BIOGRAPHICAL MEMOIRS


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ALAN FREDERICK WILLIAMS
25 May 1945 — 9 April 1992
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Elected FRS 1990

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Alan Williams is noted for his seminal contributions to the field of leucocyte membrane glycoproteins (that is, differentiation antigens). He played a leading role in the development of approaches to the purification and structural analysis of cell surface antigens. His comprehensive characterization of the structure of the rat Thy-1 antigen, as well as the application of monoclonal antibodies to the designation and subsequent isolation of multiple new leucocyte antigens, were exemplary. His discovery that Thy-1 is structurally related to immunoglobulin led directly to the concept of the immunoglobulin (Ig) superfamily, which embraced a spectrum of cell surface molecules involved in a variety of cell recognition systems. He was a very strong advocate in support of the rat as a model animal in the study of immunological phenomena. He was energetic and courageous, as well as radiating enthusiasm for immunological research, inspiring others, critically analysing accepted dogmas and setting high standards. In short, he was a brilliant research scientist.

EARLY FORMATIVE YEARS

Alan Frederick Williams was born in Melbourne, Australia, on 25 May 1945, the first son and second child of Walter Alan Williams and Mary Elizabeth Williams (née Parry). His parents and grandparents were all born in Australia and were working class. His father became a foreman in a stocking factory and both parents were passionately socialist and patriotic, but whereas his father was quiet and reflective his mother was flamboyant. Alan was a member of a large family, including two sisters and three younger brothers. His parents had both left school at 14 years of age during the depression and had a strong wish to work in agriculture with an emphasis on independence and self-employment. Given the family’s circumstances at the time of Alan’s birth and infancy, especially the absence of his father during World War II in New Guinea, money was at a premium and the two older children would have been in
demand to assist the family in a variety of modes. These were circumstances that provided a fertile field for the development of maturity and independence. Alan’s childhood and teenage years were spent within and close to Melbourne; initially, in the city (East Coburg) and latterly in 1956, when the family moved 25 miles away to a small holding of about 7 acres in Templestowe, which has since been subsumed within Melbourne’s sprawling suburbs. Here they grew tomatoes and lemons, reared chickens and developed an interest in natural history, although the family’s involvement with agriculture always remained somewhat amateurish. As a consequence of this environmental change, Alan’s spare-time occupations revolved around working in local orchards, the primary motivation being to raise cash.

Although self-sufficiency had a significant impact upon his early development, his life was profoundly influenced by his parents’ being committed members of The Salvation Army. Undoubtedly, this commitment had a potent effect upon Alan and his family that, most importantly, resulted in their occupying a ring-fenced social group separate from the rest of society. In Alan’s own words it represented ‘a classical fishbowl society within sociological terms.’ Many of his out-of-school activities were dominated by the religious institution, not just all day on Sundays but also on two or three evenings during the week. One positive outcome was that he developed a pleasure in music, playing the cornet in a brass band that continued until he left the family home on the completion of his first degree. This, in turn, promoted self-confidence through performing at public concerts from an early age. However, there was a significant downside, namely that he was alienated from school friends and more worldly teenage activities, especially sport and ‘the beach’, which are such an integral part of the young Australian culture. A momentous character-forming event occurred at about the age of 14 years when he became a ‘non-believer’, although for family and social reasons he remained within the church for a further seven years until he left the family home. Later he would ascribe his choice of remaining at home to the need for him to fight this battle on behalf of his younger brothers. Such decision-making is very rare in a 14-year-old and demanded enviable levels of soul-searching, courage, self-confidence, independence and maturity, qualities that would become evident again and stand him in good stead later in life. Overall, there is a real sense that he had a happy childhood and that he grew up in an atmosphere encouraging determination, belief in yourself on an equal basis with others, self-reliance and an ability to solve practical problems.

**Education**

Although educational success was viewed within the family as being important, and being ‘top-of-the-class’ was much approved of, there was no undue parental pressure to do well. It is a compliment to his parents that, apart from Alan’s elder sister, all of the other five children went to university. In the sixth form of Box Hill High School (boys only) he specialized in English, pure and applied mathematics, physics and chemistry. Although not a star, he progressed from there to Melbourne University to read a four-year course in agricultural science, which in reality was a broad-based course in biological sciences. Given his previous close involvement with agriculture, agricultural science was perhaps an obvious choice rather than chemistry, although it could have reflected an intrinsic and growing interest in biology. The course included one year of practical work spent on the university farm, which, together with vocational farm work on a Queensland cattle station and growing wheat in Victoria, repre-
Presented the only times he had lived away from home up to the age of 21 years. In 1966 he gained a bachelor’s degree in agricultural science and was awarded the Samuel Wadham Commemorative Medal. The latter prize was the first formal indicator of Alan’s future stardom.

**POSTGRADUATE**

Following his success as an undergraduate, Alan was encouraged by Melbourne University to stay on as a graduate student. However, he was strongly motivated to divorce himself from The Salvation Army’s pervading influence and to leave the family home. He was aided in this by the award of a prestigious Commonwealth Scientific Industrial Research Organisation Studentship. First, he took a six-week placement with Professor Bede Morris at the John Curtin School of Medical Research, Australian National University, Canberra. This must have been an awe-inspiring experience. Not only was it Alan’s first encounter with immunology, at a time when immunology was immensely exciting and at the forefront of the unprecedented growth in biological sciences, but Bede Morris was a local icon in the field and was noted for the promotion of arguments and for his unconventional views. Apart from immunology, which was very well represented in the persons of Professor Gordon Ada FAA and Kevin Lafferty, the John Curtin School under the legendary directorship of Professor Frank Fenner FRS was an outstanding example of an interdisciplinary research institute noted for its multiple research achievements, as judged by international standards. After this sobering and enlightening interlude, Alan took up a position as a graduate student in the Department of Biochemistry at Adelaide University, under the supervision of Professor William (Bill) H. Elliott, from 1967 to 1970. Both Bill Elliott and the department were notable and in this respect provided a haven of quality as well as a good reason for distancing himself from Melbourne. During this period (namely 1969) Bill Elliott spent a sabbatical with Professor Rodney (Rod) R. Porter FRS in the Department of Biochemistry at Oxford.

His PhD thesis topic was ‘Avian erythropoiesis’ and involved the delineation and characterization of the biochemical parameters governing DNA synthesis during the period of transition from the dividing erythroblast to the non-dividing polychromatic erythrocyte; the key questions concerned the factors responsible for switching off the nuclear activity. This was a very productive introduction to research, resulting in the publication of one paper during the year in which he was awarded the PhD degree (1970) and two years later five papers, on four of which he was the sole author.

At the end of his first year as a graduate student Alan married Rosalind Margaret Wright (on 23 December 1967), a nurse who had grown up in Sydney. Both of her parents had graduated from Sydney University (BA degrees) and were school teachers. The Wrights had a notable ancestor, namely Joseph Wright, who was a convict on the first fleet to Australia in 1788, having been convicted at the Old Bailey on 26 May 1784 for stealing lead from a roof in Sloane Street, Chelsea.

At the age of 25 years, with his formal education completed and the principal characteristics of his personality established, the world was Alan’s oyster. Alan had inherited his father’s reflectiveness together with his mother’s flamboyancy. He was likeable and good company, his unconventional, enthusiastic and argumentative nature—overlaid with a relish of Australian brashness—being particularly appealing. As well, he spoke authoritatively and was
fiercely independent, both of which were delivered with a streak of stubbornness. However, on meeting him for the first time, one was struck especially by his maturity and self-confidence. Although he was considered by some to be occasionally difficult to handle, there were others who judged that this depended, in particular, on ‘the handler’. Rod Porter, who in time assumed the role of Alan’s mentor, belonged to the latter group.

DEPARTMENT OF BIOCHEMISTRY/MRC IMMUNOCHEMISTRY UNIT, OXFORD

On completion of his PhD degree, Alan followed the standard track of migrating to the UK. As to location, he had a strong interest in developmental biology and his first choice was the laboratory of Professor J. B. (later Sir John) Gurdon (FRS 1971), although immunology was also appealing as a discipline and Rod Porter’s laboratory came a close second. This was a time of uncertainty and ferment. The salient factors that drove the final choice of the Medical Research Council (MRC) Immunochemistry Unit within the Department of Biochemistry, Oxford, were Bill Elliott’s promotion of Rod Porter on the basis of his recent first-hand experience, Rod’s offer of a demonstratorship coupled with the opportunity to be independent, and MacFarlane Burnett’s seminal immunological text *Self and non-self*, which Alan read during the sea voyage to the UK. The final choice was crucial; it predetermined everything that came later, especially in respect of Rod Porter’s multiple influences, including inspiration, critical analysis, promotion of rigorous biochemical standards, and personal support.

His first project was to isolate and characterize the specific antigen receptors of B and T lymphocytes, by using the photoactivatable affinity hapten ε-(4-azido-2-nitrophenyl)-L-lysine, developed previously by Fleet et al. (1972). This approach failed, which at the time caused Alan significant consternation because it meant that he published no papers from his new location during his first three years in Porter’s Laboratory. Later on, he could afford to take a more circumspect and sanguine view, and used this experience to cheer up his own colleagues in similar circumstances! In spite of the lack of publications, in 1972 he was appointed to an MRC-tenured position in the Immunochemistry Unit, which demonstrated Rod’s faith in his ability. The failure of his first project was also unfortunate within the broader perspective, because the project sought to resolve directly what was at the time a salient and fundamental controversial issue, namely the nature of the antigen receptor on T lymphocytes. At the time, there was a generally held view that the T cell used a variety of immunoglobulin. Some persons were so convinced that, following on from the convention of naming immunoglobulin subtypes, they referred to it as ‘IgT’. One possible reason for this project’s failure was that the actual amount of the antigen receptor on B and T cells (namely the number of molecules per cell) was so small that the sensitivity of the biochemical methods coupled with the cell number being used were insufficient to permit detection and characterization. In what was to become Alan’s characteristic deductive process, he reduced the problem to the basic question of ‘what is the amount of immunoglobulin on B and T cells?’ The answer was provided, in collaboration especially with Jens Jensenius (Porter’s last graduate student), through the development of sensitive and quantitative assays with 125I-labelled purified F(ab’)2 antibodies against immunoglobulin that circumvented problems due to binding to Fc receptors (1, 2)*.

* Numbers in this form refer to the bibliography at the end of the text.
Application of this assay revealed that if rat thoracic lymphocytes and thymocytes possessed surface-bound immunoglobulin, the amount was less than 50 molecules of Ig L chain per cell (3). Although this result did not categorically rule out the T-cell antigen receptor’s being an immunoglobulin subtype, from the quantitative perspective it made it extremely unlikely, a conclusion that contrasted strikingly with the conventional view at the time. In fact, this issue was not definitively resolved until a decade later, by the cloning of the genes specifying the T-cell receptor (Yanagi et al. 1984; Hedrick et al. 1984). This showed that both previous perspectives embraced an element of truth, namely that although the T-cell receptor was not formally an immunoglobulin subtype, it nevertheless possessed partial homology to immunoglobulin. The rigour and success of Alan’s approach depended critically upon sensitivity and quantification, the dual hallmarks of what has become the new discipline of quantitative biology. An important bonus of this work was that the saturation binding assay using $^{125}$I-labelled purified F(ab')$_2$ fragments, when coupled with the use of glutaraldehyde-fixed cells, enabled the development of quantitative assays for the purification of cell surface antigens solubilized in detergents (4). These assays were a key element of his future work.

In late 1972, a switch was made to the long-term aim of describing at the molecular level the architecture of the T-lymphocyte surface, through the identification and purification of its cell surface antigens. Two major approaches were adopted: the purification of the rat Thy-1 antigen, and the identification of new cell surface molecules, by using initially xenoinmunization and later monoclonal antibodies.

**Purification and characterization of the Thy-1 antigen**

By the end of 1970, some of the basic principles underpinning approaches to the solubilization and purification of lymphocyte surface glycoproteins had been established through the work in the laboratory of Mike Crumpton (FRS 1979) (Allan et al. 1972) at the National Institute for Medical Research, Mill Hill. Rod Porter promoted interaction between the two laboratories, and a good proactive relationship was established with visits by Alan and his co-workers (Ron T. Acton and Michelle Letarte-Muirhead) to Mill Hill and with a free exchange of information and ideas. The established methodologies were transferred to Oxford, where they were refined and extended in an enlightened way. Out of these exchanges grew a long-lasting friendship between Alan and Mike that incorporated a succession of stimulating and enjoyable meetings. The choice of the rat Thy-1 antigen as a candidate T-lymphocyte surface molecule deserves some comment. From a biochemical perspective, the abundant expression of Thy-1 on rat thymocytes and the ready availability of rat thymi were prerequisites, if the ultimate aim was to determine structure by X-ray crystallography; the key to success in 1972 was the availability of hundreds of milligram amounts. Also on the positive side, it was the first differentiation antigen described for mouse (and rat) T lymphocytes and had an intriguing tissue distribution, being also expressed in brain. However, the fact that the antigen was (and still is) of unknown biological function was a downside. The purification of Thy-1 from both thymus and brain was strikingly successful (6), providing amounts of material that enabled a series of notable chemical and physical studies leading some years later to a comprehensive picture of the structure of the antigen (figure 1). These studies also resulted in three significant discoveries. Of especial importance was the revelation that the thymus and brain antigens possessed different carbohydrate moieties (5), whose subsequent detailed structural analysis in collaboration with Raymond Dwek (FRS 2000) revealed site- and tissue-specific patterns of glycosylation (17). Although this result had been implied by previous observations...
that stages in T-lymphocyte differentiation were distinguished by different patterns of reactivity with lectins, it demonstrated unequivocally the differential glycosylation of the same cell surface molecule in different cells/tissues. It also raised the possibility that the same molecule could have different biological functions in different cells. More importantly, amino acid sequencing in collaboration with Jean Gagnon (MRC Immunochemistry Unit) showed that the Thy-1 sequence was related to that of an immunoglobulin V-region domain (9, 11). This represented a notable conceptual advance, which engaged much of Alan’s intellect and time in future years (see below). A second discovery was that Thy-1 lacked a typical non-polar amino acid transmembrane segment but possessed a non-protein hydrophobic domain located at the carboxy terminus containing probably phosphatidylinositol, which was responsible for the membrane attachment (9). In 1985, this was shown by Alan’s laboratory (12) and, independently by Martin Low (FRS 1996) (Low & Kincade 1985), to be a glycosyl phosphatidylinositol (GPI) moiety. These descriptions of the so-called ‘GPI anchor’ were preceded (just) by the report (Ferguson et al. 1985) that the coat protein of Trypanosoma brucei possessed an identical moiety. However, Thy-1 was the first example of its presence in vertebrates and it was this discovery, in particular, that stimulated a body of work which revealed it to be a relatively common way of attaching glycoproteins to the cell surface membrane (18).

Identification of new lymphocyte surface differentiation antigens

Concomitantly with the commencement of the purification of Thy-1, Alan initiated a second very rewarding avenue of investigation. This was the identification of new lymphocyte surface differentiation antigens by using antibodies raised by xenoimmunization. The efficacy of the approach was proven by the detection of the leucocyte-common antigen (L-CA; CD45)
with a rabbit anti-rat lymphocyte serum (8). However, the discovery in 1975 by César Milstein FRS and Georges Kohler of a method of making monoclonal antibodies provided a potential breakthrough that could circumvent the problem of the multiple specificities of such anti-lymphocyte sera. Alan realized immediately the potential of the fact that each distinct antibody derived from a fusion could identify a separate molecule. He established a collaboration in which Milstein’s laboratory did the fusions and Alan analysed the supernatants of the clones that were dispatched to Oxford by first-class post. The first two fusions yielded nothing, but the third provided the anticipated leap forwards including an antibody (‘W3/25’) against the rat CD4 antigen (that is, the rat homologue of the mouse antigen that classically distinguished the ‘helper’ subset of T cells) and another recognizing leucosialin (CD43) (7). Other antibodies were obtained against human HLA class I and blood group A antigens. Such antibodies were immensely valuable as multi-functional tools (see below).

**Future location**

This brings us to the summer of 1977. Alan had been in Oxford for six and a half years and was riding on the crest of a scientific wave. It was the occasion of the International Immunology Congress in Sydney and by combining business with pleasure he and his family took their first holiday in Australia since arriving in Oxford. Alan was feeling somewhat unsettled with regard to his future. The visit provided a good opportunity to look for a position in Australia, possibly at The Walter and Eliza Hall Institute. However, as a consequence of the appointment of Professor James (Jim; later Sir James) L. Gowans FRS as Secretary of the Medical Research Council, the Directorship of the MRC Cellular Immunology Unit, Sir William Dunn School of Pathology, was vacant. It was a position that Alan coveted. He informed Rod before his departure that ‘if the job is advertised I will apply’ and left a forwarding address in Sydney. At the time there was general agreement that in the future immunology would increasingly embrace a molecular bias, which was very much Alan’s forte. In addition, Alan’s commitment to the rat as an immunological animal model mirrored the Unit’s and Jim Gowan’s animal focus. In all probability, the selection committee was influenced by these factors plus Rod Porter’s strong support for Alan. Anyway, a letter duly arrived in Sydney offering him the post and his future was secure—an outstanding achievement at the age of 32 years.

**MRC Cellular Immunology Unit**

His relocation to the Cellular Immunology Unit was not associated with any major changes in direction concerning the structures of lymphocyte surface antigens. Here, the two major themes remained the same: first, the detection and isolation of new antigens by using monoclonal antibodies and, second, the delineation of the immunoglobulin superfamily. However, in addition there was an increasing investment in functionality coupled with the designation of the role of T-lymphocyte subsets in immune responses, topics on which the Unit already had commendable expertise. The pursuit of this comprehensive programme was aided considerably by two persons, Don Mason and Neil Barclay, who became important colleagues (figure 2). Don was already resident in the Unit; before becoming a skilled cellular immunologist with an especial interest in the functions of T-cell subsets, he had been a physicist working on nuclear fusion. He became a most valued colleague not least for his mathematical and
statistical expertise but also for his challenging discussions. Neil was Alan’s second graduate student (1973–76) (Roger Morris having been the first); his thesis topic was the purification and characterization of the cell surface protein Thy-1. Neil joined the Unit in 1978, after holding a NATO Postdoctoral Fellowship at the Institute of Neurology, University of Göteborg, Sweden, and assumed primary responsibility for the detection and characterization of new surface antigens, with the additional assignment of embracing new technologies of which the most notable was complementary DNA (cDNA) cloning. The combined approaches of monoclonal antibodies and cDNA cloning were highly successful, yielding a veritable host of surface antigens, several of which were unique. Among the most notable were the rat L-CA (T200; CD45) (14), which subsequently became the first transmembrane phosphotyrosine phosphatase to be described; MRC OX2 (CD200) (15), a lymphoid/neuronal membrane glycoprotein possessing two immunoglobulin-like domains which endorsed the principle that members of the immunoglobulin superfamily were not restricted to lymphoid cells; and MRC OX8 (13), which was a marker of the rat cytotoxic subset of T cells.

Relocation to the Unit gave Alan the opportunity to expand his laboratory by providing accommodation for a succession of graduate students, postdoctoral workers, and visitors. The increased complement of staff, in turn, permitted a more diverse spectrum of projects, which were distributed among his colleagues. Over the next decade he grew from being a talented, forthright and outspoken young man to an exemplary leader with broad perspectives, readily
assuming the mantle of responsibility and becoming a successful Unit Director. Aside from the Unit’s staff, he continued his highly successful collaboration with Milstein on monoclonal antibodies and established important external collaborations with Jean Gagnon (MRC Immunochemistry Unit) on amino acid sequencing and with Raymond Dwek on studies of carbohydrate structure. In concert with his multiple duties, he focused his personal attention on developing the concept of the Ig superfamily. In this he was ably assisted by Neil and Don, who collectively assumed the multiple roles of critic, adviser and provider of expertise, especially in statistics. Given the state of bioinformatics at the time, particularly in respect of scoring alignments, the uncertainty of assignments and the inevitable controversies, the opportunity to argue with dedicated, informed and challenging colleagues was fundamental to progress. The starting point of this study was the finding that Thy-1 was structurally related to immunoglobulin (11). This promoted the suggestion that there could be several immunoglobulin-related molecules that act as recognition molecules controlling the movement and differentiation of cells, and that the immune system might have evolved from this more primitive function (10). The description of the amino acid sequences of an increasing number of cell surface molecules from various cell types provided the opportunity to explore this suggestion directly and to propose further ideas on these themes. Analysis of the amino acid sequences by scoring putative domains against a panel of known immunoglobulin-like domains using the ALIGN program of Dayhoff et al. (1983) provided a reliable method for predicting membership of the Ig superfamily as well as strong endorsement of the above suggestion (19). In particular, this approach enabled an accurate assignment to be made for CD4 (16) and allowed the resolution of several controversial candidates, such as CD2. By 1991 about 100 molecules had been designated as belonging to the Ig superfamily; a representative selection is illustrated in figure 3. The most notable family feature was its diversity. Members were expressed by a wide variety of cell types in addition especially to leucocytes and nerve cells; also, most but not all were cell surface glycoproteins. Apart from those members associated with immune responses, in particular antigen presentation and recognition, other known functions include acting as receptors for growth factors and cytokines, and mediating cell–cell adhesion. Overall, the diversity of function supports strongly the premise that the Ig-related domain first evolved to mediate interactions between primitive cell types, possibly by means of homophilic interactions, and that during evolution a variety of related molecules were selected to regulate especially cellular differentiation and cell movement during the development of more complex organisms.

Unequivocal confirmation of the structural homology of the designated Ig-related domains depended on the determination of their three-dimensional structures. Such structural information was also essential for comprehending the molecular basis of biological activity; in addition, it provided a valuable route to the delineation and regulation of function. Alan’s response to the above challenges was to promote a programme, in concert with Neil Barclay, to produce soluble (truncated) forms of several of the cell surface proteins, in amounts suitable for X-ray crystallography. A very important element in the success of this programme was Neil’s access to Celltech’s proprietary mammalian cell (Chinese hamster ovary) expression system (21), which enabled the expression of soluble recombinant extracellular regions of cell surface antigens at high levels (more than 200 mg l\(^{-1}\)). The outstanding rewards of this corporate initiative are exemplified by the descriptions of the X-ray crystal structures of the CD2 antigen and of domains 3 and 4 of the rat CD4 antigen (22, 23), which confirmed the earlier controversial predictions.
Figure 3. Models for molecules in the Ig superfamily. The circles show sequence segments that are predicted to fold as for an Ig domain. Intrachain disulphide bonds that are like the conserved Ig disulphide bond are shown by $\beta$ within the circles. Interchain disulphide bonds are indicated by SS between chains. N-linked carbohydrate sites, as indicated by the presence of an Asn-Xaa-Thr or Ser sequence, are shown by a filled circle on a stick, unless absence of glycosylation is known. The presence of glycopospholipid anchors is indicated by an arrow. (The figure is taken from (19).)
Late in 1991 Alan accepted an invitation to succeed Professor Henry Harris FRS as Head of the Sir William Dunn School of Pathology, Oxford. He was due to assume the position in October 1992 and to combine this with being Honorary Director of the MRC Unit. In his typical fashion he embraced the forthcoming change in status with marked enthusiasm, immediately developing farsighted plans to extend the department’s accommodation and central services to facilitate an expansion of the research portfolio. Very regrettably, this was not to be. During December 1991 he acquired a nagging cough combined with some breathlessness. A chest X-ray in January revealed some shadowing of the lung, a biopsy of which showed an aggressive tumour. The prognosis was bleak. He delivered the news to his friends and colleagues with a remarkable matter-of-factness. He did not ask for sympathy and never expressed self-pity, characteristics that were personified on one occasion when he complained that ‘it was hard for him to cheer up his friends when there was no good news to tell’. So far as possible, he continued to plan for the future, to fulfil his commitments and to follow his normal routine. At least he had the satisfaction of knowing that his plans for a new animal house and a transgenic animal facility for the department had been approved. On 21 February 1992 he delivered his last seminar at the Institute of Molecular Medicine on ‘White cell differentiation’. I am grateful to Professor Andrew McMichael (FRS 1992) for the following account of this occasion:

By now Alan was increasingly breathless and he arrived in some respiratory distress. His spirits were good, which was extraordinary because the day before he had learned that the chemotherapy was failing and that tumour spread ruled out the last desperate chance of a lung transplant. The lecture theatre was packed. He started breathless but as he developed his theme his breathing eased and he re-entered his normal world, brilliantly illuminating his life’s work on the lymphocyte surface; from those early polyclonal rabbit antisera, to the monoclonals, to the immunoglobulin superfamily, to the phospholipid anchor, to the structure of CD2 and finally to the functions of the molecules acting in concert as they bind their ligands. At the end he devoured the questions in his invincible style. For those who were there it was a privilege and vivid memories will stay with us.

Alan died of his cancer on 9 April 1992. He kept abreast of his research work and continued to work, with his colleagues, on a reference book documenting all of the known leucocyte cell surface CD antigens (24) up to the day he died.

EPILOGUE

Alan had a wealth of talent, which when combined with his exceptional insights, expertise and broad perspectives resulted in a very gifted scientist. He was strongly committed to progressing immunology into the molecular arena and had a considerable impact upon the advancement of the discipline. As well, he profoundly influenced the way in which immunology was practised locally within Oxford. He was noted for his careful scrutiny and critical analysis of propositions, dogmas and experimental data and was generous with his advice, always finding time to share his expertise and to help colleagues as well as ‘out-of-the-blue’ visitors. An especial characteristic was his commitment to sharing his reagents with others. In particular, he provided samples of purified antibodies against mouse immunoglobulin G to a host of laboratories as well as making his own monoclonal antibodies generally available immediately...
upon publication of the data. The MRC OX series of monoclonal antibodies, of which there are currently 124 different specificities, are used worldwide and are the most extensively distributed monoclonal cell cultures in the European Collection of Cell Cultures. Their widespread use is a fitting tribute to Alan’s belief that the advancement of science should not be inhibited by man-made barriers.

At home he was ably supported and, especially during the last months, comforted by his wife, Ros, and their two children, Ben and Eliza. Everything Alan turned his hand to was embraced with enthusiasm and total commitment. He was a vigorous gardener, specializing in espalier fruit trees. Modern art became a passion and when he acquired some additional income from acting as a consultant to Imutran he spent all of it on collecting fine prints; Arthur Boyd, Sidney Nolan and Graham Sutherland were particular favourites. As the collection grew, it became a serious pastime and he had aspirations to open an art gallery. On Saturday afternoons, he watched football from the sofa and loved listening to music and reading. Typically, he devoured Salman Rushdie’s *Midnight’s children* over a weekend and pronounced it ‘the best book ever’.

It is difficult not to speculate about what might have been his additional scientific achievements and influence if he had lived an average life-span, but it is my belief that the current status of molecular immunology would be somewhat different, not least because those of us who were privileged to know him as a colleague or friend would not have been deprived of his wisdom, perceptions, stimulus and criticisms.

**ACKNOWLEDGEMENTS**

I am deeply indebted to Alan’s wife, Ros, for her great help especially in respect of the information on Alan’s early life and for all her other recollections. I am also very grateful to Neil Barclay and Jim Gowans FRS for sharing with me their knowledge and insights. Neil kindly provided me with a complete copy of Alan’s collected works as well as the photograph of Alan with the senior scientific staff of the MRC Cellular Immunology Unit. Obituaries written by his colleagues Professor Ken B. M. Reid FRS and Professor Andrew J. McMichael FRS have proven very useful in deriving a complete picture.

The frontispiece photograph was taken in 1990. (Copyright © The Royal Society.)

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