

LION and Degussa apply genomics to fermentation

LION Bioscience (Heidelberg, Germany) will analyze and sequence the genome of a wild-type strain of the amino acid-producing organism, *Corynebacterium glutamicum*, in a collaboration with Degussa (Frankfurt). This will represent the first application of full genome sequencing to an organism involved in bulk chemical production.

Rather than adopting the traditional shotgun cloning approach, LION will sequence an ordered overlapping cosmid library constructed by Alfred Pühler and his team at the University of Bielefeld (Bielefeld, Germany) as part of a long-running collaboration with Degussa. Pühler says that the ordered cosmid map is nearly complete, and he estimates that the sequencing work—of around 3 million bp—will be finished by the end of 1998.

Degussa is the only manufacturer producing all three essential amino acid supplements—lysine, methionine, and threonine—used in animal feeds. It supplies 140,000 tonnes of methionine (produced chemically), 13,000 tonnes of L-lysine, and 4500 tonnes of threonine per year. Degussa's animal feeds additives division generated DM741 million revenues in fiscal 1996/7.

Through Fermas (Slovenská Lupca, Slovakia), a joint venture with Biotika established 1992, Degussa started to produce L-lysine via *C. glutamicum*. Then in July 1997,

New lysine-producing strains resulting from sequencing could be used commercially within 3 years.

it set up Mid West Lysine (Blair, Nebraska), a joint venture with Cargill (Minneapolis, MN) to build and run a 75,000 tonne capacity L-lysine fermentation plant.

Manfred Kircher, Degussa's director of research and development feed additives (project development in biotechnology), believes that Degussa has, in *C. glutamicum*, the most economical production process for these feed amino acids. "But," he says, "to keep this position we have to improve further." Degussa hopes that the genomics project gives the company access not only to the genes that

code for the amino acid synthetic pathways ("which we have already," says Kircher), but also to genes for excretion, metabolism, and energy utilization. It is hoped this will lead not only to higher yielding organisms, but also possibly to understanding better the metabolic pathways of other amino acids, with the expectation that they too can be made cost efficiently through fermentation.

The next stage of the work will be to identify the mutations that have led to the high-yielding production strains of *C. glutamicum* that are used industrially (and by Degussa). The major impacts of the work are expected to be an increase in the efficiency of lysine production, a possible switch from *Escherichia coli* to *Corynebacterium* in the production of threonine, and even the production of other amino acids—such as tryptophan—in *Corynebacterium*. According to Kircher, the new improved lysine-producing strains resulting from sequencing could be used commercially within three years, following a period of process development that will necessarily stem from any change in the physiology of the producer organism.

John Hodgson

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