Building up cell division by design

Summary

Constructing autonomous division machinery within minimal cell models is one of the major goals of bottom-up synthetic biology to decipher the fundamental prerequisite of life, such as the self-organization of cytoskeletal proteins that govern higher-order functions, e.g., division, motility, etc. Here, we present two recent achievements in this regard; 1) in vitro reconstitution of a bacterial divisome formation within minimal cell models, in which E. coli FtsZA-based contractile ring is positioned into the mid-cell by MinCDE proteins. The success of in-vesicle protein synthesis allowed us to observe the entire sequence of self-organization events and the constriction of lipid vesicles by the division ring, making an essential step toward constructing a minimal cell model. 2) machine learning (ML) based generative protein design for de novo proteins with a higher-order protein function that organizes the cellular interior. We successfully validated ML-designed proteins by a comprehensive in silico, in vitro, and in vivo screening pipeline (i3-screening) that eventually found the fully functional substitution of a natural gene by an ML-designed gene in E. coli cells, giving rise to the next level of synthetic biological applications, where the cell division will be built up by design.