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Title: Expanding the Synthetic Capabilities of Yeast

Abstract:
In vitro directed evolution allows biomolecules with new and useful properties to be engineered—mimicking natural evolution on an experimentally accessible time scale by creating large libraries of DNA mutants using PCR and then carrying out a high-throughput assay for variants with improved function. To provide a breakthrough in the complexity of libraries that can be readily searched experimentally for synthetic biology and to allow systems to be directly engineered in the cell, my laboratory is engineering *S. cerevisiae* so that both the mutagenesis and selection steps of directed evolution can be carried out entirely *in vivo*, under conditions of sexual reproduction. We have built a modular chemical complementation assay, which provides a selection for diverse chemistry beyond that natural to the cell using themes and variations on the yeast two-hybrid assay. In addition, we devised a heritable recombination system, for simultaneous mutagenesis and selection *in vivo* under conditions of sexual reproduction. Finally, we have begun to utilize these mutagenesis and selection technologies to engineer yeast to carry out new functions themselves ranging from being a biosensor, to a therapeutic, to a self-organizing community.