NEWS AND VIEWS

The Genetics of Antibiotic Formation Comes of Age

It was amply evident at the ASM Conference on Genetics and Molecular Biology of Industrial Microorganisms (Bloomington, IN, 30 Sept.–3 Oct., 1984) that the recent advent of molecular cloning methods in manipulating antibiotic-producing microorganisms has generated a renewed excitement in both the academic and industrial communities. Although the main focus of the academic scientists remains on the commercially unimportant antibiotics produced by *Streptomyces* species (model systems), the industrial scientists are making steady progress in developing the genetic tools for studying poorly characterized but commercially valuable organisms. Furthermore, two publications, one by Hopwood's group on the cloning of actinorhodin genes (*1*), and the other by Beppu's group on the cloning of A-Factor regulating gene (*2*), have proved that both the structural as well as regulatory genes involved in antibiotic biosynthesis are accessible by the existing techniques of molecular biology.

It is apparent that before too long a genetically engineered strain will be available for the large-scale production of some antibiotic(s). Moreover, recombinant strains may be also constructed to produce new antibiotics by splicing genes from two or more different pathways. This latter possibility is most exciting. In the past various techniques such as precursor feeding, mutasynthesis, and protoplast-fusion have been used with limited success to produce tailor-made antibiotics. Never before has there been even a remote possibility of predetermining almost every step in the biosynthesis of a totally novel and predesigned antibiotic. Although an understanding of the biochemistry and enzymology of various antibiotic pathways is necessary to carry out such an endeavor, even the least characterized species are not accessible with the techniques such as mutational cloning, transposons, transfection, etc. Moreover, the armory of enzymes in antibiotic-producing microorganisms is so vast and varied

that it will perplex even a most imaginative chemist. Also both the primary and secondary metabolism enzymes may be combined to obtain a desired sequence of biochemical reactions. Thus this new technology gives chemists and biologists an opportunity to join forces and begin constructing "Designer Antibiotics." Such a novel approach may even rescue some "new product screening labs" that are currently plagued by the diminishing returns of traditional screening techniques.

REFERENCES

1. Malpartida, F., and D. A. Hopwood (1984), *Nature* **309**, 462–464.
2. Horinouchi, S., et al. (1983), *J. Bacteriol.* **155**, 1238–1248.

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