Chemistry and Biology in the Braun Laboratories

An Introduction by Leroy Hood

THE BRAUN LABORATORIES and their commitment to immunology and molecular biology arose from a consideration in the early 1970s about appropriate future directions in biology. These deliberations led to a program, the Medical Sciences Program, which Caltech's president, Harold Brown, approved in 1975. This program had three major components. First, the direction was immunology and molecular biology, two areas that were having tremendous impact on both fundamental and applied medical problems. Second, three new professorial appointments were to be made in these areas. The emphasis was to be on selecting interdisciplinary scientists, excellent in fundamental research, but with a real commitment to the application of their research efforts. Finally, the Medical Sciences Program was to be housed in a new structure now known as the Braun Laboratories in Memory of Carl F and Winifred H Braun.

Caltech has made fundamental contributions to immunology and to the genetics that led to molecular biology for the past 50 years. The Division of Biology was founded in 1928, when Thomas Hunt Morgan moved from Columbia to carry on his classic work with the genetics of fruit flies, for which he received the Nobel Prize in

1933. Classical genetics led quite naturally to biochemical genetics, which was formulated and exploited by George Beadle in the 1930s and 1940s. Beadle received the Nobel Prize for this work in 1958. Max Delbrück worked on bacteriophage genetics in the 1940s, the 1950s, and the 1960s. These efforts, for which he received the Nobel Prize in 1969, laid the foundations of modern molecular genetics. In the 1970s, the progression of these diverse lines of genetic research had placed Caltech in an ideal position to participate in development of the new genetic engineering or recombinant DNA techniques. In the past ten years, scientists at Caltech have made substantial contributions to the development and application of recombinant DNA research.

In the past ten years Caltech also has developed a unique microchemical facility containing machines that allow scientists to analyze and synthesize genes and proteins in ways that were heretofore impossible. The development of this facility has in large part been made possible by the unique attributes of Caltech — excellent machine and electronics shops, a close relationship with the superb engineers of the Jet Propulsion Laboratory, and a casual and intimate atmosphere that has facilitated the interactions of biologists, chemists, and engineers. Approaches made possible by the microchemical facility and recombinant DNA techniques have proved remarkably synergistic in attacking fundamental problems of developmental biology.

Caltech's contributions to immunology have been almost as striking. Linus Pauling and Dan Campbell started in the 1940s to study the antibody molecule and determine how it carried out its function of protecting man against viral and bacterial infections. In the mid-1940s Ray Owen moved from Wisconsin and began to study the fascinating question of what prevents the immune system from attacking the individual's own proteins and cells. The question of immune tolerance to self is one of the fundamentally important areas in learning how to avoid the rejection of organ transplants.

In the 1960s, when I was a graduate student here with Bill Dreyer, he and a postdoctoral fellow, Claude Bennett, formulated a hypothesis which revolutionized immunology. This then radical concept, which suggested that antibody genes could jump around on chromosomes, has turned out to be a cornerstone of modern molecular immunology. Against this background, some striking advances in the understanding of immunologically relevant genes have occurred here in the past ten years, and Caltech has come to be known as a center of molecular immunology.

Caltech is currently one of the nationally ranked departments in molecular biology and will become even better with the recent acquisition of two outstanding senior molecular biologists from San Diego, John Abelson and Mel Simon, both of whom will move into the Braun Laboratories in 1983. A first-rate young immunologist, Ellen Rothenberg, also has recently moved here from the Salk Institute in La Jolla. These scientists, as well as the outstanding immunologists and molecular biologists already here at Caltech, are interested in a variety of fundamental problems. How do genes, such as those for antibodies and the transplantation antigens that cause the rejection of grafted organs, function? Can a precise molecular mapping of human chromosomes be determined? Can techniques for protein engineering be developed, that is, can genes be altered in test tubes so that the proteins they encode will have new and useful properties? Novel and innovative instruments continue to be developed in the microchemical facility.

As Caltech looks to the 1980s and 1990s, we would like to move in several new directions — plant molecular biology and molecular developmental neurobiology — and at the same time maintain and extend our strengths in molecular and cellular biology and neurobiology. The opportunities for future research appear practically unlimited. It will be possible to isolate biomedically interesting human genes rapidly. These genes can be placed in bacteria, yeast, or human cells to synthesize large quantities of their respective proteins for diagnostic or therapeutic purposes. Antibody molecules will be fashioned with almost any desired specificity. We will come to understand how cancer genes function and use this knowledge to design rational diagnostic and therapeutic approaches for tumors. We will be able to synthesize complete human genes. We will be able to synthesize small fragments of proteins that can be used to generate vaccines that are difficult to produce now for a variety of technical reasons. Thus the Braun Laboratories will not only represent a point of enormous excitement now, but in many ways they will serve as a focus for the development of new biotechnologies and new avenues for scientific exploration in the future. The future is indeed bright, and Caltech and the Braun Laboratories perhaps occupy a unique position in being able to take advantage of these opportunities. For all of this, we must thank John Braun, his family, and all the rest who made the Braun Laboratories possible. This issue of *Engineering & Science* presents, in the first four articles, a discussion of some of the work in progress. □