R O B E R T - K O C H - S T I F T U N G e . V .

Laudatio

for

Prof. Dr. Max Dale Cooper

by Prof. Dr. Jules A. Hoffmann

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[Address],

I am both honored and delighted to have been invited to give the laudatio of my colleague and friend Max Cooper.
Max Cooper is one of the most distinguished figures of modern Immunology. Over a period of more than 40 years, he has made seminal contributions to the study of adaptive immunity, and in fact, is credited with having set that field in the mid-sixties to mid-seventies on the course it has followed since, paving the way for some of the greatest discoveries in the science of immunology with far-reaching implications for human medecine.

Max Cooper was born in rural Mississippi, the son of school teachers. He attended medical school at Tulane University, receiving his doctoral degree in 1957. His earliest scientific work was performed as a Research Assistant at the Hospital for Sick Children in London, England, in 1961. After a year spent at the University of San Francisco, Max Cooper worked as a postdoctoral fellow and Assistant Professor at the University of Minnesota until 1967. He was then appointed Associate Professor at the University of Alabama, Birmingham, where he remained for the next 41 years, rising through the academic hierarchy to become a Professor and Division Director. Cooper was also an HHMI Investigator between 1988 and 2006. He is presently a Professor in the Department of Pathology at the Emory University School of Medicine in Atlanta, Georgia, and an Eminent Scholar with the Georgia Research Alliance. The early years of scientific peregrinations of Max Cooper were sweetened by a particularly happy family life with Rosalie Lazzara, who is with us to-day, and four wonderful children successively born at each milestone city of Max's early career : Melinda in London, Bo in San Francisco, Michael in Minneapolis and Christopher in Birmingham.

The earliest contributions of Max Cooper defined the cellular basis of adaptive immunity. In 1964, while a postdoctoral fellow in the laboratory of Robert Good, he discovered the dual origin of lymphoid cells in the chicken, showing that some cells originate in the thymus while others arise from the bursa of Fabricius. Subsequently (in 1966 and 1968) Max Cooper deduced that lymphocytes derived from the bursa are responsible for immunoglobulin synthesis. This paradigm led directly to the understanding that two developmentally separate populations of lymphocytes, B cells and T cells, comprise the adaptive immune system, not only in birds but also in mammals (and other vertebrates as we have learned since) and that these two populations make very different contributions to immunity. Cooper performed extensive studies to establish the properties of these two subsets of cells, to recognize them in peripheral blood, and to determine what the mammalian equivalent of the bursa of Fabricius might be. He could finally demonstrate in 1975 that hematopoietic tissues, in particular in the bone marrow, are the sites in which B cells are generated in mammals. T cells on their behalf originate from the thymus.

Throughout his academic career, Max Cooper divided his efforts between patient care and laboratory research. His clinical activities have mostly centered on immune system disorders, including immunodeficiency diseases and lymphoid malignancies. After having refined the model of B lymphocyte development in humans, he set out to use this information as a guideline to identify the stages at which B cell differentiation was aborted in patients who had recurrent infections because of their inability to make antibodies. To illustrate just a few ground-breaking results here, Max Cooper and his associates showed that boys with X-linked agammaglobulinemia suffer from an early arrest of B-cell lineage differentiation and that

patients with late onset agammaglobulinemia fail to undergo plasma cell differentiation. Of the more than 100 different types of primary immunodeficiency diseases that are known to affect humans, the cellular and clinical levels of the diseases are now fairly well understood and have often been nailed down to specific genes. Importantly, some of these diseases are correctible by hematopoietic stem cell transplantation and, already in a few instances, by gene therapy.
A half dozen years ago, Max Cooper made an astonishing advance that has impelled a fundamental reconsideration of how adaptive immunity evolved. It had been believed that adaptive immunity arose in cartilaginous fish, as immunoglobulins are found only in jawed vertebrates including cartilaginous fish, bony fish, amphibians, reptiles, birds and mammals. By contrast, jawless vertebrates and invertebrates, such as insects, lack immunoglobulins, and were not known to have adaptive immunity. Using classical observational methods reminiscent of those he applied in the discovery of B and T cells many years earlier, Max Cooper determined that lymphocyte-like cells present in a specialized organ named the typhlosole of jawless vertebrates (notably the sea lamprey and the hagfish) do indeed have properties reminiscent of lymphocytes and express many of the genes characteristically induced in their mammalian counterparts. Cooper then demonstrated that like the lymphocytes of jawed vertebrates, these cells exhibit a recombinatorial system for production and secretion of antigen binding proteins with a highly diverse repertoire of specificities (10^{14} or more clonotypes are now estimated to exist). However, the antigen binding proteins are not based on immunoglobulin motifs in contrast to the situation observed in jawed vertebrates; rather they are based on repeat motifs rich in leucine residues (similar to those in the quintessential Toll-like receptors, known to be used by cells of the innate immune system in the detection of microbes). Cooper thus discovered that two adaptive immune systems arose independently, each built upon the principle of genetic recombination within somatic cells, but utilizing different molecular building blocks. In an extraordinary coda to this work, Cooper recently reported that two types of lymphoid cells exist in the lamprey: one with remarkably “T-cell like” properties and the other with “B-cell like” properties. One possible interpretation of this discovery is that the precursors of B cells and T cells actually antedated the evolution of a recombinatorial system, and were utilized in a similar manner by both jawed and jawless vertebrates.

This absolutely unexpected new development in the study of the evolution of the adaptive immune system has attracted considerable interest world-wide and no major conference in immunology on the five continents takes place where Max is not one of the keynote speakers reporting these new insights into the evolution of the basic mechanisms which underlie our capabilities to fight microbial infections.

Max Cooper is a member of the National Academy of Sciences and of the Institute of Medecine of the USA. He is also a Member of the American Academy of Arts and Sciences, the Royal Society of Medicine of Great Britain, the Association of American Physicians, and the American Society for Clinical Investigation. Among many other honors, he has received the Sandoz Prize for Immunology (1990), the 3M Life Sciences Award (1990), the American Association of Immunologists Lifetime Achievement Award (2000) and recently the Avery-Landsteiner Prize (2008). It is an immense pleasure, Dear Max, to be present to-day at this ceremony which honors your immense scientific contributions with the attribution of the 2010 Robert Koch Prize for Immunology.