

# CHRONICLE

**A working party convened** by the European Federation of Biotechnology has singled out microbial physiology as a key specialty in which incomplete knowledge is constraining innovation in biotechnology. Chaired by Wim Harder of the State University of Groningen in Holland, the group terms microbial physiology "generally healthy" in Europe, but highlights eight areas requiring further development, including:

- behavior of organisms from unusual environments (including extremophiles able to grow at high temperatures, high or low pH values, and low water activity);
- post-translational modification of proteins, including selective import into cellular compartments and excretion;
- micro-environmental regulation of the cell cycle and metabolic fluxes with a view to improving product formation;
- interactions in, and stability and performance of, consortia, including biofilms and microbe-plant interactions;
- the physiology of microbes in immobilized systems; and
- the performance and function of production organisms under simulated process conditions.

"The efforts of each individual country in Europe are not adequate to ascertain a sufficient level of competence," says the report (*Microbial Physiology and Biotechnological Innovation in the EEC Countries, Portugal and Spain*). "In view of developments in the USA and Japan, we recommend that a coordinated effort in Europe is undertaken to stimulate both basic and applied research in selected areas of microbial physiology so as to successfully meet current and future world-wide competition." The working party is now preparing material for an EEC Research Action Program in Biotechnology, as well as organizing symposia designed to focus attention on the links between microbial physiology and biotechnology.

**Holland's program to attract** biotech companies seems to be working. Centocor (Malvern, PA) and Molecular Genetics (Minnetonka, MN) have announced plans to form Dutch subsidiaries at the Leiden Bio-Science Park, and a spokesman from the Leiden town council says talks are going on

with three other U.S.-based firms and one company from the United Kingdom. Centocor, the first to announce a Dutch effort, hopes that production of monoclonal antibody-based pharmaceuticals in Leiden can start by the end of the year.

Apart from support from Holland's Maatschappij voor Industriële Projecten (MIP) fund, companies can count on subsidies and tax breaks from the government and, currently, the favorable exchange rate of the U.S. dollar against Dutch currency. Holland, which boasts a formidable scientific and industrial infrastructure, can also be viewed as a gateway to Europe and the Middle East.

**New agreements** involving biotechnology companies:

- Calgene (Davis, CA) and DeKalb-Pfizer Genetics (DeKalb, IL) will jointly develop and market varieties of hybrid corn that tolerate the herbicide glyphosate. Calgene has a similar agreement with Phytogen (Pasadena, CA) for glyphosate-tolerant cotton. Calgene recently announced the first successful expression of the glyphosate-tolerant *aroA* gene in regenerated tobacco plants.

- Genetic Diagnostics Corp. (Great Neck, NY) signed five contracts with Hoffmann-La Roche (Nutley, NJ) for the development of monoclonal antibodies to detect drugs like marijuana, cocaine, amphetamines, and barbiturates in blood or urine samples.

- Becton, Dickinson & Co. (Paramus, NJ) doubled its equity stake in Applied Biosystems by exercising its option to buy another 10 percent of the company for \$18.4 million. Applied also announced a two-for-one split of its common stock.

**The U.S. Patent and Trademark Office** has officially allowed Cetus Corp.'s (Emeryville, CA) patent application covering novel forms of interleukin-2 made via genetic engineering in bacteria, yeast or animal cells. Cetus says this is the first patent on a recombinant IL-2. The patent covers IL-2 muteins—proteins altered using site-directed mutagenesis—that have novel amino acid sequences giving them advantages over the natural protein, the company reports. Cetus says it expects that similar patents will be granted for other countries, as well as for its beta interferon muteins.

**A U.S. patent on alpha interferon** has been issued to Hoffmann-La Roche (Nutley, NJ), which developed the product with Genentech (South San Francisco, CA). Roche says the patent will prohibit competitors from testing or marketing their own alpha interferons. Schering-Plough Corp. (Madison, NJ), which is working on a genetically produced alpha interferon with Biogen (Geneva), says it is confident that Roche's patent will not affect Schering's product.

**Technology transfer to the People's Republic of China** continues with the formation of the Sino-American Biotechnology Co. (ZhengZhou, Henan Province, P.R.C.). Promega Biotech (Madison, WI), the Luoyang Prefecture Biochemical Reagents Factory (Henan Province), China International Trust and Investment Corp. (Beijing), and SinoGenetik (Vancouver, British Columbia) are partners in the venture, which will make biochemicals and reagents for use in genetic engineering. Production is slated to begin within a year; the collaborators plan to expand the project to include agriculture, diagnostic research, and instrumentation. As a start, nine Chinese scientists will train at Promega.

**The U.S. Food and Drug Administration has granted licenses** to Abbott Laboratories (North Chicago, IL) and Electro-Nucleonics (Fairfield, NJ) to produce and sell tests to screen blood for evidence of HTLV-III virus, which is believed to be associated with acquired immune deficiency syndrome. Abbott says it is making 2 million tests a month. Both companies' tests work by detecting antibodies to the AIDS virus. Also, Genetic Systems Corp. (Seattle, WA) announced that it is starting clinical trials on a similar blood test it is developing with the Institut Pasteur Production (Paris).

**Stanford University Medical School** (Stanford, CA) is developing a vaccine to prevent the spread of urinary tract infections to the kidneys. A purified protein made from *Escherichia coli* via recombinant DNA techniques elicits antibody production that prevents virulent *E. coli* from attaching to tissues lining women's bladder and kidneys. Human clinicals could begin by the end of the year.