

Obituaries



Helen Muir (1920–2005)

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Helen Muir had a remarkable life and career. She was born in India in 1920, where her father was part of the British Administration. Helen only had formal education when she came to school in Europe when she was 10, but her father was greatly interested in natural history and that was a starting point for her interest in science and nature. At school in Switzerland and in Berkshire she was “well educated”, but typical of the age, she received little teaching in science. Undaunted by this handicap, she managed to cram science at a college in London so as to gain entrance to Somerville College, Oxford.

Initially, this was to read Medicine, but she quickly changed to Chemistry, which, under the guidance of her tutor, Dorothy Hodgkin, she found much more interesting.

Helen graduated in 1944 and stayed on at Oxford to do research and a doctorate in the Department of Chemistry. Her first work was on the synthesis of antimalarial compounds under the supervision of Dr F.E. King and then with Professor Robert Robinson on the chemical synthesis of penicillin — it was during World War II, and the supply of penicillin to stop wound infection was a high priority. Unfortunately, the structure of penicillin was a source of controversy and the structure favoured by Professor Robinson’s team, on which Helen was asked to work, later turned out to be incorrect. However, she received a sound grounding in organic synthesis in the Dyson Perrins Laboratory and she learnt much from others there at the time, including John Cornforth, Norman Heatley and Ernst Chain. Helen completed and defended her DPhil in 1947.

After spending a further year at the Sir William Dunn School of Pathology she was recruited by Albert Neuberger, who was establishing a new group in London at the National Institute for Medical Research, which was initially based at Hampstead, before moving to Mill Hill in 1949. This also began her move further into biology, as Albert’s interests were in using radioactively labelled precursors to determine the origin of haem biosynthesis, and Helen published her first major papers with Albert Neuberger in the *Biochemical Journal* in 1949 and 1950 on the biogenesis of porphyrins^{1,2}. This work was carried out with ¹⁵N-

labelled glycine (chemically synthesized by Helen), which was injected into rabbits; this strategy led to Helen investigating the labelling of collagen from glycine, which helped establish the concept of metabolic pools and precursors of what were then, these intractable components of connective tissues. She also formed friendships here with others interested in collagen, including David Jackson, Robert Harkness and Dennis Lowther.

This began Helen’s interest in human connective tissues and she was awarded an Empire Rheumatism Fellowship with research space at St Mary’s Medical School, London. She found St Mary’s a shock environment after the well-equipped labs at Mill Hill; however, she received strong support from the Professor of Medicine, Stanley Peart, and she used it as a launch pad to move into even more unexplored territories — chondroitin sulphate and protein polysaccharides. The accepted view at the time was that chondroitin sulphate formed ionic complexes with proteins and effects, such as co-acervation, caused the non-ideal physical properties. However, with Helen’s careful chemical training, she used rigorous purification methods to show that by all methods, even by Tiselius electrophoresis, the protein and chondroitin sulphate were linked by an alkali-sensitive bond and her paper chromatograms showed that serine was the site of linkage. This was a revolution in the field and the data published in the *Biochemical Journal* in 1958³ showed that chondroitin sulphate was covalently

linked to protein. This work led to the recognition that all glycosaminoglycans, with the exception of hyaluronan, were linked to protein. It marked a major change in understanding, as hyaluronan was the first glycosaminoglycan to be characterized and it was shown to have no attachment to protein. This had led to speculation that other glycosaminoglycans were also unattached to protein. Having discovered the basis of this new class of linkage and a new family of macromolecules, Helen's reputation was now well established, and with further fellowship support she developed her work with protein polysaccharides, which were soon to be renamed proteoglycans.

Much of Helen's career was spent at The Kennedy Institute of Rheumatology in Hammersmith, which was the world's first specialist rheumatology institute and was funded by the Arthritis Research Campaign. Helen was recruited to The Kennedy Institute to head a research division in 1966 and she went on to become Director in 1977. Helen's group at The Kennedy Institute carried out fundamental work on the structure and functions of proteoglycans from cartilage and were the first to establish that the supramolecular organization of these proteoglycans involved their binding in the extracellular matrix to another polysaccharide, hyaluronan⁴. This was also heretical at the time, as who would predict that one polyanion would specifically associate with another polyanion? Yet the data stood the test of time, as it was a

property of the protein part of the proteoglycan to bind to hyaluronan and it provided the first example of the family of hyaluronan-binding proteins. Other work developed studies of cartilage degeneration in experimental joint disease with a long collaboration with ICI Pharmaceuticals. This work was fundamental in establishing that degenerative joint diseases were not just caused by 'wear-and-tear', but that an active process was involved⁵⁻⁷. Thus Helen's major achievement was in moving research in joint diseases from an era of observational descriptive pathology to the molecular and cellular analysis of the processes underlying these diseases. Basically, this involved using better science to tackle these tough chronic medical problems.

Helen's interest in glycosaminoglycans also led her to another area of disease and therapy, the mucopolysaccharidoses, a range of progressively debilitating lysosomal storage diseases, including Hurler's and Hunter's syndromes. Through this work, Helen was involved with enzyme replacement therapy, as it was established that lysosomal enzymes were released and taken up by other cells and therefore delivery of enzymes, or enzyme-making cells, was a strategy for correction of the medical problem⁸. Unfortunately this was insufficient to reverse the serious pathological changes caused by the prolonged lack of functional enzyme prior to treatment.

Helen's work at The Kennedy Institute on cartilage degeneration

and osteoarthritis was recognized internationally and she was given many prestigious awards, including the Heberden Medal of the British Society for Rheumatology (1976)⁷, the Feldberg Foundation Award (1977), the Bunim Medal of the American Arthritis Society (1978), the Neil Hamilton Fairley Medal of the Royal College of Physicians (1981), the Ciba Medal of the Biochemical Society (1981)⁹ and the Steindler Award of the American Orthopaedic Research Society (1982). She was awarded the CBE in 1981 for her contribution to medical research. She was also elected to become a Fellow of The Royal Society in 1977 and a foreign Member of the Royal Swedish Academy of Sciences in 1989. She was also awarded many honorary degrees including from the University of Edinburgh, where her great grandfather had been Principal.

Helen was well-known for speaking her mind in a clear and objective way and she did not go out of her way to court influence. Perhaps because of these qualities, Helen became the first woman appointed to the Council of the Medical Research Council (MRC) (1973-1977) and was an active participant in the strategic development of the MRC's activities. She was also later appointed a Trustee of the Wellcome Trust (1982-1990). This was at a time when the Trust was evolving to become the major biomedical research funding agency in the UK; indeed it became even larger than the Government's funding through the MRC. Helen played a major part in the expansion of the

Trust and developing the new responsibilities it had in leading the support of UK biomedical research. She was also able to promote the development of research on the role of extracellular matrix in biology and in disease.

It is a measure of the high regard in which Helen was held that she was selected for these prestigious positions. In 1998, she was the subject of a Channel 4 documentary, *Our Brilliant Careers*, on three women in science and it should remind us that Helen, as a woman in the era in which she lived, had to be not only exceptional to succeed in the male-dominated world of science, but also very determined and that was certainly a trait that she had in abundance.

The important positions that Helen held were onerous and required much hard work and endeavour; however, they did not come entirely without perks. The MRC Council is chaired by a non-scientist and when Helen was on Council, the Chair was the Duke of Northumberland. Coincidentally, he was a keen hunting man and Helen was also very keen on hunting, so much to her delight she was on occasion invited to hunt at Alnwick Castle. To say that Helen was keen on hunting is perhaps an understatement, indeed at one point it almost cost her life. She had a serious riding accident in the mid-1950s, but, typical of Helen, it didn't stop her hunting and she continued to ride for another 35 years. Much of her riding was done in Bedale, Yorkshire, where her parents had retired when they returned from India. However, she also man-

aged to ride in London and she had the dubious honour of being cautioned by the police for speeding in Richmond Park; the park police that is... Helen was on her horse on a Sunday morning and she was galloping when she shouldn't. Helen's interest in horse riding was also matched by a liking for fast cars and it was known that a green Mark 2 Jaguar was regularly seen as a blur on the A1 heading north from London to Bedale, where she escaped from the confusion of London to sample the clear air of Yorkshire. She also liked ballet and she regularly went to ballet classes, as she put it, to keep fit. She admitted that she wasn't as agile, poised or elegant as the young ballerinas also in the class, who were incidentally less than half her age, but this far from fazed Helen.

Helen also had a great influence on people, particularly the many national and international scientists who spent time at The Kennedy Institute. Indeed, there is a league of Helen's friends that straddles the globe and whose science was influenced by her direct and insightful example. Helen retired from The Kennedy Institute in 1990, but even in post-retirement she was active in research immortalizing chondrocytes¹⁰ in Roger Mason's Department at Charing Cross Hospital Medical School. She was the focus of many retirement parties and frequently these were scientific meetings in her honour, including a Biochemical Society Symposium in Bath when she was 67, an International Research Meeting in

London, when she was 70 and a special 2-day meeting in Manchester in 2000 with 65 scientists from around the world to honour her 80th birthday. Basically, it was clear from the start that one thing that she would never do was retire. Helen was many things, but she was certainly never dull. She couldn't stand fools and often let them know it. She couldn't stand pomposity and, although she became a grand lady, she had a wry sense of humour and liked a good laugh. She was very much without prejudice and judged people on their merits.

Helen's last few years were not without difficulty, there was pain, discomfort and increasing personal frailty and she typically bore it with stoic resolve. She was ably supported by a team of carers at her home in Yorkshire and she continued to be interested and concerned about science, which was the principle focus of her life.

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