GENOME ENGINEERING TECHNOLOGIES FOR PROGRAMMING AND RECODING ORGANISMS

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A defining cellular engineering challenge is the development of high-throughput and automated methodologies for precise design and manipulation of genomes. To address these challenges, we develop technologies – MAGE (multiplex automated genome engineering) and CAGE (conjugative assembly genome engineering) – for versatile genome modification and evolution of cells. Our methods treat the chromosome as both an editable and evolvable template and are capable of simultaneously targeting many locations on the chromosome to fundamentally re-engineer genomes from the nucleotide to the megabase scale. I will first describe the use of these technologies to diversify pathways and recode genomes in bacteria. These Genomically Recoded Organisms (GROs) contain an alternative genetic code, in which all 321 UAG stop codons have been eliminated from the genome of E. coli. GROs exhibit improved properties for incorporation of nonstandard amino acids that expand the chemical diversity of proteins in vivo, establish genetic isolation and multi-virus resistance, and enable the engineering of GROs to depend on synthetic amino acids for robust biocontainment strategies. Finally, I will describe extensions of these genome engineering technologies into industrially relevant eukaryotic microorganisms. This work increases the toolbox for genomic and cellular engineering with the goal of expanding the functional repertoire of organisms.