A giant step toward creating better fats

Enzymes are the designers that fashion fats. Like most couturiers, they tailor their creations in secret—away from the prying eyes of engineers who would copy both their designs and their techniques.

Now, an international team of biochemists and structural biologists has uncovered the active elements that allow one of the most important enzymes to convert a saturated fat into an unsaturated one. By applying this insight, the researchers have already begun creating novel enzymes, with the eventual goal of designing equally novel fats.

They say that the new findings lay the genetic groundwork for a host of new crops—for example, a canola that manufactures its own low-calorie margarine or produces the raw material for nylon, now obtained from petroleum.

Today, the market for oils from crop plants exceeds $80 billion annually, notes John Shanklin of Brookhaven National Laboratory (BNL) in Upton, N.Y., who led the study. He predicts that as genetic engineers develop plants to produce new fats—whether fats that other plants had evolved to make or fats that had never existed before—"farmers will be able to plant the same acreage but dramatically boost the dollar value of their crops."

Moreover, this research holds the prospect of turning into renewable resources many commodities now derived from petroleum. For instance, Shanklin says, "you could decide how much nylon you wanted to make next year and then plant that much canola."

At the core of each fatty acid is a chain of carbon atoms, usually from 8 to 20 units long. Shanklin's team has been focusing on desaturase enzymes, which create a double bond between a pair of carbons in that molecular backbone. Each desaturase works on a fatty acid of a specific length, placing its double bond at a certain location in the backbone.

A desaturase called stearoyl delta-9, from the black-eyed Susan vine, places a double bond between the ninth and tenth carbons in a straight, 18-carbon-long fat. This transforms the saturated stearic acid into oleic acid, the monounsaturated fat that predominates in olive and canola oils. Besides introducing a kink into the molecule, this double bond dramatically lowers the fat's melting point—making oleic acid liquid at room temperature—and inserts in the molecular backbone a weak point where any later chemical reactions will tend to begin.

In the May 13 Proceedings of the National Academy of Sciences (PNAS), Shanklin's team reports that substituting different amino acids for just 5 of the 360 that make up stearoyl delta-9 converts this enzyme into one that places its double bond after the sixth carbon in palmitic acid, a 16-carbon-long saturated fat.

By mapping the placement of those substitutions onto the crystal structure of the original desaturase enzyme, "we could begin to understand why some of those changes worked," he says. With these new insights, Edgar B. Cahoon, also of BNL, engineered a two-amino-acid change to stearoyl delta-9 to make an enzyme that inserts a double bond at the normal place—after the ninth carbon—but almost exclusively in palmitic rather than stearic acid.

"While this manufactured enzyme doesn't exist in nature," Shanklin notes, "it produces the same fatty acid as a structurally different enzyme that his team has just isolated from the milkweed plant. Moreover, "when we compared the enzyme from milkweed to the [novel] one, the manufactured enzyme was much more efficient," Shanklin notes. His team reported the findings in the April 6 Plant Molecular Biology.

"What is exciting is that this work involves enzymes that determine the fatty acid composition of vegetable oils and therefore has immediate prospects for producing useful products," says John Browse of Washington State University in Pullman.

Tony Kinney, a lipid biochemist at DuPont Experimental Station in Wilmington, Del., describes the new work as "seminal." The locations of a fat's double bonds is pivotal, for example, to whether the compound will make a good paint hardener versus a raw material for nylon. "We're really interested in this [PNAS] study, and other companies are too," he says, because it "suggests how we might modify existing enzymes by manipulating genes to put double bonds into fats where we want them."

Indeed, Shanklin says, if the canola plant could be engineered to make the novel enzyme that his team developed—and is in the process of patenting—"perhaps instead of canola, you could call the plant canylon." —*J. Raloff*

News flash! A burst goes the distance

After more than 25 years of debating whether gamma-ray bursts come from within our galaxy or from far beyond it, astronomers report the first proof that one of these energetic flashes originates outside the Milky Way.

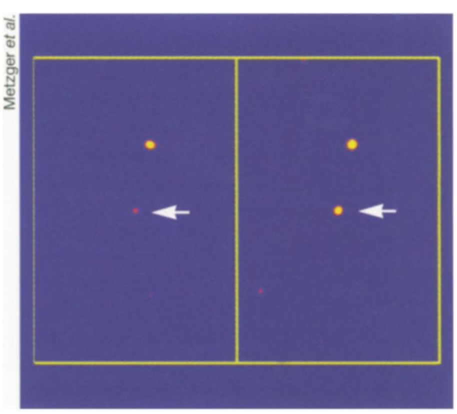
The burst, dubbed GRB 970508, was observed May 8 by the Dutch-Italian satellite BeppoSAX and lasted only 35 seconds. Within a few hours, astronomers had found a visible-light counterpart—a starlike object fluctuating rapidly in brightness at the burst's position. Howard E. Bond of the Space Telescope Science Institute in Baltimore and his collaborators detected this afterglow from the Kitt Peak National Observatory near Tucson, Ariz., while Mark R. Metzger of the California Institute of Technology in Pasadena and his colleagues found it in observations from the Palomar Observatory near Escondido, Calif.

These findings rank as a milestone. Astronomers have only once before identified the visible-light counterpart of a gamma-ray burst; that burst was also detected by BeppoSAX (SN: 5/17/97, p. 305; 3/22/97, p. 174).

On May 11, Metzger and his collaborators made an even more momentous discovery. Using Keck II, the newer of the two 10-meter telescopes atop Hawaii's Mauna Kea, the astronomers measured spectra of the counterpart. The spectra revealed that light emitted by the object had passed through an intergalactic cloud, which absorbed certain wavelengths of the radiation. The wavelengths that the researchers detected indicate that the cloud lies some 7 billion light-years from Earth, about halfway to the edge of the observable universe. At this distance, the burst must be highly energetic to have been detected.

The finding that the visible-light afterglow, and therefore the burst itself, must lie beyond the cloud clinches the notion that this burst originated far from our galaxy. The astronomers don't know whether the counterpart resides immediately behind the cloud or much farther away, but other evidence from the spectra suggests it cannot be more than 12 billion light-years from Earth. Metzger and his colleagues report their findings in the May 11 circular of the International Astronomical Union.

Gamma-ray theorist Bohdan A. Paczynski of Princeton University says the data provide "proof that the distance to the burst is cosmological." He notes, however, that the jury is still out on whether other bursts are extragalactic. —*R. Cowen*



Metzger et al.

Visible counterpart (arrows) of a gamma-ray burst brightens from May 9 (left) to May 10 (right). It has since dimmed.