

tein in fragments than functional enzymes using his vectors.

Silhavy, Benson, and their colleagues have pursued their transport research at NCI's Frederick Cancer Research Center for Litton Bionetics under an NCI contract. Michael Hanna, director of Litton's Institute of Applied Biotechnology, believes that this technology may also lead to new methods of immunization. The current competing biotechnology in this area, the cloning and production of pure antigen for vaccines, is not completely satisfactory. Robert Fildes, president of Cetus, remarks about the cloning method: "Although you can make these pure antigens, they are not necessarily in the most active form in terms of eliciting good immune response." Fildes thinks it would be useful to investigate whether or not the presence of a bacterium would increase the immunogenicity of an antigenic molecule, as this would allow development of more effective vaccines.

Benson believes that further work on protein export will allow him to

place a functional enzyme or functional fragment of an enzyme onto the surface of *E. coli* and develop a biocatalytic bed. Researchers at Litton Bionetics are reportedly pursuing research on such a project.

Don Oliver, a senior scientist at the Genetics Institute in Boston, speculates that secretion in *E. coli* might be achieved by engineering a site sensitive to proteolytic cleavage into a protein expressed at the cell surface and clipping it off at that site. Hanna agrees and says that such a system could be useful. "Even though we have insulin being produced by genetically engineered bacteria," he notes, "it is really not that much better economically than the old procedure. You're getting production in the bacteria, but you're not getting secretion." According to Oliver, bacteria that normally secrete proteins, such as those in the genus *Bacillus*, are not used because little is known about their gene regulation and their genes tend to be unstable when cloned.

Although Benson and others have expressed optimism about the success

of future research in this area, that path is certainly not assured. Benson acknowledges that little other information about protein export to the outer membrane is available and that the generality of the export signals in lamB might be limited. Other researchers have conducted research which indicates limits to the evolving model. For example, Joseph Hedgepeth at the University of California has shown that the export of the lambda protein can be prevented by a deletion in the lamB gene which results in a loss of about 100 amino acids from (and including) the C-terminal end of the protein. He suggests that export may involve more signals than those indicated in Benson's work.

Silhavy remains optimistic, noting that the export of  $\beta$ -galactosidase may indicate that the transport system is applicable to proteins. Benson tentatively agrees but cautions that other proteins must be examined before the general model can be confirmed for commercial development.—William Netzer

#### INDUSTRIAL MICROBIOLOGY

## SCIENTISTS TARGET ALGAE FOR OIL PRODUCTION

LAKE BUENA VISTA, Florida—Microalgal culture may be useful for producing valuable chemical products such as oil, according to two speakers at the seventh Energy From Biomass and Wastes conference recently held here.

"Since these organisms are simpler than plants, it may be easier to manipulate them with genetic engineering techniques," says Michael Heller, supervisor of the Illinois-based molecular biology group at Standard Oil Company of Indiana. The ability to genetically manipulate algae, howev-

er, is just developing. "Most workers, ourselves included, are trying to develop suitable vector systems to carry out routine cloning in these organisms," he says.

Traditionally, algal culture systems have been envisioned as potential sources of food and biomass, but scale-up has been limited by high-cost factors such as harvesting. The ability to extract oil from these organisms could make algal culture cost-effective, says Heller.

The green unicellular alga *Bobbyococcus braunii*, which contains over 70

percent oil on a dry weight basis, has piqued the interest of researchers in this area. Because of its high oil content the organism floats on the surface of water, making it easy to harvest. However, the slow doubling time of this organism—75 hours under laboratory conditions—currently precludes its use as an economical photosynthetic oil-producer. So Heller's group is focusing their genetic engineering work on three other groups of organisms: the green algae *Chlamydomonas* sp., the blue-green algae *Anacystis nidulans*, and the photosynthetic bacteria *Rhodospseudomonas sphaeroides*.

Researchers at the Solar Energy Research Institute in Golden, Colorado, have also been interested in oil-producing algae. They have developed a cytochemical staining technique for lipids that is being used to identify organisms capable of producing intracellular oil.

"We have established the first comprehensive collection of oil-producing algae—31 species within 11 genera and five taxonomical orders of eukaryotic microalgae," says Stephen Lien, senior scientist at SERI. Among them are algae from the *Chlorella* and *Chlorococcum* genera. One species of *Chlorella* species isolated at SERI has a mass doubling time of 10–15 hours, according to Lien. This organism also accumulates about 30–50 percent of its total mass as intracellular storage oils and lipids.—Jeffrey Howell

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REASONS

**A comprehensive search of wild-type algae and the use of new genetic engineering techniques could result in the economical production of oil from these microbes.**