INVITED SPEAKER

CONTEXT-DEPENDENT INHIBITION OF PROTEIN SYNTHESIS BY RIBOSOME-TARGETING ANTIBIOTICS

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Antibiotics are a mainstay of modern medicine, but their effectiveness is threatened by the spread of antibiotic-resistant bacteria. While prevention of antibiotic misuse in humans and animals is necessary to address this global public health crisis, it is also essential to develop new antibiotics that can bypass existing resistance mechanisms. Of the antibiotics currently in use, more than half act on the ribosome, the large ribonucleoprotein complex responsible for translating the genetic information encoded in messenger RNA into proteins. For the most part, ribosome-targeting antibiotics are derived from natural compounds extracted from soil microbes during the golden age of antibiotic discovery (1950-1960), and the precise molecular mechanisms by which many inhibit the ribosome are only partially understood. Here, I will present our recent efforts to decipher the mechanisms of action of various antibiotics by a combined approach involving cryo-EM and high-throughput biochemistry. In particular, I will focus on how the precise substrate composition of the ribosomal complex can result in context-dependent inhibition of translation by certain antibiotics. Ultimately, understanding how antibiotics work at the molecular level could help develop improved versions of existing drugs to counter the spread of resistant pathogens.