

FOREWORD

The last quarter of a century has witnessed phenomenal growth in the discovery and development of new antibiotic agents, so that they now hold a highly important place in modern medicine. Chemical science has advanced sufficiently to permit the synthesis of antibiotics once thought impossible to synthesize, and methods have been devised that permit ring modifications that hold promise for reducing sensitivity reactions and slowing the evolution of bacterial resistance. Among synthetic organic chemists who have led these advances, an outstanding leader has been Professor Hamao Umezawa, Director of the Institute of Microbial Chemistry.

Under the talented leadership of Professor Hamao Umezawa, the Institute has contributed to the world a very large number of antibiotics, many of which have proved to be effective against microorganisms of medical and agricultural importance. Even a partial list of outstanding antibiotic contributions establishes this Institute at the very forefront in the discovery of new antibiotics, perhaps unrivaled by any laboratory in the world.

For example, one could cite Professor Umezawa's discovery in 1957 of Kanamycin, which historically provided the basis for the founding of the Institute in 1962.

A good illustration of his ability to follow up on the clinical progress of an antibiotic is the work of the Institute in 1967. Microbial strains resistant to kanamycin were reported in the medical literature. Immediately Dr. Umezawa discovered the enzymes responsible for the inactivation and determined the structures of the inactivated kanamycin. It then became possible to devise derivatives not susceptible to the inactivating enzymes, thus making possible new kanamycin derivatives which were clinically effective against the newly developed resistant strain.

In the area of antitumor antibiotics, Dr. Umezawa conducted some of the earliest and most significant studies. A prominent example are the bleomycins, which were first reported in 1966. The therapeutic effects of the bleomycins on squamous cell

carcinoma and Hodgkins disease represent substantial progress in the clinical management of these malignant-type diseases.

In the important field of small and medium size molecular enzyme inhibitors, Dr. Umezawa's pioneering research in 1966 is an important milestone. Some of the protease inhibitors, such as pepstatin, have attracted medical attention and stimulated research all over the world.

The discovery by Dr. Umezawa's group of the small molecular weight enzyme inhibitors has led to the possibility, now being widely explored, of isolating products from microorganisms which exhibit various biological or pharmacological properties without necessarily inhibiting the growth of the parent microbe itself.

More recently, Professor Umezawa's laboratory has been interested in the so-called "T" or transfer-effect. The "T" effect is probably involved in the development, perhaps by means of plasmids, of cross-resistance by micro-organisms to widely different types of antibiotics.

It was approximately 1957 that it was my privilege to meet Dr. Umezawa through the efforts of Dr. Amel R. Menotti, who introduced us. Dr. Menotti was then Vice-President and Director of Research at Bristol Laboratories in Syracuse, New York. I was most interested in Dr. Umezawa's recently announced discovery of kanamycin, as he was in my own recently announced total chemical synthesis of penicillin V.

Later on, Dr. Umezawa's son, Kazuo, came to MIT for a Ph. D. in organic chemistry. He completed his doctoral dissertation in my laboratory in 1972. Upon graduation he spent approximately a year at Oxford studying with Professor E. P. Abraham. It is of interest to note that not only are Professor Hamao Umezawa and his son Dr. Kazuo Umezawa brilliant organic chemists, but other members of the family as well. A brother of Dr. Hamao Umezawa is Dr. Sumio Umezawa, Professor of Chemistry at Keio University and is one of Japan's outstanding organic chemists and the author of a leading textbook. A third brother, Dr. Hiromi Umezawa, is a Professor of physics at the University of Wisconsin, USA.

During the past ten years, it has been my privilege to visit both Professor Hamao Umezawa at the Institute of Microbial Chemistry and Dr. Sumio Umezawa at the Institute of Bioorganic Chemistry. From personal observation I can attest to the outstanding quality of the personnel and facilities of both institutes.

It is a great personal pleasure to have the opportunity to provide this brief Foreword for the birthday issue of Heterocycles reflecting so much of Professor Hamao Umezawa's scientific influence and distinguished contribution.

Professor John C. Sheehan

August 10, 1979

Massachusetts Institute of Technology

Cambridge, Massachusetts

U.S.A.