder and CSO of the company Metagenom Bio, which applies metagenomic and microbial community analysis to challenges in the agriculture and environment sectors.*

Tuesday, 20th August 2019 | 12pm
MD6-10-01T

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Hosted by: A/Prof Yew Wen Shan

