U.K. START-UP

XENOVA BLENDS OLD WITH NEW

SLOUGH, U.K.—“Our main competitor is Merck,” proclaims Louis Nisbet, R&D director of Xenova Ltd., “not Celltech.” For a new biotechnology company with a staff of just 25, this statement seems little short of ludicrous. But as an indication of Xenova’s scientific approach to drug discovery, it makes perfect sense.

Xenova’s strategy is classical with modern trimmings: Today’s biotechnology is viewed as a means to an end rather than an end in itself. Recombinant DNA technology has defined precise new targets for drugs, and candidate drugs can be tested in sensitive assays that depend on monoclonal antibodies. But the drugs themselves, insists Nisbet, are still best sought among the myriad metabolites of microorganisms via the old-fashioned approach of screening culture broths.

What makes screening less laborious than before is the automation and miniaturization of sample production and assay. As a result, Xenova expects to screen about 80,000 samples a year, comprising duplicate preparations of the metabolites produced by 10,000 microorganisms, each grown in four different broths. Nisbet anticipates that, on average, such a screen will produce five low-molecular-weight compounds of sufficient therapeutic potential to warrant characterizing fully.

The company will focus on fungi and actinomycetes, the vast majority of which will be isolated in-house from soil and other samples collected from a diversity of locations and environments. Xenova chose in-house isolation rather than tapping into existing collections because of the cost of accession, questions over ownership, and the increased chance of success when using fresh rather than stabilized isolates.

While negotiating a variety of contracts and collaborative ventures, Xenova has initiated searches for interleukin-1 (IL-1) antagonists, metalloproteinase inhibitors, and compounds active against the human immunodeficiency virus and cancer.

So, although screening will depend on the kind of products for which nearby Celltech Ltd. (Slough, U.K.) is renowned, it is Merck’s (Rahway, NJ) discovery of Mevacor®—a microbial metabolite that specifically inhibits a key enzyme in cholesterol synthesis—that Nisbet holds up as an example to follow.

—Peter Newmark

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