DEPARTMENT OF CHEMISTRY & CHEMICAL BIOLOGY

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Putting synthetic in biosynthetic chemistry: Increasing the diversity of natural product space with engineered systems

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Chemicals produced by biological systems have had a tremendous impact on society. In the field of medicine, these natural products and their derivatives account for about one third of small molecule drugs approved over the last 30 years. However, natural products have evolved to provide the organism that produces them with a competitive advantage, rather than to be used as drugs in humans. One approach to accessing natural product like compounds with desired activities or other characteristics is to engineer natural product biosynthetic pathways to produce “unnatural” natural products. To explore this approach, during my graduate work in the laboratory of Michelle Chang, I studied the organofluorine metabolism of Streptomyces cattleya, a bacterium that produces fluoroacetate and fluorothreonine, and used what I had learned to engineer the incorporation of fluoroacetate building blocks into model polyketide natural products. During my postdoctoral work in the laboratory of Wilfred van der Donk, I developed and validated yeast surface display as a platform for screening libraries of lanthipeptides, a class of cyclic peptide natural product, for the ability to disrupt protein-protein interactions. These studies highlight the potential of using biosynthetic enzymes to explore and expand the chemical space of natural products.