Cyclic dinucleotide and quorum sensing revolutions could solve the antibiotic resistance problem

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Abstract:

According to the US centers for disease control and prevention (CDC), antibiotic-resistant pathogens make over 2 million Americans sick every year and over 23,000 deaths per year could be attributed to these bugs. Worryingly there are a few pathogens, the so-called super-bugs, that are resistant to a plethora of antibiotics. In the last decade most of the antibacterial agents that were approved by the FDA met the same antibiotic resistance fate, probably because these agents were mere derivatives of existing drugs, for which resistant bacterial strains already existed. The current antibiotic resistance crisis and the projection that this problem will worsen calls for immediate action to identify new tactics to tackle multi-drug-resistant bacteria. About three decades ago, Benziman and his colleagues discovered an interesting signaling pathway in bacteria that involved the conversion of GTP into cyclic dinucleotides but this seminal discovery remained largely unexplored until the last few years when scientists began to appreciate that cyclic dinucleotide signaling in bacteria is widespread and that these second messengers control a plethora of processes that affect bacterial fitness. We are currently witnessing a cyclic dinucleotide revolution that promises to usher in a new class of antibacterial agents. In this talk, I will discuss some of our efforts to develop novel antibacterial agents that target bacterial communication networks, including cyclic dinucleotide signaling.