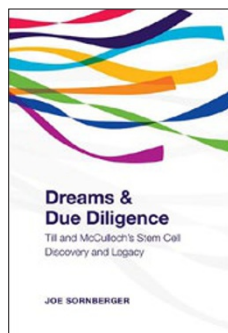


Founding a new field



Dreams & Due Diligence: Till and McCulloch's Stem Cell Discovery and Legacy

Joe Sornberger

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Reviewed by David Nathan

Joe Sornberger is a professional writer commissioned by the Canadian Stem Cell Foundation to create a monograph on the Canadian legacy of the collaborative efforts of James Till and the late Ernest 'Bun' McCulloch, whose seminal work was the discovery of a mouse bone marrow cell that they called the spleen colony-forming cell.

In a study designed to determine radiation sensitivity of mouse bone marrow cells, they noticed unexpected lumps on the spleens of the irradiated and bone marrow transplanted mice. Several of those lumps turned out to be colonies of blood cells derived from progenitors capable of giving rise to granulocytes, megakaryocytes or erythrocytes.

A splendidly written foreword by Alan Bernstein, a leader of Canadian biomedical science and a former student of the researchers, puts their work in clear scientific perspective. Their discovery, as well as the vital contributions of Donald Metcalf and his co-workers in Australia and of Leo Sachs in Israel, both of whom developed culture conditions that permitted much simpler growth of hematopoietic colonies *in vitro*, set the stage for a subsequent explosion of information on the regulation of normal and malignant hematopoiesis.

The book is based on a series of interviews with Till and McCulloch and with many of their most distinguished students at the Ontario Cancer Institute (aka the Princess Margaret Hospital) in Toronto whose independent careers have brought substantial credit to Canadian biomedical science.

Sornberger profitably explores the relationship between the two men. Unlike many successful scientific collaborators, such as Nobel Prize winners Michael Brown and Joseph Goldstein, who discovered the pathways that regulate serum cholesterol, or Michael Bishop and Harold Varmus, who demonstrated the role of oncogenes and their derivation from viruses, the approaches of Till and McCulloch to scientific work were totally orthogonal. They also came from widely disparate social and scientific backgrounds. But friendships are often built because each of the partners sees in the other qualities that they desire in themselves. Till and McCulloch made a landmark discovery

largely because they were capable of observing and appreciating the importance of completely unexpected findings. The ability to notice and pursue the unanticipated result is key to both excellent science and clinical care.

Sornberger is a writer, not a critical scientist, so readers will not gain much insight into the history of the study of hematopoiesis before and after Till's and McCulloch's seminal finding. And there is a bit of Canadiocentric chauvinism expressed in the pages. For example, Ronald Worton, former Scientific Director of the Ottawa Health Research Institute, is a splendid geneticist and a major contributor to inherited muscular diseases, but he is not *the* discoverer of the muscular dystrophy-associated gene, as Sornberger seems to suggest. It is strange that he does not mention that Louis Kunkel of Children's Hospital in Boston and his colleagues made key contributions to that discovery. Tak Mak of Toronto is an outstanding molecular biologist, but not *the* discoverer of the T cell receptor. But this criticism might be considered caviling. The fact is that the students of Till and McCulloch are highly distinguished members of the scientific, and particularly hematologic, communities.

In the final section of the book, Sornberger launches into a discussion of the controversy over human embryonic stem cells. However, it is a very long stretch from the classic experiments of Till and McCulloch, who focused largely on the relatively mature myeloid stem cells that produce granulocytes, platelets and red blood cells, to the totipotent embryonic stem cells that are capable of giving rise to all of the cells of the body. Nonetheless, the author plunges into the furiously debated morass of embryonic stem cell research without adding very much resolution to the conflict. He is properly outraged that unscrupulous hucksters are selling injections of so-called 'stem cells' to desperate patients, but hucksterism has been part of the US if not the Canadian medical culture since colonial days. That it persists is a terrible disgrace.

Toward the book's end, the author decries the fact that Till and McCulloch never received a Nobel Prize. But that is probably not due to lack of appreciation of their work. In my opinion, this failure relates to the difficulty that the Nobel Committee must have had when they tried to limit the assignment of the prize to three people. The development of the field depended on both *in vivo* (Till and McCulloch) and *in vitro* (Donald Metcalf and Leo Sachs) experiments, and four researchers are simply one too many for the Nobel Prize. That particular prize notwithstanding, theirs was truly a seminal discovery.

In summary, this is an interesting short book because the author interviewed some of the best experimental hematologists in the world to gather the data he needed to write it. Their thoughts about the field and about Till and McCulloch are valuable archives. The writing style is clear, but the material is not groundbreaking. It stands as a tribute to a collaboration between two totally disparate individuals who came together to do a great experiment and expanded a great cancer center, the Ontario Cancer Institute. That may be reason enough to catch the attention of basic and physician scientists.

COMPETING FINANCIAL INTERESTS

The author declares no competing financial interests.

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