In Memoriam

Sandford Lloyd Skinner (1933–2005)

Sandford Lloyd (“Sandy”) Skinner, one of the pillars of the renin-angiotensin system, died on May 29, 2005, after a long illness. Sandy was a gentleman, scientist, teacher, and family man who touched the lives of the many who were fortunate to know him.

Sandy was born in Clare, South Australia, on August 6, 1933. He graduated MBBS from The University of Adelaide in 1957. Following his medical studies, he researched the effects of vasoactive substances on the circulation and respiration of humans in the Department of Physiology, The University of Adelaide, for which he was awarded an MD degree in 1962. He also reported the artifactual elevation of plasma potassium levels during venepuncture. His first postdoctoral position during 1962–1963 was at the Cleveland Clinic working with Irvine Page and James McCubbin. This was the start of his life-long passion for the renin-angiotensin system.

At the Cleveland Clinic he performed seminal studies demonstrating the role of the baroreceptor mechanism of control of renin release. Importantly, his studies demonstrated that renin release could be stimulated by reduction in renal perfusion pressure within the physiological range without significant change in renal blood flow, thus demonstrating that renin release was caused by a baroreceptor mechanism and not renal ischemia. He also showed that renal compression could stimulate renin release. These studies were important in showing that variation in renin release may have a physiological, rather than an entirely pathological, function. After the Cleveland Clinic he spent 12 months during 1963 and 1964 in Sir Stanley Peart’s department at St. Mary’s Hospital, London, where the peptide sequence for angiotensin II had recently been determined. While there he rubbed shoulders with Tony Lever, Ian Robertson, and Joyda Brown, who subsequently established the MRC Blood Pressure Unit in Glasgow. This further cemented his bond to the renin-angiotensin system.

The difficulties of renin measurement at that time stimulated Sandy’s interest in the need for an improved method of renin measurement. On his return to Adelaide he developed methods for the separate measurement of plasma renin activity (PRA) and plasma renin concentration (PRC). His method for measurement of PRC was based on the use of nephrectomized sheep plasma; the success of this assay was because of the much higher affinity of human renin for sheep angiotensinogen than human angiotensinogen. These assays were adopted in many laboratories throughout the world, and Sandy played a key role in the international collaborative study of renin assay and the establishment of the international reference preparation of human renin.

With Malcolm Symonds and Margaret Stanley, Sandy demonstrated the production of renin by human chorionic membranes and uterine muscle. This stimulated Sandy’s long-term interest in “tissue” renin systems and the role of renin in the female reproductive tract. Together with Eugenie Lumbers and Malcolm Symonds, he studied the effects of oral contraceptives on plasma renin and angiotensinogen and proposed that failure of feedback inhibition of renin secretion by increased angiotensinogen levels may contribute to oral contraceptive–induced hypertension. Eugenie Lumbers subsequently demonstrated that amniotic fluid contains inactive renin that could be activated by pH <4, the significance of which was immediately apparent to Sandy, given that plasma was treated at pH 3.3 for his PRC assay. Thus, in his studies with Malcolm Symonds and Eugenie Lumbers of renin levels during pregnancy, Sandy was able to demonstrate a dissociation between PRA and PRC, leading to the proposal that the PRC method measures both active and inactive renin and that early pregnancy is associated with increased amounts of inactive renin in plasma. Sandy subsequently modified his methods to measure the separate concentrations (with sheep angiotensinogen) of active and total (acid- or trypsin-activated) renin, the difference between active and total renin representing inactive renin (prorenin).

In 1968 Sandy was appointed Reader in Physiology at The University of Melbourne, where he remained for the remainder of his career. Sandy’s interest in extrarenal renin led to his studies of the (mRen-2)27 rat. With Darren Kelly, Jennifer Wilkinson-Berka, Terri Allen and Mark Cooper, he produced the first rodent model of rapid onset diabetic nephropathy, by streptozotocin treatment of the (mRen-2)27 rat. This model is invaluable for investigation of the effects of therapies on diabetic nephropathy. Together with his collaborators he also demonstrated the value of the diabetic (mRen-2)27 rat as a model of diabetic proliferative retinopathy. These models of diabetic nephropathy and diabetic retinopathy will continue to serve the research community for the foreseeable future. His studies also demonstrated the contribution of the thymus and gut to circulating levels of renin. Sandy’s last article addressed the potential functional significance of differential glycosylation of tissue renin.

Sandy’s research encompassed many other aspects of physiology, particularly exercise physiology, where he also...
made an outstanding contribution. He maintained a large undergraduate teaching load, teaching both physiology and research ethics, in addition to his administrative responsibilities that included Chair and Deputy Chair of the Department of Physiology at different times. He supervised more than 40 higher degree students, who benefited greatly from his mentoring, and many went on to successful scientific careers. He also worked as a physician at the Austin Hospital.

Sandy was a very special person. He had an open, generous personality. He always had time to talk. He loved and enjoyed life. He loved and enjoyed his family. He was a gifted tennis player, so much so that he and his wife Lesley built and maintained a grass tennis court at “Sandles”, their beachside holiday house. An invitation to play there was equivalent to an invitation to Wimbledon. Sandy was spontaneous, with an infectious enthusiasm, particularly for science in general and for the renin-angiotensin system in particular. His ability to generate new ideas and concepts and to endlessly debate all aspects of renin from its phylogeny to its cellular location and molecular basis of action made Sandy a special kind of scientist. He was a great collaborator, always curious, always thinking of new experimental approaches, overflowing with ideas. He was generous in his discussions with other scientists and with his suggestions for new experiments. He would happily volunteer to rewrite manuscripts for those for whom English was a second language. He was an honest man—in all aspects of life and science. In science, he was committed to finding the truth. When he found one of his reports contained an error, he was quick to set the record straight. In addition to his erudition, Sandy obviously had an inborn talent for friendly discussion with his competitors—discussion that was no less robust than might be expected, but so open and friendly that all participants could walk away and say, “Not only was that exchange worthwhile, it was invigorating.”

Sandy made many life-long friendships during his sabbaticals in Denmark, France, and the United States and was host to many international visitors. His many friends from many different walks of life and many different continents will dearly miss him.

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