Natural product antibiotic biosynthesis

Most antibiotic drugs in use today are natural products or natural product derivatives. These drugs are produced by living organisms such as bacteria, fungi, and plants. Our research is focused on understanding how nature synthesizes large and complex antibiotic drugs. In particular, we have investigated how *Streptomyces* bacteria synthesize echinomycin and lasalocid A. Echinomycin is a member of the quinoxaline family of non-ribosomal peptide antibiotics and it acts by intercalating double-stranded DNA. Echinomycin contains an unusual thioacetal linkage that is derived from a disulfide bond. This thioacetal group confers structural rigidity, chemical stability, and target selectivity. Lasalocid A belongs to the polyether family of antibiotics and derives its antimicrobial activity from its ability to carry cations across the cell membrane. The structure of lasalocid A is particularly interesting from a synthetic chemistry perspective because it contains a six-membered cyclic ether moiety that is produced from an enzymatic epoxide ring opening reaction. Our work opens up the possibility of using synthetic biology to produce novel natural product analogues.