BIOCHEMISTRY SEMINAR

Elucidating the Natural Product Signaling Systems of the Genus Streptomyces

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Abstract: More than 60% of antifungal, antimicrobial, and anti-cancer drugs come from natural sources, such as plants, fungi, and bacteria; we call these nature-derived drugs Natural Products (NPs). One 'super producer' of NPs is the bacterial genus Streptomyces, with over 70% of therapeutic NPs sourced from Streptomyces. These chemical weapons are regulated by sensitive signaling systems that respond to environmental conditions and subsequently activate expression of 'NP biosynthetic gene clusters', enzymes that biosynthesize NPs. Essential components of these signaling systems are cluster situated regulators (CSRs), transcription factors that can repress NP gene cluster expression until they sense a chemical signal. Previous research identified gamma-butyrolactones and butenolides (GBLs) -small, low-concentration signaling molecules that effect morphological development- as ligands of CSRs that can induce NP expression, including therapeutically relevant NPs such as avermectin or streptomycin. This regulatory strategy is bioinformatically predicted to regulate potentially hundreds of novel NPs. My research objective is to elucidate the signaling systems of Streptomyces which elicit NP production to induce or enhance NP expression. To execute this objective, I have developed a plasmid-based fluorescence reporter assay to identify CSR/GBL pairs. These assays can aid in Natural Product discovery, as well as having broad applicability for building novel genetic circuitry for use in synthetic biology applications.

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