RESEARCH PAPER ANALYSIS

rDNA AND ANTIBIOTICS—A MAJOR ADVANCE

CAMBRIDGE, Mass.—The pioneering efforts of David Hopwood and his colleagues at the John Innes Institute (Norwich, U.K.) have led to an understanding of actinomycete genetics, and also to the idea that antibiotic biosynthetic genes and genes coding for resistance to the antibiotic in the producing-actinomycete are clustered either on a plasmid or on chromosomal DNA (Chater and Bruton, *EMBO J.* **4:**1892, 1985). In 1984, Malpartida and Hopwood (*Nature* **309:**462) placed the chromosomal genes of actinorhodin biosynthesis, present on a 34-kilobase insert from *Streptomyces coelicolor*, onto a plasmid and thus cloned the entire antibiotic pathway in *S. parvulus*. This caused great excitement because it meant that recombinant DNA technology might be used to increase antibiotic titers, to produce new antibiotic derivatives, and to carry out basic studies on the organization and regulation of genes coding for antibiotic biosynthesis.

A major advance in the application of recombinant DNA technology to the production of medically useful antibiotics is described in this issue by Richard Baltz's group at the Lilly Research Laboratories (Indianapolis, IN). These investigators cloned the genes for the entire erythromycin biosynthetic pathway plus a resistance gene from *S. erythreus* into *S. lividans*. Unlike actinorhodin, erythromycin is an extremely important medical antibiotic used against Gram-positive bacteria, mycoplasma, chlamydia, and the organism causing Legionnaires' Disease. It is the most well-known macrolide antibiotic. Despite this, its 30-step biosynthetic pathway is not yet completely understood. Still, the studies of Weber, Wierman, and Hutchinson (*J. Bacteriol.* **164:**425, 1985) at the University of Wisconsin indicated that the genes coding for the relevant enzymes are probably clustered.

The beauty of the present work lies in its simplicity. The large number of biosynthetic genes did not have to be characterized or even studied. The work was merely based on the assumption that the genes were linked to each other and to the resistance gene. A genomic library of *S. erythreus* DNA was prepared in pKC462a, a bifunctional cosmid vector that replicates in *Streptomyces* and *Escherichia coli*. An *E. coli* clone, which hybridized to a plasmid containing the *S. erythreus* erythromycin resistance gene, was used to prepare DNA which then transformed *S. lividans* TK23 to erythromycin resistance. As a result, *S. lividans*, which produces no macrolide antibiotic, was now able to produce erythromycin.

The authors seem correct in predicting that their approach—cloning antibiotic resistance genes to identify antibiotic biosynthetic genes—will be used to isolate other clinically important genes. Antibiotic strain improvement programs are also likely to adopt this strategy.

—Arnold L. Demain

EUROPEAN ECONOMIC COMMUNITY

UPGRADING BIOTECHNOLOGY ACTION IN EUROPE

LONDON—By the middle of this year, the European Economic Community's Biotechnology Action Programme (BAP) 1985–9 should be firmly under way. With a budget of 55 million European Currency Units (about $48 million), it will support work in over 150 laboratories, grouped into some 55 research projects (each involving trans-national collaboration). The Concertation Unit for Biotechnology in Europe (CUBE) will play a major role in orchestrating the BAP, as well as in monitoring developments worldwide.

Also poised for development are the Community's Bio-informatics Collaborative European Programme and Strategy (BICEPS), designed to improve access to information important for biotechnology. But, as CUBE head Mark Cantley pointed out at a recent seminar here, these various initiatives are unlikely to succeed fully unless there is action to deal with Europe's twin handicaps of unfavorable patent laws (see *Bio/Technology* **4:** 87, Feb. '86) and high feedstock prices.

"The recent OECD [Organization for Economic Cooperation and Development] review of biotechnology patent law carried a worrying message," Cantley pointed out. "The USA and Japan operate systems that are much more open than those in Europe. They also give inventors adequate legal protection."

Just as urgent is the need to reduce the prices of feedstocks such as starch, which are held artificially high in the EEC and which could induce fermentation industries to establish themselves elsewhere, probably in Third World countries where costs are substantially lower.

"This debate is still bogged down in the Council of Ministers," Cantley said. "The problem is one of political persuasion. To reverse the current situation, industry must communicate its need much more effectively."

—Bernard Dixon

BIO/TECHNOLOGY STOCK INDEX

NEW YORK—The much-discussed "public window" for biotechnology companies is now wide open, and the breeze blowing in is pleasant indeed.

On the initial public offering front, Oncogene Science Inc. (Mineola, NY) plans to raise $10–12 million by going public with a 2 million-share offering, and diagnostic specialist Hygeia Sciences (Newton, MA) intends to offer 1 million shares at a price between $8 and $10 each. Other private biotech firms, including Repligen (Cambridge, MA), Genzyme (Boston, MA), Synergen (Boulder, CO), and NPI (Salt Lake City, UT), are looking seriously at taking the public plunge, too.

Publicly held companies are also capitalizing on the favorable market to make secondary stock offerings. Such companies include Cetus Corp. (3 million shares), Immunex Corp. (1.4 million), Monoclonal Antibodies Inc. (775,000), Amgen (2 million), Chiron Corp. (1.5 million), California Biotechnology Inc. (2 million), and Damon Biotech (2.5 million).

As for the *Bio/Technology* Index of 23 Specialty Firms, this weighted average rose 51 points to 1647 between January 8 and February 12, 1986. The index was set at 1000 on July 15, 1983.

—Arthur Klausner