Ernest McCulloch

First identified stem cells

It was half a century ago when Ernest McCulloch told his research partner, James Till, the good news. This moment of scientific triumph marked the official beginning of stem cell research. It also was a personal moment that became Till's favourite memory of McCulloch.

"He was coming toward me, waving a piece of graph paper," recalled Till, now professor emeritus of medical biophysics at the University of Toronto. "This was on a Monday morning after the Sunday when he had first observed the presence of bumps on the spleens of irradiated mice that had received transplants of normal bone marrow cells. On the graph paper he had plotted the number of bumps as a function of the number of nucleated marrow cells transplanted. The result was a straight line. Twice as many marrow cells transplanted: twice as many bumps."

Both scientists later admitted that their observation was accidental. Nonetheless, Till said, "We knew from the beginning that we were involved in research that would be interesting." In 1961 they published their findings in *Radiation Research* (1961;14:213-22). In a 50th anniversary tribute to the paper, Irving Weissman, director of the institute of stem cell biology and regenerative medicine at the University of Stanford, writes that he learnt of the paper soon after publication in a basement hallway at Stanford (2011;175:143-4). His mentor, the radiation therapy pioneer Henry Kaplan, brandishing the journal in his right hand, advised his student, "You should read this. It will be important."

Ernest Armstrong McCulloch was born on 27 April 1926 in Toronto. His father was a doctor, as were two brothers of his father. After graduation from the exclusive Upper Canada College preparatory and high schools for boys in Toronto, he enrolled directly at the University of Toronto medical school, earning his medical degree in 1948. He spent the next year as a research fellow at Lister Institute in London, returning to Toronto for additional research and clinical training in internal medicine.

Rumpled tweed suits

In 1954 he became research fellow at the National Cancer Institute of Canada and in 1957 joined the newly formed Ontario Cancer Institute, the research arm of Princess Margaret Hospital at the University of Toronto. McCulloch, who was short and stocky and wore rumpled tweed suits and bow ties, was joined by fellow Canadian James Till, tall, elegant, and polished, having just earned his doctorate in biophysics from Yale University.

JOHN SMOCK/PA/AP

They injected the mice with marrow cells to help the mice survive. Ten days later, McCulloch observed the nodules of new cells on the spleen

"One important reason why the team worked so well is that Dr McCulloch had the MD that I lacked, and I had the PhD that he lacked," said Till. "He had a background in haematology and I didn't. I had a background in radiation biology and he didn't." But he graciously added, "Without him, what turned out to be pioneering work [in stem cell research] wouldn't have happened."

In the 1960s, with tensions high during the cold war between the United States and former Soviet Union, the two young scientists began to study the potential effects of atomic bomb radiation on the production of new blood cells. They exposed mice to radiation levels high enough to kill them within a month, and then they injected the mice with varying amounts of marrow cells to learn what quantities were necessary to help the mice survive. Ten days later on a Sunday, McCulloch observed the nodules of new cells on the spleen. And the next morning, triumphantly waving the graph paper, he told his partner the exciting news.

In their 1961 paper "the term stem cells was not mentioned," notes Weissman in his 50th anniversary tribute, "but then we had no important definition of such a cell at that time." He adds, "the major finding came in just a few sentences—each colony had at least four blood cell types (monocytic, granulocytic, erythroid and megakaryocytic), and they proposed that each colony was derived from a single clonal progenitor. They mentioned that the spleen colony-forming cell was probably from an undifferentiated cell."

In 1963 in a paper published in *Nature* the team confirmed that the different blood cells were produced from a single cell (1963;197:452-4). During the 1960s they continued research that laid the foundation for bone marrow transplantation in humans and for stem cell research. The two scientists eventually separated to pursue their own research interests, but they remained friends for life.

McCulloch held a variety of top research, academic, and administrative positions at the University of Toronto and Ontario Cancer Institute and served as president of the Royal Society of Canada's Academy of Science. Elected in 1999 to the Royal Society of London, he held nearly a dozen editorships during his career, including editor of the *Journal of Cell Physiology* from 1968 through 1991.

Alternative view

After retirement in 1991 he continued his quest as a senior scientist emeritus to find a cure for acute myelogenous leukaemia (AML), and from 1991 to 1993 he was visiting professor at the University of Texas M D Anderson Cancer Center in Houston. "He was determined to try to link laboratory findings to clinical outcomes," Till said, adding, "He wasn't afraid to contradict conventional wisdom if he preferred an alternative view."

He leaves his wife, Ona, and four sons and a daughter.

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Ernest McCulloch, internist and hematologist (b 1926; q 1948, Toronto), died on 20 January 2011.

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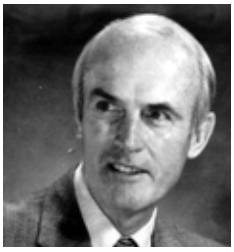
Edward Barry Adams



Foundation professor of medicine University of Natal, Durban, South Africa (b 1918; q Witwatersrand, South Africa, 1944; BSc (Oxon), FRCP, MD), d 18 November 2010.

Edward Barry Adams ("Barry") was professor in Durban during 1954-78. He published on iron deficiency, megaloblastic anaemia, and protein deficiency, and studied the treatment of neonatal tetanus, establishing a unit for its management in his department. As a teacher, he questioned received wisdom and offered new insights, and he believed that respect for colleagues and compassion for patients underpinned the daily practice of medicine. During the apartheid era, he stood against forces threatening to undermine the high ideals of his department, and the main lecture room in the department of medicine was named for him. He leaves Sybil, his wife of 67 years, and four children.

Oscar Jolobe
Y K Seedat

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Robert John Oriel Davies

Consultant and professor of respiratory medicine Churchill Hospital and University of Oxford (b 1961; q Southampton 1985; DM, FRCP), d 19 November 2010.

Robert John Oriel Davies ("Rob") graduated with honours and clinical distinction. He moved to Oxford for postgraduate training, becoming interested in sleep apnoea (the subject of his DM) and pleural diseases. Passionate about evidence based care for respiratory disease, he set up the Respiratory Clinical Trials Unit at Churchill Hospital, coordinating several multicentre studies on empyema, malignant pleural effusions, and sleep medicine. He instigated a network of collaborating departments throughout the UK; was instrumental in the British Thoracic Society's guidelines on pleural disease, further contributing to his international reputation; and inspired many of his juniors to a higher research degree. He was also an accomplished jazz saxophonist. He leaves a wife, Penny, and two children.

John Stradling
Colin Mumford

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Jean Drinkwater

Former general practitioner Brierfield, Nelson, Lancashire (b 1925; q Manchester 1949; DObstRCOG), d 12 January 2011.

Jean Drinkwater met her husband, Peter, at medical school and in 1954 they entered general practice in Brierfield, Jean having decided against a research career. Known as Dr Jean and Dr Peter, they ran their practice for 34 years, first from their home and then a purpose built health centre, also training and mentoring many young doctors. Jean was active in the local branch of Cruse and supported many national and local charities, including Marie Curie and Pendleside Hospice. She was a keen gardener and walker, completing the Pennine Way in sections over several months with Peter in their 60s. Predeceased by Peter (obituary, *BMJ* 2001;322:367) in 2000, she leaves three sons and eight grandchildren.

Andrew Drinkwater

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Ian William Ballantyne Grant

Former consultant physician in respiratory medicine Northern General Hospital, Edinburgh (b 1918; q Edinburgh 1941; FRCPEd), died from bronchopneumonia on 10 December 2010.

Soon after qualifying, Ian William Ballantyne Grant served with the Royal Tank Regiment in India. He became consultant at Northern General Hospital in 1952 and helped to eradicate tuberculosis from Edinburgh in the 1950s. Especially interested in asthma, interstitial lung disease, and respiratory intensive care, he discovered malt worker's lung and co-established a self referral emergency asthma service. He had over 150 publications in peer reviewed journals and contributed chapters to many important textbooks, as well as lecturing all over the world. President of the Scottish Thoracic Society and of the Thoracic Society, he was also professor of medicine in Malaysia. Predeceased by his wife, Betty, in 2003, he leaves three children and nine grandchildren.

Ian S Grant

Cite this as: *BMJ* 2011;342:d1027

Theodore Inslee Jones

Former general practitioner Isle of Mull (b 1922; q Cornell, USA, 1952; FACS), d 30 October 2010.

Theodore Inslee Jones ("Ted") first came to Scotland in 1941 as a fighter pilot in the US Army Air Force. He was associate professor at Rochester, New York, and visiting surgeon at two teaching hospitals before he set sail for the UK in 1973 to practise medicine. In 1976 he took over the practice in Mull, and was surgeon in the cottage hospital in Tobermory. He learned to speak Gaelic and threw himself into supporting island life. He visited elderly patients in remote areas because he distrusted "five minute office consultations" that ignored domestic and environmental aspects of illness. On retiring in 1985, he moved to and thrived on the isle of Ulva. He leaves a wife, Ann; five children; and four grandchildren.

Gordon Stewart

Cite this as: *BMJ* 2011;342:d1024

Peter Timmis

Former consultant ear, nose, and throat surgeon Luton and Dunstable Hospital (b 1922; q St Bartholomew's Hospital, London, 1945; FRCS), died from colon cancer on 15 December 2010.

Peter Timmis was the first in his family to enter medicine. Appointed consultant ear, nose, and throat surgeon in Luton in 1960, he serviced a one in two rota, building a high quality department and training many visiting surgeons from around the world. Following retirement in 1987, he enjoyed golf and bridge, and in his 80s was marching in London against the Iraq war. But the garden was the main beneficiary of his energies, and he was a regular exhibitor at the local horticultural event, a magnificent cucumber winning "best in show" only three months before his death. He leaves a wife, Kathreen; three children; and seven grandchildren.

Jane Timmis
Adam Timmis
Ben Timmis

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