



In Memoriam Dr. Ian M. Orme (1952 – 2018)

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University Distinguished Professor, Emeritus

The tuberculosis research community mourns the loss of the well-known tuberculosis immunologist Dr. Ian Michael Orme, age 65, who died peacefully in his sleep Tuesday, June 19, 2018, while at his summer home in Onchiota, New York, shortly after apparent recovery from a heart attack. He is survived by his wife Eileen Orme (nee Aquavella), R.N., and his two sons, Joseph Allen Michael Orme and Robert James Steven Orme.

Born and raised in England, Ian completed his primary school education in London. He attended Paddington College in East London and the University of London, graduating with a first class honors B.Sc. degree in Physiology in 1977 and a Ph.D. degree in immunology in 1981. In that year, as a post-doctoral fellow, he joined the eminent group of tuberculosis immunologists (Drs. George Mackaness, Frank M. Collins, and Robert North) at the Trudeau Institute, Saranac Lake, New York. That period (1981 – 1986) proved highly productive for Ian with 15 publications co-authored with Frank Collins, many on the use of “adoptive transfer” to address the nature of the T-cells acquired during the height of the primary immune response to tuberculosis infection in the mouse, and published in prominent journals such as *J. Exp. Med.*, *J. Immunol.*, *Infect. Immun.*

In August 1985 I met Ian Orme at a meeting of the Tuberculosis Panel of the U.S.-Japan Cooperative Medical Science Program at NIH, Bethesda, MD and encouraged him to apply for the vacant immunologist faculty position in the Department of Microbiology, Colorado State University. Ian joined our faculty in 1986 and has remained at CSU for his entire career. We both founded the Mycobacteria Research Laboratories at CSU in the early years of our careers, now one of the more prominent laboratories devoted to basic experimental research on the bacteriological, immunological and pathogenesis aspects of the biology of tuberculosis and other mycobacterial diseases, and application of that research to disease control and elimination.

Ian Orme, following on the work of George Mackaness, provided the first evidence, using passive cell transfer technology, that CD4 T cells mediate protective immunity in tuberculosis. Much of Ian's early research involved the application of this technology (“adoptive immunity”) to the study of the immune response to vaccines and the various phases of tuberculosis infection in mouse models. He also described the role of gamma delta T cells in tuberculosis, and with other members of his laboratory, and others laboratories, advanced knowledge of the role of macrophages in tuberculosis. With members of his lab he described the important role that CD8 T cells play in the chronic stages of tuberculosis disease. He also tested DNA, subunit, and whole

cell vaccines in mouse models. He reflected, and wrote extensively on the different strategies important in pre-exposure vaccination and tested several post-exposure vaccination alternatives. He pioneered the use of low dose aerosol infection in mice and guinea pigs and proved the importance of working with clinical tuberculosis strains due to their higher virulence compared to what he called “wimpier” laboratory strains. More importantly, he showed that the degree of protection provided by the BCG vaccine varied for different *Mycobacterium tuberculosis* strains. Another area of research was non-tubercloid mycobacteria (NTM), more specifically how they interfered with protection conferred by vaccination against tuberculosis. Using the mouse model, he evaluated several immune alterations in the host that could explain the higher rates of secondary infection experienced by tuberculosis patients after successful antibiotic treatment of the primary infection. In 2009 Dr Orme was honored with the title of University Distinguished Professor, the highest academic award conferred by Colorado State University.

Throughout his years at the Trudeau Institute and Colorado State University Ian was a prolific author, having published 313 peer-reviewed articles, 31 book chapters, several editions of his self-published book on Basic Immunology (mostly intended for undergraduate and graduate students studying immunology; his 1995 book “Immunity to Mycobacteria” published by R.G. Landes Co./Springer-Verlag is still relevant for students). Ian was very supportive of me in my editorial duties as the former Co-Editor-in-Chief of the journal *Tuberculosis* and its predecessor *Tubercle and Lung Disease*. He was a member of the Editorial Board of *Tuberculosis* since its inception in 1997 until recently. Ian was a perceptive, dependable, always prompt reviewer (although his penchant for use of British English as distinct from American English - a favorite word of Ian's was “whilst” - tended to unmask his anonymity, and his sometimes acerbic comments often required editorial intervention!). Ian also published extensively in our journal (43 of his documented 313 peer-reviewed articles, by my account).

Ian in his earlier years was outstanding as a didactic teacher of undergraduate level immunology. One of Ian's earliest department heads commented: “He had already established an excellent reputation in research on the immunology of tuberculosis; however, at that time we were a small department and all faculty members participated in classroom teaching as well as research. We were fortunate that Ian took over responsibility for teaching undergraduate immunology courses, both in the classroom and the laboratory, because his unique sense of humor, as well as his comprehensive and up-to-date knowledge of

immunology, really engaged our students and made him a favorite". Ian was also a mentor to many who went on to establish strong careers in both research and teaching. Among these that I can call to mind are: Dr. Bernadette Saunders, Senior Lecturer, School of Life Sciences, Faculty of Science University of Technology, Sydney; Dr. Andrea Cooper, Professor of Cellular Immunology, University of Leicester; Dr. Joanne Turner, Vice-President of Research, Texas Biomedical Research Institute; Dr. Ana Junqueira-Kipnis, Professor, Federal University of Goiás, Brazil; Dr. Catharine Bosio, Chief, Immunology of Pulmonary Pathogens, NIAID, NIH; and Drs. Mercedes Gonzalez-Juarrero, Anne Lenaerts, Diane Ordway, Marcela Henao-Tamayo, Angelo Izzo, all current faculty members at Colorado State University and now continuing on the lines of research pioneered by Ian Orme. Indeed, Ian was a type of mentor to the current President of Colorado State University, Dr. Anthony (Tony) A. Frank, D.V.M., Ph.D. Dr. Frank's early career at CSU was as an administrator (Head of the Department of Pathology and later Vice-President for Research, before elevation to University President). He was a trained veterinary pathologist and Ian engaged him extensively early in histological and immunochemical analysis of diseased tissues. In a tribute to Ian, Dr. Frank wrote: "We traveled the world together, and he really made the science part of my career".

In his early life in England Ian had ambitions to be a professional soccer player and throughout he retained a passion for soccer and rugby. While at the Trudeau Institute in Saranac Lake he was responsible for organizing the Canadian-American (Can-Am) Rugby Tournament and in Fort Collins later on he was founder, manager and coach of the "County Cork Pub Soccer Club" for over 40 year-olds. Perhaps in recognition of my own love of rugby football from my boarding school upbringing in Dublin, Ian expressed great admiration of Ireland's defeat of England at Twickenham and hence Triple Crown champions and 'Grand Slam' winners of the 2018 Six Nations Rugby Tournament. Ian was a talented soccer/football player himself in his early days here and I saw his score from 40 meters out.

Ian was described accurately by some on his passing as "ornery, funny, generous, and visionary", "passionate and innovative", "no fear in facing bureaucracy or precedent". Another department head wrote: "Orme delighted in scientific debate and particularly enjoyed challenging the dogma and paradigms of his field...Ian delighted in challenging those in administrative roles and was most happy when he was stirring the pot...His approach was not necessarily kind and for that, he

was not apologetic. His goal was to stimulate thought and action. Those who accepted Ian's challenge were rewarded with interesting debate and camaraderie. Ian leaves a legacy of students and trainees who he inspired to be curious and think critically." A former colleague of his wrote: "The junior Orme was very much in his element as the rebellious other, attacking shaky sacred shibboleths. Later on, when he was confidently expounding the best that rigorous analysis had to offer, I often wondered whether there might not be some part of him that would actually be happier back on the other side of the fence attacking his own accepted ideas".

Here at home in Colorado, Ian will be remembered by me for his unstinting support over 32 years, his friendship, generosity, and vision. He was the one whom in the mid-1980s brought tuberculosis research to our fledgling mycobacterial research program and helped give us national and international recognition and the research funding necessary for the training of new generations of researchers. He was the co-creator of that pioneering research that emanated from here not only on the immunological basis of mycobacterial diseases but also an understanding of the chemical composition, biogenesis and genetics of the cell wall armament of *Mycobacterium spp.*, research which has already resulted in the emergence of new interventions, drugs and vaccines, leading to the control of tuberculosis, leprosy and other mycobacterial infections.

In the wider University community, Ian Orme will be remembered as one "larger than life", "a mentor to many"; "had an incredible heart"; "an independent thinker; a beautiful mind"; "his unique and refreshing sense of humor"; and to quote myself: "appreciation of the originality of Ian Orme in his scientific pursuits and achievements, his mental quickness, his writings, but also that English sense of humor and irreverence that only the Irish and the English themselves can fully appreciate".

Ian Orme would have appreciated two stanzas from the poem "Crossing the Bar" by the greatest of all English poets, Alfred Lord Tennyson:

"Twilight and evening bell, /And after that the dark!/ And may there be no sadness of farewell,/When I embark;

For though from out our bourne of Time and Place/ The flood may bear me far,/I hope to see my Pilot face to face/When I have crost the bar"