



Brigitte Askonas

1923–2013

Emil R Unanue

Brigitte Askonas, known to her friends as 'Ita', passed away peacefully on 9 January 2013 after a brief illness with cancer, a few months short of her 90th birthday. Ita lived a long, full and enjoyable life and made major contributions to the understanding of the immune system. She made countless friends in and out of science and was highly influential in molding the careers of many. She was universally loved and respected and, in return, she genuinely cared deeply for her many friends. Her curiosity and enthusiasm for biology, and her keen and critical eye for scientific excellence, never dwindled one bit over her long and illustrious career.

Ita thoroughly relished her entire career that spanned her entrance into the field of immunology in the mid-1950s (when the cellular basis of immunity was poorly understood) to more recent times. She contributed throughout all those years. After initial studies at McGill University, she obtained her graduate degree at the University of Cambridge in 1952 and then moved to the National Institute of Medical Research in Mill Hill, where she remained for most of her active research career. A biochemist by training, Ita focused her first immunological studies on the mechanisms that underlie antibody formation, a field that attracted her after she attended a lecture by John Humphrey. She went on to collaborate with Humphrey, joining him at the Division of Immunology, which he created. The National Institute of Medical Research in Mill Hill became, over time, a major center for immunological research in the world and attracted many additional major scientists that most prominently included Peter Medawar, who became the institute director, and Avrion Mitchison. Ita became director of the Division of Immunology in 1976, a position she held until her retirement in 1988.

Ita first studied antibody formation *in vitro* in tissues obtained from immunized rabbits and guinea pigs. One of her first important contributions was the finding that bone marrow has a high capacity for antibody formation, some of which is nonspecific. Ita then became more and more interested in the cellular basis of immunological reactions but continued to approach her investigations with a characteristic biochemical and molecular slant. Her interest in B cells eventually led her laboratory to examine and characterize the development and specificity of hapten-specific B cell clones, and her laboratory became an undisputed leader in this area.

I did a postdoctoral fellowship at the Division of Immunology in 1967 to gain further insight into the basis of immunological specificity. Ita wanted to investigate the interactions of live macrophages with lymphocytes, so we set up a system to examine the effect of antigen-fed macrophages using cell transfer; these were the initial studies on antigen presentation. Ita was a great mentor: tough and demanding, but fair. She knew how to focus on important issues—issues that could move the field vertically. Notably, she was able to

pass that unique trait on to her trainees. I had a great experience with her, and my time spent under her mentorship changed my career. She was incredibly unselfish, and when I formed my own laboratory after leaving Mill Hill, she allowed me to continue the work that she and I had started. We kept in touch over the years, and she continued to follow my work. Ita was always there to provide me with her objective opinions, criticisms and suggestions on the work. She would let me know when she disagreed with me. I came to value these interactions greatly and I respected the time and effort she spent helping not only me but also others. The reason I have emphasized my experiences in her laboratory and afterward and her influence on my future is to make the point that such experiences were not restricted to me. I was no exception but the rule; this was the experience of all who were fortunate enough to work and interact with her. Indeed, she helped launch and advance the careers of many major immunologists who populate the field today. I would like to name them all, but that is not possible in this context.

Ita continued for a time to investigate various aspects of cellular immunology, in particular, responses to infectious agents. But it was her examination of the cellular response to viruses and in particular influenza virus starting in the late 1970s that became the central focus of her career. She became interested in the major histocompatibility complex and was influenced by, among others, Hugh McDevitt who, while at Mill Hill, conducted the first successful studies that defined high and low immunological responsiveness of various strains of mice to simple synthetic polypeptide antigens. Ita went on to examine the specificity and function of cytolytic T cells to influenza virus and was the first to establish lines and clones. Mill Hill was an ideal place for such studies, as researchers there had considerable expertise in the field of influenza viruses and many collaborated with her on these projects. The end result of this was a series of major papers on the nature of influenza virus-specific T cells and, notably, on the components of the virus recognized by such T cells. Moreover, Alain Townsend, while a PhD student in her laboratory, collaborated with John Skehel to make the seminal findings on the specificity of cytotoxic T lymphocytes to the internal viral nucleoprotein that led to the realization that T cells recognize processed peptides. All these are now classical studies in the field of cellular immunology and form an important part of the understanding of the origins of lymphocyte specificity.

Ita received many honors for her multiple contributions to immunology. She was a Fellow of the Royal Society, received honorary degrees from the University of Cambridge and the University of Oxford, was elected a foreign associate of the United States National Academy of Sciences and received the Robert Koch medal. Like so many all over the world, I was very fortunate to be one of her friends.

Emil R. Unanue is in the Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, Missouri, USA.
e-mail: unanue@wustl.edu