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“Discovery and Design of WMDs (Weapons of Microbial Destruction)”

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12:00 Noon
SciTech Room 136
Antibiotics have proven to be one of the most important innovations of the 20th century, and much of modern medicine is predicated upon physicians’ ability to prevent or cure bacterial infections. In response to the strong selective pressure of widespread antibiotic use, microbial pathogens have evolved resistance to most of the antibacterial drugs in the clinician’s toolkit, and the rapid spread of drug-resistant and multidrug-resistant bacteria constitutes a looming public health crisis.

In the near future, biotechnology may enable a genuine paradigm shift in physicians’ approach to treating bacterial infections. One exciting development on the immediate horizon is antibacterial enzyme therapies, which kill infectious pathogens by actively degrading cell wall peptidoglycan causing bacterial lysis and death. This concept shows enormous promise, including early success in clinical trials. However, there exist technical barriers to widespread discovery, development, and deployment of antibacterial biocatalysts. First, effectively mining the global biome for undiscovered yet potent bacteriolytic enzymes will require sophisticated, ultra-high throughput screens that go beyond conventional antibiotic discovery technologies. Second, the vast majority of antibacterial biocatalysts are of non-human origin, and administering any such exogenous protein to a human patient runs the risk of eliciting a detrimental anti-drug immune response. This talk will introduce the concept of enzymatic antibiotics, discuss innovative screening technologies for discovery and engineering of antibacterial enzymes, and highlight T cell epitope deletion as a means of engineering less immunogenic and safer biotherapeutic agents.