In Memoriam

Charles Philippe Leblond, 1910 - 2007

“The quality of the radiographs was so much better than before, and that made things easy to see, compared with earlier, crude contact techniques. And dogged persistence, tenacity, and stick-to-itiveness helped, too.” One should also add a lively curiosity for the big questions of cell biology and an intuitive genius for the patterns of nature. These features marked the amazing career of cell biology giant Charles Philippe Leblond, who died on April 10 at age 97.

Leblond was past president of the American Association of Anatomists (1962–1963) and winner of many awards, including Fellow of the Royal Society of Canada (1951), the Flavelle Medal (1961), the Medal Leo Pariseau, the Gairdner Foundation Award (1965)—often a predictor of the Nobel prize—Fellow of the Royal Society of London (1965), honorary member of the American Academy of Arts and Sciences (1970), NIH Fogarty Scholar (1975), Officer - Order of Canada (1977), the AAA’s Henry Gray Award (1978), the American Society for Cell Biology’s Wilson Award (1982), McLaughlin Medal (1983), the Quebec government’s Prix Marie-Victorin (1992), inductee into the Canadian Medical Hall of Fame (1995), and honorary doctorates from Acadia, McGill, and York Universities and from the Universities of Montreal and Sherbrooke. In 1999, he was appointed to the prestigious Companion of the Order of Canada and in 2001, he was made a Grand Officer of the National Order of Quebec.

Although awards were appreciated, the world of biological discovery always came first. For lovers of science, there is much to be gained by rereading his classics. His early discovery of stem cells has many insightful nuggets that still lead the field. One learns, for example, that stem cell-driven renewal is actually less common than the mechanism used by “expanding cell” populations, where mitotic cells are dispersed rather than focused in niches. Prominent acknowledgement and confirmation of this under-appreciated observation came recently in Nature.3 Other classics include: identification of how skeletal bones grow through osteoblast deposition and osteoclast remodeling,4 early discovery of the biogenesis and metabolism of thyroxine5 and detection of triiodothyronine,6 early prediction of DNA semiconservative replication7 (published days after the Watson and Crick Nature article), the discovery of axonal transport,8 the Warshawsy et al.9 finding that nascent proteins are processed from the rough endoplasmic reticulum through the Golgi apparatus into pancreatic zymogen granules (made in hot competition with the Palade lab at Rockefeller University), the first realization that the Golgi apparatus is the site of terminal glycosylation,10 the discovery of the cell coat,11 the cellular biogenesis of collagen,12 and new insights into the ultrastructure of basement membrane.13 The breadth and originality of his contributions to science are astounding.

Charles Leblond was born in the northeastern border city of Lille, France, and entered science after medical school as a student of histochemist Antoine Giroud at the University of Paris. While a Rockefeller Fellow at Yale University, he met and married Gertrude, his beloved companion of 64 years. After two years, he returned with Gertrude to Paris (1937–1940) and joined the lab of Antoine Lacassagne, director of the Biology Section of the Institut du Radium.14 In 1920, Lacassagne had begun injecting rabbits with radioactive polonium. Organs were removed, paraffin sectioned and applied to photographic plates. Also at the Institut du Radium were physicist Frederic Joliot and his wife Irene Joliot-Curie (daughter of Pierre and Marie), who shared the 1935 Nobel Prize in Chemistry for their discovery of a method to generate radioactive elements. With a new Rockefeller-funded cyclotron in place, there was much excitement about the power of radio-labeled precursors as an emerging tool in biological research.15 Here
Leblond made the landmark discovery that iodine is taken up and stored by the thyroid gland at saturating levels under the control of TSH then released over days to other organs. In 1940-1941, Leblond studied the role of phosphates in bone growth as a research fellow in anatomy at the University of Rochester, then joined McGill University as a lecturer in histology in 1941, rising to assistant (1943), associate (1946) and full professor (1948) of anatomy in short order and serving as chairman of the Department of Anatomy from 1957–1974.

His early period at McGill was interrupted by the war years 1944–1945, during which time Leblond served in the Free French Forces in France and Britain helping to organize personnel that numbered more than one million by the end of the war. The return from the war was transformative. “In 1946,” he wrote, “after returning to Montreal from service with the Free French Forces, it was clear to me that the crude technique previously used for radioautography had to be improved.”

Radioautography (autoradiography) is the histological detection of incorporated radiolabeled precursors. State-of-the-art was to tightly appose glass slide-mounted histological sections onto photographic plates, then develop the plate and compare the two. By melting photographic emulsion directly onto histological sections, resolution improved to the level of individual cells. Radioautography introduced the dimension of time to histological cell biology, a “dynamic histology.”

Leblond’s childlike openness to the possibilities of new data (“study every opportunity, learn from every situation”), his courage in controversy with faith in the precision of the data (“Always, above all, be precise”) and his ambition to always do better than his best was matched by his enduring gentle humor and personal concern for his associates and students. A remarkable 120 graduate students matriculated under his supervision. As we graduate students reported our new data to him, the Heraclitus quotation over his desk—“Rien n’est permanent sauf le changement” (Nothing is permanent, except change)—reminded us of the flow of science and life.

A beginning student’s introductory interview with Leblond might include a gentle query about the periodic acid Schiff stain whose lively purple-magenta coloring of carbohydrate 1-2-glycol groups inspired his Golgi and cell coat discoveries. The student would later realize that it also elegantly inspired the Leblond wardrobe, automobile, and even home interiors. His popular histology lectures were accompanied by large, carefully rendered multi-color (some purple-magenta) chalk drawings and had a significant historical narrative. As Nobel Laureate George Palade noted on the occasion of the 1992 Prix Marie-Victorin to Leblond, Charles Leblond’s discoveries are so fundamental that they are taught in schools and colleges throughout the world.

The 1975 international stem cell symposium honoring Leblond on his 65th birthday was not, as it turns out, the expected transition into retirement. Instead, Leblond was awarded an NIH Fogarty Scholarship for a year of retooling in George R. Martin's lab at the National Institute of Dental Research, where a benign, misidentified mouse tumor was soon to revolutionize extracellular matrix biology.

Armed with the powerful new technique of immuno-histochemistry, Leblond returned to McGill to elegantly document previously uncharted steps in the cellular biosynthesis of thyroglobulin and collagen I in bone and teeth. Soon, antibodies to collagen IV, a new basement membrane molecule designated ‘GP-2' - later named ‘laminin’, and to a heparan sulfate proteoglycan ('perlecan') began appearing in the Leblond lab from George Martin. This launched a 20-year molecular exploration culminating in the concept of the basement membrane as an integrated polymer, rather than as layers of separated macromolecules initially favored by others.

This remarkable productivity did not get in the way of new contributions to the understanding of
epithelial renewal, nuclear and nucleolar shape, and bone remodeling—including a September 2006 article detecting the MMP9 cysteine activation switch for the first time in remodeling cartilage. A whole career in itself beyond age 65!

Gertrude died in December 2000. Charles Leblond’s card of “Best wishes for year 2000 and the millennium” displayed pictures of a younger Gertrude and himself on the inside. On the back page was a beautifully drawn version of the much-maligned fibroblast. His caption states, “Even the shapeless fibroblast can get beautifully oriented. Here is hope.”

A zest for beauty and humor in life and work. A year later, Leblond married Odette Lengrand, a childhood acquaintance from Lille. Both were 91. “I married the best of North America first and now the best of France,” he declared. Odette died in July 2004.

Gordon W. Laurie, Ph.D., Department of Cell Biology, University of Virginia

References


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