THE FACULTY OF MEDICINE
Harvard University

Fritz Heinz Bach

Fritz Heinz Bach, a brilliant transplant immunologist and the Lewis Thomas Distinguished Professor of Surgery at Harvard Medical School died of a cardiac arrest on Sunday, August 14, 2011 at his home at Manchester-by-the-Sea, Massachusetts. He was 77 years old.

Fritz was one of a small group of young biological scientists with the genius, insight and good fortune to be associated with a discovery that had a profound, long-lasting impact on their field. He was generally regarded as one of the early giants of transplant immunology, a visionary with legendary ability to identify big concepts and ideas among masses of data and observations whose contributions changed transplant immunology as we know it. He was one of the most articulate and dynamic speakers in the field who could explain the complex in simple understandable terms. He could converse fluently in several languages, including French, German, Italian, and of course English. His early observations on cell transformations which occur in in vitro cultures of peripheral blood lymphocytes (PBL) from unrelated individuals (for which he coined the term mixed lymphocyte cultures - MLCs), his studies on the relation of these changes to the alloimmune response and histocompatibility antigens, and his early application of the MLC assay to the selection of compatible tissue and organ donors unleashed a veritable perfect storm of related progress in experimental and clinical transplantation that persists to this day. He later made major contributions to our understanding of xenograft rejection and to the importance of "protective genes" in protecting against stress and disease.

Fritz H. Bach was born April 5, 1934, into a Jewish family in Vienna, Austria, the younger of two sons of Leo Bach and Gertrude Rosenfeld. After the infamous Kristallnacht pogrom in November 1938, he and his brother, Bertholdt, were sent to safety in England in 1939 via the legendary Kinder Transport organized by the British to rescue over 10,000 predominantly Jewish children that were cared for by British families. They were later joined by their parents in Bath, England. As with many of their generation, Fritz's

In tribute to their dedicated efforts to science and medicine, deceased members of the Harvard Faculty of Medicine (those at the rank of full or emeritus professor) receive a review of their life and contributions with a complete reflection, ***a Memorial Minute****.*

maternal grandparents stayed in Vienna after hostilities began. They were subsequently deported to the Theriesenstadt work camp in 1942 and later died in the Treblinka death camp. A United States soldier sponsored the Bach family's immigration to Burlington, Vermont in 1949. Fritz graduated from Burlington High School before attending Harvard College as a scholarship student and obtaining a Bachelor's degree in 1955. He went on to Harvard Medical School where he became interested in immunology and genetics and graduated in 1960.

Fritz undertook internal residency training at New York University where he came under the influence of Dr. Lewis Thomas whom he always credited as being the inspiration for his scientific career. It was Dr. Thomas who apparently persuaded Fritz to attend a lecture by Peter Medawar given at NYU in 1961 on the antigens and mechanisms involved in allograft rejection. It was at this lecture that Medawar allegedly encouraged the young, recent medical graduate to study these problems in vitro. In 1964, Bach and Hirschorn described experiments involving the culture of peripheral blood lymphocytes from two unrelated individuals in vitro for 7-8 days in which some of the cells underwent large cell transformation and division. They estimated the percent of blast cell transformation and mitosis by microscopic examination of fixed smears. They noted that PBL cultures of individuals in whom the probability of sharing HLA antigens had been determined by skin grafting (by a group led by another future transplant luminary, Felix T. Rappaport) had the lowest number of large cells and mitoses. Bach and Hirschorn suggested that it might be possible to develop mixed lymphocyte cell cultures (MLC) as a typing test for potential recipients and donors of kidney allografts that could identify the most compatible pairs. This potential application was complicated by the fact that as described it was a two-way reaction since both donor and recipient cells reacted to each other. Only later could the recipient's cells reaction to the donor's antigens be quantitated by using stimulator (donor) cells whose transformation potential had been eliminated by prior exposure to x-irradiation or Mitomycin C – a culture modification graciously attributed by Fritz to a suggestion by Leslie Brent. Later work by Fritz and others showed that lymphocytes generated in MLC cultures were cytotoxic to stimulator cells thereby connecting in vitro alloreactivity with in vivo graft rejection, i.e. the MLC reflected activation of the immune response and the derivative CML reaction (cell mediated lymphotoxicity) represented its effector arm.

Fritz moved to the University of Wisconsin in 1965 and remained there until 1979 during which time he made additional major contributions to clinical and experimental transplantation. In 1967, he used the MLC assay to select non-reactive, compatible donors for the first successful matched bone marrow transplants performed for immunodeficiency diseases first by Robert Good in Minnesota and then in Wisconsin with both cases subsequently reported together as twin papers in The Lancet. This was a milestone in clinical bone marrow transplantation (BMT) that presaged the widespread successful application of BMT in the treatment of diseases. In the laboratory, Fritz and his group performed extensive studies utilizing the MLC and the derivative CML reaction to study multiple aspects of allograft effector mechanisms and histocompatibility antigens which eventually led to his being among the first to conceptualize that there were two kinds of HLA antigens – those defined by serological methods and those defined by MLC techniques (later called Class I and Class II respectively). Fritz subsequently worked at the University of Minnesota from 1979 through 1992 where he continued and expanded his basic studies on T-cell immunogenetics and cytotoxicity, HLA function and structure and the H-2 locus. While at Minnesota, he developed an interest in xenotransplantation which fostered productive experimental collaborations with J.L. Platt and A.P. Dalmasso and others that examined numerous aspects of xenotransplant rejection such as the significance of xenoreactive antibodies, the endothelial antigens they recognized, the role of complement and endothelial cell activation in discordant xenograft rejection, the concept of accommodation as a possible mechanism to enhance

discordant xenograft survival as well as numerous pharmacologic, molecular and genetic strategies to prolong xenograft survival.

In 1992, Fritz was recruited by the Department of Surgery of the New England Deaconess Hospital (now part of the merged Beth Israel Deaconess Medical Center) and Harvard Medical School to be the Director of the Sandoz Center for Immunobiology. This center was built with the financial support and endowment of the Sandoz Corporation (now Novartis) to support basic research on discordant xenotransplantation that hopefully would lead to eventual clinical application. A tenured chair was created at the Harvard Medical School to support the Director that was named at Fritz's request after his old mentor Lewis Thomas. He became the Lewis Thomas Professor of Surgery at HMS in 1995. The purpose of the new Sandoz Center was to focus collaborative, multidisciplinary research on xenotransplantation and related research areas. Over the next eleven years, Fritz did just that: he fostered multiple creative and productive collaborations with Wayne Hancock, Simon C. Robson, Christiane Ferran, Miguel Soares, Leo Otterbein and others which examined in depth the immunologic, molecular, coagulation/hematologic and genetic mechanisms involved in the genesis and evolution of the endothelial cell activation/coagulation series of events leading to xenograft rejection and destruction. A very important outgrowth of these collaborations was that Fritz recognized the importance of genes whose purpose it was to provide protection against stress and disease and the need to study how to take advantage of these cytoprotective and homeostatic systems in order to apply them to prevention and treatment of clinical diseases and inflammatory states. One of his last interests was the homeostatic protective gene heme oxygenase and its product carbon monoxide and its potential application to organ protective strategies. It is noteworthy that in spite of a strong interest in and commitment to xenograft research and to the eventual use of xenografts in human clinical transplantation, Fritz strongly urged caution against their premature use because of the possibility of introducing serious infections and other diseases into human beings. At a United States Public Health Conference in 1998, he and others urged that a moratorium on the use of pig cells and tissues to treat people be instituted until a public commission was created to examine the problem and to educate the people in any potential dangers.

Through his long and illustrious academic career, Fritz Bach exerted a profound and sustained impact on the transplantation field. He was author/co-author on approximately 800 papers, many of which were published in the highest quality journals. He was a gifted, dedicated, and charismatic teacher. His talks and scientific presentations given in a clear, confident, resonant voice to meetings and societies around the world were models of precision and clarity that exuded his obvious joy at the task at hand. He trained, mentored, sponsored, and encouraged hosts of postgraduate students, fellows, and junior faculty who later rose to academic positions of great prominence and responsibility. He was editor of Clinical Immunology (with R.A. Good), and editor-in-chief of Xeno. He held several important leadership posts: International Transplant Society (Council Member), International Bone Marrow Transplant Advisory Committee (Member), International Histocompatibility Testing Workshops (Chair) and NIH Experimental Medical Study Sections (Member). He was also a respected and important member of the Society of Clinical Investigation, the American Association of Immunologists, the Transplantation Society, the American Society of Transplant Surgeons (named an honorary member in 1992), and a charter member of the International Bone Marrow Transplant Registry. He also served on the Weizman Institute International and Board of Governors. It is therefore not surprising that Fritz's prodigious scientific accomplishments and contributions were acknowledged with numerous awards. These included the Distinguished Scientist Award of the American Red Cross (1983), the Medal of the College de France (1984), Foreign Membership of the Royal Dutch Academy of Sciences (1987), the Emilio Trabucchi Foundation Award (1989) and the Medawar Prize of the Transplantation Society (1995). He

also gained very unique honors late in his career (2004) when his Austrian citizenship was restored and in 2005 when the University of Vienna, the major university of the country he fled during the Nazi era, had recently started a laboratory to train young scientists, awarded him an honorary doctorate for his services and scientific contributions.

Fritz Bach was married twice. His first marriage was to Marilyn Brenner, a Massachusetts Institute of Technology Ph.D. graduate with whom he had three children, a daughter, Wendy, and two sons, Peter and David, both of who later became successful academic physicians. Marilyn and Fritz Bach were close scientific collaborators for years before they divorced in 1979. Bach married his second wife, Dr. Jeanne Gose, a pediatric allergist in 1983 with whom he had three daughters, Kathryn, Erika, and Dana. This marriage also ended in divorce. In addition to six children, he is also survived by four grandchildren, Maya, Jonathan, Andreas, and Caiden.

Although Bach was passionately and totally engaged in his scientific endeavors – one of his collaborators (Paul Sondel) stated he spent every waking minute dreaming and hypothesizing the mechanisms of how the immune system worked and that the most exciting thing in his life was always next week's experiment – he also did enjoy wide-ranging interests in classical music, sailing, tennis, travel, food, spy novels and Sunday news shows. He was a regular participant in the Walter Brendel Symposium in Austria where he impressed all not only with his scientific and skiing prowess but also with his interest and understanding of music, literature, and even the culinary arts. He was a warm, friendly, extroverted bon vivant who enjoyed the good things in life and was fun to be with. He genuinely enjoyed being with and socializing with his many friends. They will miss him dearly.

Respectfully submitted,

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