Diving into Chemistry from the Sea: Marine Bacteria as Sources of Natural Products with Unique Biosynthetic Pathways and Biological Functions

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Over half of marketed drugs are derived from natural products. Elucidation of biosynthetic pathways by which living things assemble these metabolites offers insights into Nature’s chemical synthesis toolkit as well as opportunities for genetic engineering to increase natural product diversity and enhance drug development. The marine-derived bacterium Nocardiopsis sp. CMB-M0232 is a talented producer of structurally intriguing natural products that hold potential as future pharmaceuticals. These metabolites include the nocardiopsins, which modulate FK506-binding proteins (FKBPs), and the nocardioazines, which reverse drug resistance among cancer cells. To unveil the biosynthetic pathway responsible for production of each metabolite, we sequenced the genome of Nocardiopsis sp. Bioinformatics analyses of these data revealed that Nocardiopsis sp. harbors genes predicted to encode production of nearly a dozen chemically distinct groups of natural products, including the nocardiopsins and nocardioazines. Selected genes from the bioinformatics-predicted nocardiopsin and nocardioazine pathways were heterologously expressed, and the resulting enzymes characterized in vitro to unveil their biosynthetic functions. These experiments revealed that both the nocardiopsin and nocardioazine pathways include unprecedented features, which shall be discussed in this STEMinar.