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Genome-scale engineering: A new frontier in metabolic engineering

Advances in reading, writing and editing genomes have greatly expanded our ability to reprogram biological systems at the resolution of a single nucleotide and on the scale of a whole genome. Such capacity has drastically accelerated the cycle of design, build and test in synthetic biology to construct organisms as cell factories for synthesis of fuels and chemicals. In this presentation, I will introduce three new strategies for genome-scale engineering of *Saccharomyces cerevisiae*, a prominent industrial production host. These strategies include: (a) a CRISPR/Cas9 and homology-directed repair assisted genome-scale engineering (CHAnGE) method for rapid engineering of *S. cerevisiae* with single nucleotide resolution; (b) a tri-functional CRISPR-Cas system for simultaneous gene activation, interference, and deletion in *S. cerevisiae* either for a set of pre-selected targets or on a whole genome scale; and (c) design and construction of the RNA interference machinery for automated genome-scale engineering in *S. cerevisiae*. Coupled with our recently developed Illinois Biological Foundry for Advanced Biomanufacturing (iBioFAB), these strategies should greatly accelerate the metabolic engineering of *S. cerevisiae* for production of value-added products and provide new insights into cellular metabolism and physiology.