BIOCATALYSTS FOR ABIOLOGICAL CHEMISTRY: BRINGING NEW CHEMISTRY TO LIFE

Frances Arnold, California Institute of Technology
frances@cheme.caltech.edu

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We create enzymes that catalyze reactions not known in living systems. We direct the evolution of new enzymes by starting from the 'promiscuous' activities of existing proteins, identifying catalytic activities that may be known to synthetic chemistry but that nature has not (yet) discovered. We have found that heme proteins are a wonderful source of new biochemistry: engineered cytochrome P450s and other heme proteins catalyze a wide range of synthetically useful carbene and nitrene transfer reactions, from alkene cyclopropanation to Si-C bond formation to direct amination of C-H bonds. It's fascinating to observe how members of nature's vast catalog of proteins can be evolved—with only a few mutations—to catalyze these reactions with high efficiencies and selectivities, even forming chemical bonds that are unknown in biology. These results demonstrate the ease with which evolution can innovate and enable life to respond to new challenges or opportunities. In the future these fully genetically-encoded catalysts may access vast areas of chemical space that life has not explored. These catalysts already offer an efficient, cost-effective, green biocatalytic alternative to the use of stoichiometric reagents, rare transition metal catalysts, and organic solvents in production of a variety of fine chemicals and pharmaceutical intermediates.

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