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Hugh Robson MacDonald (1946–2023)

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Hugh Robson (Rob) MacDonald, former director of the Lausanne Branch of Ludwig Institute for Cancer Research (LICR) passed away unexpectedly after surgery for a pelvic fracture following a fall at home. Rob was an exceptional immunologist and his research group made seminal contributions to a broad spectrum of topics in T cell biology. His more than 500 publications, 35,000 citations and h-index of 102 were central in making the Lausanne LICR internationally recognized.

Born in Willowdale in Ontario, Canada, Rob obtained his first degree in astrophysics from the University of Toronto. He then moved to the Department of Medical Biophysics at the Ontario Cancer Institute and obtained his PhD in 1972 for studies quantifying the generation and biophysical properties of cytotoxic T cells developing in mixed lymphocyte cultures, carried out with R. G. Miller and R. A. Phillips. This background in immunology and biophysics profoundly influenced Rob's subsequent research focus, practicing a very quantitative and statistical approach to biology.

To expand his knowledge of cellular immunology, Rob became a research fellow in the group of Theodore Brunner and Jean-Charles Cerottini at the Swiss Institute for Experimental Cancer Research (ISREC) in Epalinges, Switzerland. Following this very productive period from 1972 to 1975, Rob joined the Ontario Cancer Treatment and Research Foundation as an assistant professor. It was here that Rob teamed up with his research assistant Rosemary Lees and they continued working together for 30 years.

When the Ludwig Institute of Cancer Research established its Lausanne branch in 1977, Rob returned as an associate member and group leader, becoming deputy director in 1989 and a director in 2006 until his retirement in 2013. Within ISREC were groups studying mouse and human immunology, genetics, experimental hematology, radiation biology, biochemistry, virology and immuno-parasitology. This was an ideal environment for Rob's scientific passion to flourish. He immediately established the first and one of the pre-eminent flow cytometry facilities in continental Europe, thereby enabling the quantification and isolation of phenotypically defined cell types. Combined with the availability of monoclonal antibodies and

limiting dilution analysis to establish the frequency of antigen-specific T cells, a new era in immunology began. Long before recombinant cytokines were available, Rob and his associates perfected T cell cloning. The T cell cloning efficiency at Lausanne was second to none, and clones were established by micromanipulation rather than by limiting dilution at an 'average' of one cell per well. Thus, the heterogeneity of cytotoxic T cells and later 'helper' T cell clones could be dissected.

Rob's contributions to immunology were broad, but generally focused on T cell biology. Beginning with the thymus, his laboratory identified and quantified the development of functional subpopulations of T cells and their blood-borne stem cell precursors. He defined subsets of early developing thymocytes based on the expression of CD25. In 1987, he identified CD44 as a marker of memory T cells, which has remained one of the best memory markers to this day. In the same year, he identified natural killer T cells for the first time. His group's research showed that these cells develop intra-thymically by alternative selection processes.

Three seminal contributions by Rob's group warrant particular emphasis. First, to investigate the oncogenicity of mouse mammary tumor viruses (MMTV), the ISREC virology group generated MMTV transgenic mice. There was a known correlation between mouse strain expression of MMTV and their T cell receptor (TCR) repertoires. Rob's laboratory established that expression of MMTV 'neoantigens' by transgenesis resulted in intra-thymic deletion (or negative selection) of T cells expressing particular TCRs, thereby confirming one of the central tenets of Burnet's clonal selection theory. Second, Rob demonstrated that positive selection of $CD4^+$ thymocytes was controlled by MHC class II. Third, initiated by the appointment of Michel Aguet as the ISREC director in 1996 and the arrival of Freddy Radtke, Rob's group developed an interest in Notch signaling, and together with many colleagues dissected the role of Notch in T cell commitment, development and homeostasis.

Paramount in Rob's legacy was not only his sterling intellect but also his incredible generosity and kindness. He could listen to proposed models of students and colleagues and easily identify the big picture and the crucial experiments worthy of further investigation. Dozens profited immensely from this guidance. He read avidly and knew the precise content of the numerous papers he kept in a tall pile on his desk. His writing skills were legendary and an inspiration for his colleagues. Many of his first drafts, written with pencil on paper and typed by others, became the final published article.

Rob rarely sought the limelight, and was a reserved individual, preferring to spend his spare time relaxing in the garden of their old Mill house deep in the Swiss countryside and listening to Chopin nocturnes or Leonard Cohen songs with his beloved wife of 54 years, Lana. He leaves behind Lana, his sisters Chris and Kathy, sister-in-law, Rita, Lana's sister, and many nieces and nephews and their families. Rob MacDonald was to so many colleagues a superb mentor, pundit, enthusiast, confidant and connoisseur of fine wines, in essence a highly civilized person. Innumerable colleagues are forever indebted to him for nurturing their scientific careers.

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