TR35

2007 Young Innovator

Kristala Jones Prather, 34

MIT

Reverse-engineering biology

Scientists are increasingly looking for ways to make compounds using -biological processes rather than -chemical reactions. Such techniques could provide environmentally


Credit: Mark Ostow

cleaner ways to manufacture everything from biofuels to drugs, avoiding the harsh solvents and toxic by-products associated with more conventional synthesis. Kristala Jones Prather, an assistant professor of chemical engineering, is developing a promising strategy for synthesizing commercial molecules biologically, from start to finish.

Organic chemists often begin with the structure of a molecule they want to make, then look for the simplest pathway of precursors to produce it. The strategy is called retrosynthesis. Prather believes that biologists can use similar reverse-engineering principles--she calls it "retro-biosynthesis"--to build compounds, stringing natural and engineered enzymes together in novel combinations inside microbial hosts such as *E. coli*.

"What I'm interested in is designing organisms to be chemical factories," says Prather, who spent four years in the -Bioprocess Research and Development department at Merck. "We used biological systems to do one reaction, and we passed that back to a group of chemists who would do the rest of the fun stuff, and I started thinking, 'Why can't biology do more?'"

In 2004, Prather left industry and joined academia so she could help -biology do more. Enzymes catalyze a wide range of chemical reactions. Prather is developing a database of these reactions; it includes algorithms that will identify the enzymes most useful for constructing novel meta-bolic pathways--in many cases leading to chemicals that are not produced through any natural biosynthetic pathway. When multiple

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enzymes might fit the bill, her software will help select the best one; when no appropriate enzyme is known, the program will help determine which existing enzyme should be modified in order to fill the hole. Prather's software should be a boon to other synthetic biologists who now construct metabolic pathways by painstakingly combing the literature for possible enzymes, says Jay -Keasling, a leading synthetic biologist at the University of California, Berkeley, who supervised her PhD thesis.

Adds John Woodley, professor of chemical engineering at the Technical University of Denmark, "It's a very clever idea."

--Jennifer Chu

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