NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

# BIOLOGY COLLOQUIUM

Friday, 22 Feb 2019 | 4pm | DBS Conference Room 1

Hosted by Dr Chae Eunyoung

# Posttranslational modifications in natural product pathways

*Brandon obtained his B.S. in Chemistry from the University of California at Santa Cruz and his Ph.D from the University of California at San Diego. During both his undergraduate and Ph.D. Studies he worked on the isolation and structure determination of marine natural products, specifically from marine sponges. He then moved overseas to the University of Bonn and the ETH Zurich for postdoctoral research with Professor Joern Piel. While there he gained expertise in biosynthesis and genome mining approaches to natural products discovery. He is currently Assistant Professor in the Department of Pharmacy at NUS where his current research interests are in the biosynthesis and isolation of ribosomally synthesized and posttranslationally modified peptides.*


## *By* **Brandon Isamu Morinaka**

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In fundamental biochemistry, ribosomal biosynthesis is based exclusively on α-amino acids of the L-configuration. Here I will discuss the genome-guided discovery of bacterial pathways that post-translationally create either D-configured or β-amino acid containing products. These enzymes are encoded in ribosomally synthesized and posttranslationally modified peptide natural product pathways. To functionally validate enzymes, we heterologously expressed substrate and enzyme genes in Escherichia coli and carried out comparative proteomics. The identified products were elucidated by a combination of analytical and spectroscopic techniques. These posttranslational modifying enzymes belong to previously uncharacterized members of the radical S-adenosylmethionine (rSAM) superfamily. The D-configured amino acids are introduced by an epimerase while the β-amino acids are introduced by a radical mediated protein splicing process. These enzymes can be used to incorporate diverse and multiple D- or β-amino acids into substrate precursor peptides in E. coli. Although these proteins are encoded in the genomes of a wide range of bacterial species, their end natural products remain cryptic and source of new small molecules. Initial insights into these reactions as well as potential applications will be shown.



Artwork by Ann Nee, DBS, NUS