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BACTERIAL GLYCOENGINEERING: FROM ENZYMES AND PATHWAYS TO HUMAN THERAPIES AND VACCINES

Life is thought to depend on 200-300 core biological processes. The vast majority of these are accomplished by large heterogeneous protein assemblies commonly referred to as machines. Unfortunately, the functional details of these cellular machines remain poorly understood. This has hindered our ability to harness them for tackling problems that cannot be solved with natural systems. Thus, our research aims to engineer the protein machinery of simple bacteria in order to solve complex problems in biology and medicine. We focus on the molecular machines of protein biosynthesis both as a toolbox for the discovery, design and manufacturing of biopharmaceuticals and as targets for reprogramming cellular physiology.

One of our approaches is exploiting the untapped mechanistic features of existing cellular machinery, such as the intrinsic mechanisms that control protein quality and ensure the correct folding and assembly of native and non-native proteins. This approach has illuminated important structurefunction relationships in protein machinery and it has provided a basis by which the machines can be harnessed for producing novel biotechnological products. A second related approach is engineering microbial cells with unnatural protein machinery, thereby expanding their repertoire of useful biological and chemical functions far beyond those bestowed by nature. In this talk, I will discuss how bacterial cells that are armed with entirely new functionalities for producing and conjugating diverse polysaccharide structures can provide a robust platform for the biosynthesis of complex therapeutic proteins and vaccines.

