

Synthetic Biology of RiPPs and Activation of Cryptic Metabolism in Actinomycetes

Hiroyasu Onaka, Gakushuin University, Japan

Abstract

Actinomycetes are well known for their prolific production of antibiotics and other bioactive natural products. Despite their importance, many biosynthetic pathways in these bacteria remain silent or poorly expressed under laboratory conditions. Our research focuses on developing strategies to access this hidden metabolic potential.

In the first part of this lecture, I will present our recent work on ribosomally synthesized and post-translationally modified peptides (RiPPs) produced by actinomycetes. In particular, we have utilized the lactazole thiopeptide biosynthetic machinery as a synthetic biology platform to generate diverse unnatural thiopeptides through precursor peptide engineering. This system provides a versatile approach for creating middle-sized cyclic peptides relevant to drug discovery.

Finally, I will describe our studies on microbial interactions in soil ecosystems. Through co-culture experiments, we have shown that interspecies interactions can activate otherwise silent secondary metabolism in actinomycetes, providing an effective strategy for discovering new natural products.

Short Bio

Hiroyasu Onaka is a Professor in the Department of Life Science at Gakushuin University, Japan. He received his Ph.D. from the University of Tokyo and has worked extensively on microbial natural products produced by actinomycetes. He also led an endowed research laboratory at the University of Tokyo for ten years, focusing on exploring microbial metabolic potential. His current research centers on ribosomally synthesized and post-translationally modified peptides (RiPPs), synthetic biology of natural product biosynthesis, and activation of cryptic secondary metabolism through microbial interactions.