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Avrion Mitchison (1928–2022)

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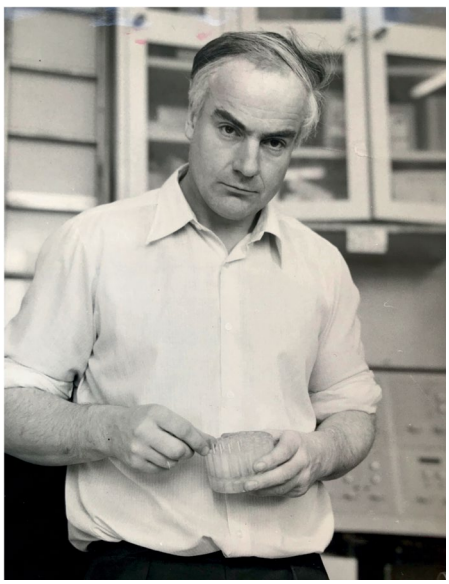
Seventy years after seminal work showing that the transfer of cells (T lymphocytes) rather than antibodies accelerated transplant rejection[1], we mourn the death of its author, the pioneering immunologist and zoologist (Nicholas) Avrion Mitchison.

Avrion (Av) died peacefully on 28 December 2022, aged 94. He was husband to Lorna, father to Tim, Mary, Matthew, Hannah and Ellen, and a proud *ceannard* to a large clan of grandchildren, whom he adored.

Av was the son of a Labour politician (Gilbert 'Dick' Mitchison) and the writer Naomi Mitchison (née Haldane), nephew to prominent geneticist J. B. S. Haldane, and grandson of the physiologist John Scott Haldane. With such a provenance, Av joked that he simply 'went into the family business' and became a scientist in Oxford under the guidance of Peter Medawar. Initially as a lecturer and then a reader at the University of Edinburgh (pictured above) and later as head of the Experimental Biology Division at the National Institute of Medical Research (NIMR), Av initiated a series of experiments that collectively provided the conceptual framework of much of today's understanding of immune rejection, tolerance and T–B cell co-operation. Av realized that B cells require T cell help to produce specific antibodies, and in now classic experiments, he demonstrated that B and T cells interact by recognizing different parts of an immunogen. One part – the 'hapten' – contained the B cell epitope, and the other – the 'carrier' – contained the T cell epitope. Clear evidence for this came from the finding that a mouse primed by injection of a hapten-carrier conjugate makes a full secondary antibody response only to the hapten as part of the same conjugate, but not to a hapten conjugated to a different carrier. This showed that two cells were involved, one recognizing the hapten and the other the carrier. Crucially, the hapten and the carrier had to be physically linked for a productive interaction between B and T cells to occur[2] and to explain this, Av imagined that B and T cells interacted simultaneously with different parts of the antigen via an 'antigen bridge'. We now know that T cell receptors interact with processed



antigen fragments presented by major histocompatibility complex (MHC) molecules[3] and that for this cooperation to occur, antigens must first be internalized and processed by hapten-specific B cells, and carrier epitopes presented on the surface of B cells in association with MHC molecules[4].

In 1970, Av moved to University College London (UCL) to become Jodrell Professor of Zoology and Comparative Biology, and he took with him the brilliant young Canadian Martin Raff. Av's style was to guide his students and postdocs towards asking clear and incisive questions and to then support them in creating the best work possible. Although this will be a familiar pattern to many scientists who had the privilege of encountering a great mentor, Av's approach was unusual because he regularly opted to remove his name from the resulting papers – with the clear intention of increasing the prominence of the other authors. This scientific generosity is exceptionally rare but also makes it hard to decipher and fully appreciate Av's huge impact on scientific progress. Some examples of such unsigned scientific masterpieces include seminal studies on the role of B and T cells in adaptive immunity[5,6] and the origin of T helper cells from $CD4^+CD8^+$ double-positive precursors in the thymus[7]. Despite a reluctance to take full credit for work he had initiated, Av received many accolades during his lifetime, including the Novartis Prize for Basic Immunology in 1995 and the Robert Koch medal in 2001, and he was made a Fellow of the Royal Society and a foreign member of the National Academy of Sciences USA. In 1956, together with John Humphrey, Rob White and Robin Coombs, Mitchison helped establish the British Society for Immunology – one of the oldest, largest and most active immunology societies in the world.

Av Mitchison was a visionary immunologist with a magnetic personality that attracted scientists from around the world to his long-term base at UCL, and subsequently to the German Rheumatism Research Center (DRFZ) in Berlin. Across the decades, scores of aspiring scientists clustered around him to enjoy his conversations, ideas, encouragement, humor and not infrequent teasing. At his funeral held recently in North London, there was standing-room only, as an entire generation of scientists gathered to remember Av's unwavering support for curiosity, truth and openness. A man of powerful intellect with an infectious zest for life. In the gathering of family, friends, neighbors and co-workers a consensus was reached – although the world was considerably diminished by the passing of Av and his wife Lorna (who also died in 2022), we were so very lucky to have known them both.

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