Invited Speaker Abstract Submission

A Semi-synthetic Organism with an Expanded Genetic Alphabet

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Expansion of the genetic alphabet to include a third base pair not only has immediate utility for a number of applications, such as site-specific oligonucleotide labeling, but also serves as the foundation for an organism with an expanded genetic code. Toward this goal, we have examined a large number of different unnatural nucleotides bearing mainly hydrophobic nucleobase analogs that pair based on packing and hydrophobic interactions rather than H-bonding. Optimization based on extensive structure-activity relationship studies and two screens resulted in the identification of a class of unnatural base pairs that are well recognized by DNA and RNA polymerases. More recently, we have engineered *E. coli* to import the requisite unnatural triphosphates and shown that DNA containing the unnatural base pair is efficiently replicated within the cell, resulting in the first semi-synthetic organism that stores increased information in its genome.