

MEETING REPORT

CAPITALIZING ON CELL ENERGY BUDGETS

BERLIN—"Energetic priorities dominate all other processes in living cells," Oense Nijssell of the University of Amsterdam reminded his listeners several times during this spring's Dahlem Conference. In a paper prepared jointly with David Tempest, Nijssell argued that by understanding and acting upon this simple truth, biotechnologists should be able to boost product formation using methods quite distinct from those of gene splicing. Yields of classical fermentation products like ethanol and lactic acid, for example, could be raised by measures such as decreasing the number of moles of ATP formed per mole of product and increasing the cells' energetic demands. "Thus if the ATP/lactate ratio could be made to fall from 1.0 to 0.5, yeasts would have to generate twice as much lactate to cover the same energetic need," Nijssell said. "That this is not pure speculation is apparent from present interest in *Zymomonas mobilis* as a potential ethanol producer. If we as-

sume that this yeast and *Saccharomyces cerevisiae* require the same amount of ATP to synthesize biomass from glucose, then *Zymomonas* will need twice as much glucose and synthesize twice the amount of ethanol to generate the same amount of biomass." He went on to describe tactics such as potassium limitation (causing a potassium leakage current) which could be employed to boost the ATP requirement of cells and thus heighten product formation.

Nijssell was less optimistic about methods of increasing the synthesis of substances such as proteins and some polysaccharides, which are made at the expense of energy rather than being linked with energy production. "Here too we must bear in mind a simple truth—that whereas a vital enzyme will have high priority for a microorganism, something like human growth hormone is a nonsense protein from the organism's point of view and has correspondingly less importance in energetic terms.

Production of such foreign proteins will be inherently unstable in a chemostat because any revertant will grow more rapidly and thus dominate the culture very quickly. The preferred approach will always be batch cultivation in which we deliberately separate the growth phase from that in which the gene is expressed."

Nijssell did, however, highlight possibilities for raising production of materials such as extracellular polysaccharides, which confer a selective advantage in nature that is lost when the organism is grown in pure culture, leading to a decline in capsule formation. "If this reasoning is correct, and manufacture of this polysaccharide endows a bacterium with a permeability barrier, it's possible that inclusion of certain antimicrobial agents in the medium will select for producing cells," he said. "The concentration of the antibiotic would, of course, have to be such that non-producers were killed and producer cells not."
—Bernard Dixon

CORPORATE FINANCING

GENEX SEEKS FUNDS; SELL-OUT RUMORS PERSIST

ROCKVILLE, Md.—Genex Corp.'s financial straits have become one of the more talked-about subjects in biotechnology. Once regarded as having unique promise because of its unusual focus on specialty chemical production, Genex has slipped drastically in the eyes of many analysts.

The company has committed \$25 million in cash to its production facility in Paducah, KY. Its strategy of depending on phenylalanine sales—a market where competition runs fierce and G.D. Searle (Skokie, IL) is virtually the only consumer—has been seriously questioned. And, after breaking even for the first three quarters of 1984, Genex lost \$7.5 million in the fourth quarter when its phenylalanine sales plummeted. With Genex stock languishing at around \$5 per share (after trading as high as \$23 in the summer of 1983), the company is officially in search of funding.

Last January, Genex announced that it had retained E.F. Hutton for advice on seeking additional investment. The firm has yet to garner such funding, and co-founder Robert F. Johnston says an agreement will probably not be reached for several months. "I would suspect that the company would not do a deal that would involve less than \$20-30 mil-

lion," says Johnston, a venture capitalist who is now on the board of directors of the company.

Genex reports that it is seeking either a joint venture or a private placement. To this end, it has been courting both European and American companies. "There are people who will be willing to invest at this bargain level," predicts Scott R. King of Montgomery Securities (San Francisco, CA). Analysts wonder, however, whether there is a portion of Genex's business that it could cleanly devote to a joint venture in the manner that Cetus Corp. (Emeryville, CA) farmed off its Cetus Madison agricultural subsidiary to a joint venture with W.R. Grace (New York, NY).

"It would be logical to say that with the stock price where it is, equity is not a desirable option," says Nelson Schneider, formerly an E.F. Hutton analyst and currently managing director of TEI Medical L.P. (Washington, D.C.). He sees two probable courses of action: Genex could form one or more R&D limited partnerships for development of explicit products, or it could "take cash out of the equity of its Paducah plant." Genex could mortgage the plant directly, or it could sell the facility to a real estate developer and then lease it

back. Schneider points out that most biotech companies tend to pay cash for their purchases—a proper move for research expenditures. "It would be a horror to incur debt on R&D. That would be inappropriate," he says. "But on something like a factory, you incur debt as a logical order of operating business."

More sensational rumors—none of them confirmed—continue to surface that Genex could be acquired entirely by a major company. W.R. Grace is mentioned most often as a possible suitor. Linda Miller, assistant vice president of Paine Webber Mitchell Hutchins (New York, NY), believes that a chemical company seeking a developed scientific program and interested in Genex's focus on specialty chemicals would be the most likely kind of acquirer.

"What will happen to us over the next six to eight months will not be atypical of what is happening to other companies," says Johnston. "I think that we are going to have at least one or maybe two corporate investors in the company, and that the company will continue to remain independent." The experienced venture capitalist hastens to add, however, that "If the price is right, then anything is for sale."
—Arthur Klausner