Artificial Strain Construction with a Minimal Genome

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Creating an artificial strain with a minimal gene set for a specific purpose is every biologist's dream. With the complete genome sequencing of more than 270 microorganisms and extensive functional analyses of their genes, it is theoretically possible to produce a genetic blueprint for a simple custom-designed microbe with a minimal gene set. Two different approaches are being considered. The first "top-down"approach is trimming the genome to a minimal gene set by selectively removing genes of an organism which are thought to be unnecessary based on functional genomics of microorganisms. The second "bottom-up" approach entails synthesizing the proposed minimal genome from basic chemical building blocks and inserting it into an environment that allows metabolic activity and replication. The "bottom-up"approach is technically challenging and an actual experiment synthesizing an artificial genome from chemical building blocksmay not be attainable in the nearest future because of the lack of the complete functional analysis of the genes needed for a life. However, the "top-down" approach starting with the genome of a well-known microorganism is more technically feasible because the top-down approach can be initiated in parallel with the progress of the functional genomic researches of microorganisms.

In this presentation, we will describe the "top down" approach for minimizing E. coligenome to create an artificial organism with "core"elements for free self-sustaining and self-replicating cells by eliminating unnecessary genes. Using several different kinds of sophisticated deletion techniques combined with P1 phage and transposons, we constructed more than 2,000 mutants and deleted about 30% of *E. coli* genome without causing any aberrations to cell growth. The minimized *E. coli* genome and a large number of deletion mutants can lead to the construction of many custom-designed strains with a myriad of practical and commercial applications.