Discovering New Antibiotics Using Old Ones

Presented by Mohammad Seyedsayamdost, Princeton University

Microbial natural products serve as a dominant source of pharmaceutical compounds and comprise some of our most celebrated cures. Recent studies, however, have been plagued by the frequent rediscovery of old molecules. The underlying reason is that the vast majority of natural product biosynthetic genes in a given bacterium are not significantly expressed, when cultured under standard laboratory conditions. These so-called ‘silent’ or ‘cryptic’ gene clusters represent a large reservoir of bioactive molecules and methods that access them would have a profound impact on natural products research and thereby on drug discovery. In this talk, I will present new strategies that my group has developed for activating silent biosynthetic gene clusters. Application of these approaches to diverse bacteria has unveiled not only the products of silent clusters, but also small molecule elicitors, which in most cases are growth-inhibitory or antibiotic in nature. These insights have led to the idea that old antibiotics may be used to find new ones. In addition, my group has been engaged in elucidating new transformations carried out by metalloenzymes during natural product biosynthesis. Recent reactions that we have discovered, along with proposed mechanisms, will be presented as well.

Hosted by Neel Shah