Donald Metcalf, ‘Father of CSF’ (1929–2014)

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Donald Metcalf, a superstar in the field of hematology, died of metastatic pancreatic cancer on December 15, 2014 at the age of 85. Don, to those who knew him, gained the respect and admiration of scientists, clinicians, and students for his pioneering research and kind mentorship. An object

of widespread admiration and respect, his loss is deeply felt by all of us in the community.

Born in 1929 in Mittagong, New South Wales, Don was educated at the University of Sydney, first receiving a BSc (Med), and then an MBBS in 1953 for his work on the ectromelia virus. The following year he accepted a Carden Fellowship in cancer research at the Walter and Eliza Hall Institute of Medical Research (WEHI), where he studied vaccinia virus, marking the beginnings of his interest in hematology. He was a postdoctoral student at Harvard Medical School between 1956 and 1958, and received an MD in 1961, after which he served a resident medical officer at the Royal Prince Alfred Hospital. He returned to the WEHI as Head of the Cancer Research Laboratory in 1958, and from 1965 to 1996 he was Head of the Cancer Research Unit and Assistant Director of the WEHI. He also served as Research Professor of Cancer Biology at the University of Melbourne from 1986 to 1996. In 1996, he became Professor Emeritus of the University of Melbourne.

He also served as an International Advisory Board of International Journal of Hematology until 1998 for nearly a decade in addition to serving as editors for many other journals. Don spent most of his career, nearly six decades, at the WEHI. His major concern was the proliferation and differentiation of hematopoietic stem cells and their progeny is regulated in a systemic and interrelated fashion. His commitment to this line of study was such that he even refused a prestigious appointment as Director of the Institute, and continued to throw himself into his work right up until he retired last year. His rigorous approach led him to his breakthrough hypothesis that there must be at least four physiological regulators involved in white blood cell production. These substances, which he termed colony-stimulating factors (CSFs), were the main focus of his studies for more than 50 years, during which time he

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led his colleagues to characterize and purify four distinct CSFs.

These studies laid the groundwork for the cDNA cloning of various CSFs. Of these, Don was most interested in G-CSF, the *in vivo* actions of which he correctly anticipated to be both comprehensible and highly valuable for clinical use. I recall that around that time he was pleased with and highly appreciated our discovery of human G-CSF-producing tumor in the 1970s, which provided clear evidence for the *in vivo* action of this cytokine. Soon after the development of its recombinant forms, lenograstim and filgrastim, respectively, in Japan and in the United States, he also manufactured filgrastim in his country, clarified molecular mechanisms of its production and action, and gained approval for clinical use in 1991, after which he initiated successful clinical trials of his own. As well as boosting the immune system in people treated with hematological and immunological disorders, this agent has revolutionized hematopoietic stem cell transplantation. He once observed that these two agents have now benefited more than 20 million people worldwide.

In recognition of his consistently stellar achievements, he received many honors and awards, including the Companion of the Order of Australia, the Albert Lasker Award for Clinical Medical Research in 1993, the Gairdner Foundation International Award in 1994, the Royal Medal of the Royal Society in 1995, the Victoria Prize in 2000, and the Prime Minister's Prize for Science in 2001. I regret that he passed away before being awarded the Nobel Prize as among the greatest pioneers in the modern hematological sciences.

It is needless to say that Don mentored hundreds of students and young researchers who worked with him, and

was an inspiration to thousands of scientists around the world. What we have learned from his example is that scientists should describe, explain, and make precise predictions from clear observations of their own experimental data. He was a frank critic of muddled data and interpretations, which he nonetheless managed to do while engaging in warm and witty conversation, and was always a source of encouraging suggestions and support. In my own case, while at the WEHI I was given the task of developing *in vitro* cancer stem cell colonies and studying their immunogenicity. Don was always available whenever I had questions or wanted his advice, which I knew I could seek even when he was bent over his microscope. He would sometimes simply tell me, 'Just keep working on something about you are really excited despite whatever your colleagues, your boss, and other people may tell you'. I suspect that other Japanese clinical scientists who joined his laboratory may have had similar experiences as well, and I am sure it is no exaggeration to say that Don was a defining influence in all of our lives, both by example and by direct, wise advice.

I heard that two things Don most wanted after being diagnosed with cancer was spend as much time as possible with his wife, Jo, and his daughters, while continuing to do his research; he did this by speaking with his family at lunch and over tea with his successors as usual, maintaining his interest in stem cells through it all. Looking back on those exciting days with Don at the WEHI, I wish I could have joined in those lunch and tea-time talks once again.

I offer my sincere condolences to Don's wife, Jo, four daughters, and six grandchildren.