

History 6 - Leblond to Hermo

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47. Charles Philippe Leblond (McGill: 1941-2007)



C.P. Leblond

NOTE: Much of the material in the following section is taken from an article by the author in Biographical Memoirs of Fellows of the Royal Society. 54: 175-191 (2008) in which references are found ^{Bennett 2}.

It was during this exciting era in the history of Anatomy and Cell Biology that C.P. Leblond began his long career at McGill, starting as Lecturer in 1941. The destiny of institutions and disciplines can often change with the arrival of an outstanding individual, and this was certainly the case with Charles Leblond. To appreciate the significance of Leblond's scientific contributions, we must examine our current concepts of biology compared to those of the world which he was entering .

In the modern world of Cell Biology, it is understood that virtually all cells in the body continuously synthesize a multitude of proteins, and the pathways of synthesis and secretion of these proteins are well established. The continuous turnover of cells in many tissues is also an accepted idea, and embryonic and adult stem cells are of central importance for the cellular economy, in malignant transformation, and more recently in terms of exciting new therapeutic treatments. None of these phenomena were understood at the beginning of Leblond's career, and his extraordinary contributions to these fields have fundamentally changed our understanding of Cell Biology.

This was an era in which radioactive isotopes were beginning to be used to investigate the fate of various molecules in biological processes – an approach that would overturn many long-held concepts. Leblond

virtually introduced and developed the technique of autoradiography which permitted an accurate localization of radioactive molecules in tissues and cells, and thereby could trace the migration of these molecules from their site of synthesis. His work almost single-handedly “transformed the descriptive science of Histology into a dynamic one” ^{Frost 2:383}.

Beginnings

C. P. Leblond was born in Lille, France, in 1910. His father died when Leblond was only 10 years old, leaving his mother to raise him and his three brothers. A brilliant student with an insatiable curiosity, he debated on becoming a film producer, an architect or a biologist. In the end, he decided on Biology, and enrolled in Medicine at the University of Paris. He was fascinated by his first course in Histology and decided to pursue this field as a career. Friends tried to dissuade him, saying ‘Histology is a dead horse ... the future is in Biochemistry.’ He nonetheless became a histologist, and 50 years later reflected on the wisdom of his choice and the many exciting developments that had occurred in this field, including the rebirth of histochemistry, immunocytochemistry, electron microscopy and autoradiography—which he concluded were ‘all powerful kicks for a dead horse’.

Leblond obtained his M.D. degree from the University of Paris in 1934. His doctoral research thesis described the histochemical localization of ascorbic acid, which he found to be predominant in steroid-secreting cells. This study led him, with a Rockefeller postdoctoral fellowship in hand, to the endocrinology-orientated Department of Anatomy at Yale University in 1935. It was here that he met his remarkable wife Gertrude Sternschuss, to whom he remained married for 64 years.

From the beginning of his career, Leblond realized that just as past research had shifted its focus from Gross Anatomy to cellular structure, future research would center on Cell and Molecular Biology, and would include using tools developed mainly by Biochemistry. In 1937, following his interest in radioisotopes, Leblond joined the Laboratoire de Synthèse Atomique in Paris, which was involved in preparing such isotopes. This move was to set the stage for his future contributions to our understanding of the dynamic nature of tissues and cells.

Under the guidance of Antoine Lacassagne, Leblond injected ¹²⁸I into a rat and found that the radioactive label promptly accumulated in the thyroid gland, presumably incorporated into the thyroid hormone precursor thyroglobulin. To localize this label more precisely within the thyroid tissue, Leblond attempted a novel technique that used a photographic emulsion to detect radioactive molecules in histological tissue sections. This technique, called ‘radioautography’ or ‘autoradiography’, had been first used by Lacassagne in 1924, albeit crudely, to localize radioactive polonium in the intestinal wall.

Unfortunately, Leblond’s first attempt to use radioautography in the thyroid failed, the reason being that the radioiodine isotope used, with its extremely short half-life (25 minutes), disintegrated so quickly that too little radioactivity remained in the tissue to be detected by the photographic emulsion.

The invasion of France by Hitler in 1940 brought great difficulties. At that time, Leblond was serving as a doctor in the French army in Casablanca while his family remained in Paris. Since Leblond’s wife Gertrude was from a Jewish family, her life was at real risk. Finally, as the German troops were nearing Paris, Gertrude and her infant son Philippe, accompanied by Leblond’s mother and grandfather, escaped by car

over the back roads of France, and across the Pyrenees. They crossed into Spain, just hours before the border closed, and finally made their way via Lisbon to the USA.

Early Studies at McGill: Developing the Technique of Radioautography

In 1941, C.P. Leblond came with his family to McGill, where he became a full-time faculty member of the Department of Anatomy, a post he held for more than six decades. During this time his family expanded to include two more sons and a daughter. In the subsequent five years he also obtained a Ph.D. from the Université de Montréal (1942) and a D.Sc. from the Sorbonne (Université de Paris) (1945).

It is possible that Leblond may have come to our Department at McGill in order to work with Hans Selye who was doing endocrinological research. As mentioned previously, this was a period of spectacular developments in the field of endocrinology. During the three year period in which they were together in the Anatomy Department, Selye was the Associate Professor of Histology while Leblond held a very junior position as Lecturer. The two scientists published three papers together on the effects of steroid hormones on the hypophysis and kidney. However this work constituted only a very small part of Selye's publication output of 300 papers. Also it did not form a significant part of the main theme of Leblond's research. In 1944, Leblond left McGill to serve with the Free French Army in Rio de Janeiro and London. By the time of Leblond's return at the end of the war, Selye had left McGill for the Université de Montréal.

At McGill, Leblond became intimately linked with our Department of Anatomy to a much greater extent than Hans Selye and influenced its whole future. His main interest from the beginning was the development of the radioautographic technique in order to investigate cellular processes. At McGill, he repeated his Parisian radioautographic experiment on thyroid tissue using the newly available radioiodine isotope ¹³¹I with a half-life of eight days. In this procedure he clamped a glass histological slide with a radioactive tissue section tightly against a photographic plate (in darkness), and after allowing sufficient exposure time, the plate was removed and developed to produce an image of silver grains. When the plate and the histological slide were carefully realigned, one could localize the radioactivity within the tissue section. With this method the resolving power was less than 100 µm, but he was nonetheless able to localize the radioactivity to specific thyroid follicles. In this radioautographic study, Leblond showed that all follicles, with both large and small epithelial cells, incorporated label.

It was the results of this study that challenged the first of several concepts that were strongly held regarding the functioning of cells and tissues in the early part of the twentieth century. According to this first concept of 'activity-rest alteration', all cells were thought to undergo cycles of cellular activity, followed by rest periods during which this activity ceased. This study provided the first evidence to refute this concept, indicating that iodine was being incorporated continuously into newly synthesized thyroglobulin in all cells.

When he returned to McGill from his military service, Leblond continued, with Leonard Bélanger and Rita Bogoroch, to search for ways to increase the resolution of the radioautographic technique. They were advised by physicist Pierre Demers to melt the emulsion from Eastman-Kodak lantern slides, paint it directly onto the sections and then develop the emulsion while it was still attached to the histological sections. This resulted in a tenfold improvement in resolution. As recalled by Leonard Bélanger 20 years later: "It was on a bright and crisp Saturday of February 1946, that a striking radioautographic record was first seen over the tissue. It reminded me of the biblical story of a message written in letters of fire on the wall of the palace of the wicked Assyrian king. But the imprint in the photographic emulsion was not recording a message of doom, but one by which to understand life."

In 1948, Leblond and J. Gross developed a technique in which the histological slides were dipped directly into liquid emulsion. This 'coating technique' was later refined by Beatrix Kopriwa, an associate of Leblond's who became one of the best specialists in the field. In particular, she devised a semiautomatic coating instrument that made it possible to achieve a constant thickness of the emulsion coat. This enabled the quantification of radioautographic reactions by counting the number of silver grains per unit area over reactive histological structures.

The use of thinner sections and emulsion coats led to further advances in resolution, and the introduction of tritium (^3H) was a technical milestone. With the low energy of its β -rays (averaging 0.018 MeV), the emission from tritium travelled over only a very short pathway in the overlying emulsion, and a 100-fold improvement in resolution was finally achieved. This led to an explosion in the use of radioautography in cell biology.

Other novel studies performed by Leblond and his co-workers in the 1950s used radioautography, after administration of radioactive phosphorous and calcium, to reveal the mechanism of bone formation through osteoblast deposition and osteoclast remodelling ^{Frost2:384}.

Studies on the Turnover of Cells: Discovery of the Adult Stem Cell

The next dramatic result of this technique, achieved in Leblond's laboratory with labeled DNA precursors, challenged a second entrenched concept, that of 'stability'. According to this concept, all adult tissues were considered to be essentially static, with cells that did not divide.

The first evidence to challenge this concept had been the observation of mitotic figures in the crypts of the small intestine. This had been documented as early as the 1890s, but this cell division had been interpreted as occurring simply to replace damaged cells in the villus. In 1946 Leblond and Catherine Stevens carefully examined the small intestine of rats, and even in the absence of any detectable epithelial damage to villous cells, they observed frequent mitoses in the crypts. These results led them to the conclusion that all of the villous epithelial cells were replaced physiologically every two days—a concept originally dismissed by critics as 'too silly for words'. To prove their case, Leblond and his colleagues made use of their new radioautographic technique after the administration of DNA precursors, including ^{32}P -phosphate with Stevens and Bogoroch in 1948, ^{14}C -adenine with B.E. Walker in 1958, and finally ^3H -thymidine with B. Messier and Kopriwa in 1958. These studies conclusively revealed a constant dynamic turnover of epithelial cells in the small intestine. Subsequent studies with W.L. Chang in 1971 showed a similar turnover in the large intestine. In 1974, studies in the small intestine with Hazel Cheng showed that stem cells in the crypt gave rise to four different epithelial cell types, namely columnar, mucous, Paneth and enteroendocrine cells.

The other landmark work leading to the concept of an adult stem cell was the classic morphological and histochemical study by Leblond and Yves Clermont in the early 1950s on the epithelium of the male seminiferous tubules. Spermatogonia in the outer regions of the epithelium give rise to one or two generations of spermatocytes. These are succeeded by one or two generations of spermatids which differentiate into mature sperm cells. These generations were found to be associated with one another in fixed compositions such that, in any given area of seminiferous epithelium, the cellular associations followed one another in time in a continuous cycle. In order to identify the different generations of germ cells, it was necessary to identify the different stages of their maturation. The key to solving this complex

problem lay in using a histochemical technique, the periodic acid-Schiff (PAS) technique which selectively stained the Golgi complex and acrosomic system of the cells. By observing the morphological changes occurring in these organelles, one could identify the different generations of germ cells. This led to a seminal publication of Leblond and Clermont which precisely defined the 14 different stages of the adult rat seminiferous epithelium.

Analysis of these stages then brought these authors to a second seminal finding, i.e. the discovery of stem cells in the seminiferous epithelium. Their publication thus stated that: “At each cycle, there is the reappearance of a new dormant cell which acts as the stem cell of spermatocytes ... This is described as the “Stem Cell Renewal Theory”. This article is the first in which nests of cells dividing in an adult organ were designated as ‘stem cells’.

The significance of this discovery was not fully appreciated at the time, but over the years its monumental importance has come to be understood. In 2013, John Fleischman wrote an article in the American Society of Cell Biology Post entitled: “The other big paper of 1953” in which he compared the initial discovery of adult stem cells by Leblond and Clermont to the elucidation of the structure of DNA published by Watson and Crick in their famous 1953 Nature Paper. He mentioned that “unlike DNA, Leblond’s theory of stem cells met with a storm of criticism, but, in the fullness of time, “stem cells” turned out to be real and the hypothesis confirmed The ASCB Post. May 14, 2013. Based on this historic contribution, Leblond was nominated on two more occasions for a Nobel Prize in the two years before his death.

This stem cell concept synergized with that proposed independently by Till and McCulloch in 1960–63, who recognized that the ‘regeneration nodules’ transiently present in the spleen of irradiated mice that had been transplanted with donor bone marrow were derived from a single cell, ultimately defining a form of haemopoietic stem cell.

The above studies had shown the presence of adult stem cells in ‘renewing cell populations’, characterized by continuous cell replacement. However, Leblond and his colleagues also found evidence for the presence of occasional adult stem cells even in tissues such as muscle and brain that are composed almost entirely of non-dividing cells. In a review paper written in 1964, Leblond concluded that the body has three types of cell population: 1) ‘renewing cell populations’ in which adult stem cells are an essential feature; 2) ‘expanding cell populations’ in which small numbers of adult stem cells exist and give rise to skeletal fiber nuclei or glial cells of the brain; and 3) ‘static cell populations’ that are composed of non-dividing cells and include no adult stem cells. These last have the ‘stability’ formerly attributed to all adult cell populations.

Studies on Protein Synthesis

The radioautographic studies of Leblond and his colleagues in the 1950s also challenged another established concept, that of ‘specificity’, which postulated that each cell type in the body had a distinct, unique function. It was initially believed, for example, that only cells of the liver and pancreas synthesized proteins, and all circulating body proteins were derived from these cells.

To investigate protein synthesis, Leblond and his colleagues carried out studies using ¹⁴C-bicarbonate in 1953, and then ³⁵S-labelled amino acids in 1957. They were astonished to find that virtually all cells in the body incorporated label. This led to the conclusion, considered heretical at the time, that all cells synthesized proteins continuously. This was one of the first pieces of evidence to replace the specificity concept with the idea that most cells are multipotential in their functions.

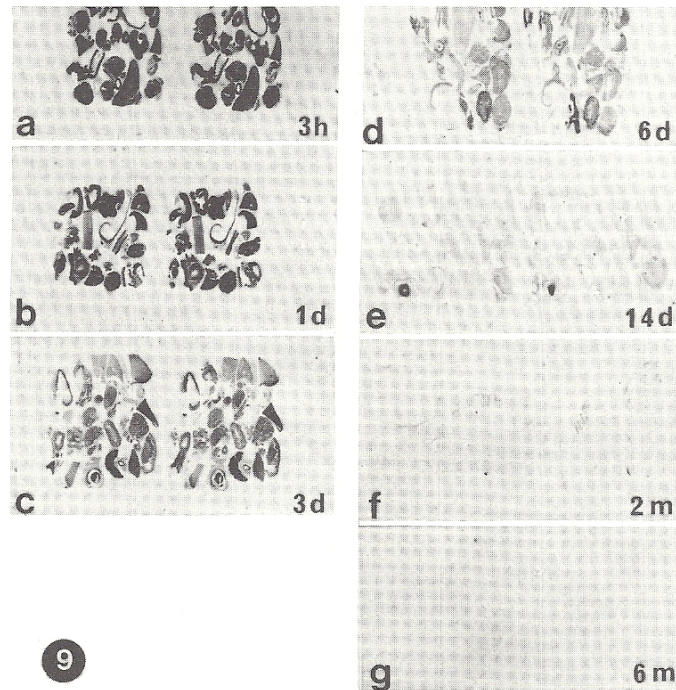


Fig. 8.9. When substances such as ^3H -methionine, ^{14}C -bicarbonate, or ^{14}C -glucose are injected into young animals, all cells become labeled, as these various labels find their way into newly synthesized protein. However, the label is eventually lost, indicating that proteins turn over.

This figure represents photographs of whole histological slides bearing unstained radioautographs from rats given $30\ \mu\text{Ci}$ of ^{14}C -glucose at the age of 3 days, and sacrificed from 3 hr to 6 months later. Exposure has been equal in all cases.

Three hours after the injection (a), an intense blackening outlines the shape of the various organs and tissues. By 1 day (b), there is a slight decrease in the intensity of the reactions, indicating some loss of labeled material, presumably as a result of secretion or turnover. At later intervals (c and following), the intensity of the reactions progressively decreases. By 14 days (e), reactions are weak, except for a black spot due to the presence of radioactivity in the lens, a unique structure in which proteins do not seem to turn over. At 2 months (f), very little radioactivity is retained in organs and tissues, with the exception of line reactions in bone and dentin. At 6 months (g), the decrease in dentinal reactions is due to wear of the tooth surface and in bone reactions is due to resorption processes.

In conclusion, proteins and other substances are rapidly synthesized in all tissues of young animals, but they turn over eventually in nearly all sites.

Radioautography

These radioautographic studies gave no indication as to the intracellular site(s) of protein synthesis. This was partly due to the poor level of resolution obtained with ^{14}C and ^{35}S labels (with their relatively high-energy β -emissions). In addition, however, the design of these early experiments was somewhat flawed, because the rapidity of the biosynthetic process was not realized at that time. Thus the earliest time interval examined was 4 hours after injection of the label, at which time, radioautography showed the presence of label throughout the cells.

By 1963, ^3H -labelled amino acids had become available, enabling better resolution. Experiments included much shorter time intervals after administration of the labelled precursor. In a light microscopic study of

pancreatic acinar cells performed by Leblond, Hershey Warshawsky and Bernard Droz, the label was at first localized at 15 minutes over the basophilic base of the cells (enriched in rough endoplasmic reticulum). It then peaked over the supranuclear Golgi region by 30 minutes, and over apical secretory granules by 4 hours.

The introduction of electron microscopic radioautography at this time permitted more precise localization of labelled proteins to intracellular compartments. In the same pancreatic acinar cells, studies in 1964 by Caro & Palade at the Rockefeller Institute, and by Van Heyningen in our McGill Anatomy Department documented the migration of labeled protein molecules from the rough endoplasmic reticulum to the Golgi apparatus and then to secretory granules. In the same year, a similar migration of labelled proteins from the rough endoplasmic reticulum to the Golgi apparatus was shown in thyroid follicular cells by Leblond, Norman Nadler and colleagues.

Studies on the Role of the Golgi Apparatus in Glycosylation

But did the Golgi apparatus simply package proteins, or were they modified? Studies by Leblond and Yves Clermont in the 1950s, had shown that the Golgi region in most cell types was dramatically stained by the periodic acid-Schiff staining technique, indicating the presence of carbohydrate. In 1969, an electron microscopic study using a similar periodic acid silver technique, was carried out by Leblond, Alain Rambourg and William Hernandez. This revealed a gradient of staining intensity from the *cis* (immature) to the *trans* (mature) side of the Golgi apparatus, suggesting that carbohydrate residues were added to proteins at this site.

To test this hypothesis, light- and electron-microscopic radioautographic studies were performed by Leblond and Marian Neutra between 1964 and 1966, in which rats were injected with ^3H -glucose or ^3H -galactose. Within 10 minutes, the label was markedly localized to the Golgi apparatus of intestinal goblet cells, indicating that this was the cellular site of addition of sugar residues in the synthesis of the carbohydrate side chains of mucous glycoproteins. This discovery had a tremendous impact on the scientific community, being the first evidence for a functional role of the Golgi apparatus in the synthetic process.

Evidence from several biochemical studies in later years has shown that the glycoprotein side chains of the mucous glycoproteins produced by intestinal goblet cells are mainly of the O-linked type, in which all sugar residues are added in the Golgi apparatus (reviewed in Roth 1984). The majority of glycoproteins in most cell types, however, have N-linked side chains, and radiographic studies in these cells provided a different picture.

Thus in 1969, Leblond, Paul Whur and Annette Herscovics studied thyroid follicular cells after incubation of rat thyroid lobes with either ^3H -mannose or ^3H -galactose. This work showed that the label of ^3H -mannose (a core sugar in N-linked side chains) appeared first in the rough endoplasmic reticulum and only later in the Golgi apparatus, whereas incorporation of the label of ^3H -galactose (a more peripheral sugar) occurred in the Golgi apparatus. Leblond had at first been hesitant to accept the idea that mannose residues were added in the endoplasmic reticulum. These results had been predicted, however, by a biochemical study published earlier in the same year by Annette Herscovics, and clearly showed that N-linked glycoprotein side chains are initiated in the rough endoplasmic reticulum and are further modified in the Golgi apparatus, a concept that is now part of our basic knowledge.

In 1971, ^3H -Fucose (another peripheral sugar) was also found to be added in the Golgi apparatus by Leblond along with Antonio Haddad, Meredith Smith, Annette Herscovics and Norman Nadler. Similar

results with ^3H -galactose and ^3H -fucose were observed by Leblond and his colleagues in several other cell types: i.e. small intestinal villous columnar cells with Gary Bennett in 1971, parathyroid gland cells with K. Nakagami and Hershey Warshawsky in 1971, ameloblasts with Alfred and Melvin Weinstock in 1971 and 1972, and kidney tubule cells with Antonio Haddad and Gary Bennett in 1977. All of this evidence indicated that in the common N-linked side chains of most glycoproteins, synthesis of the carbohydrate side chains is initiated in the rough endoplasmic reticulum and completed in the Golgi apparatus.

The importance of the work of Charles Leblond and his colleagues on biosynthesis of proteins and glycoproteins was recognized world-wide, and Leblond was nominated for the Nobel Prize. The prize in 1976 ultimately went to Palade, Albert and DeDuve but it was felt by many that Leblond should have been included in this group. During the decades of the 1960's and 1970's, the Institute for Scientific Information surveyed the literature to discover the one hundred most-quoted articles in each decade. Leblond was an author in two of these articles.

Migration of Proteins and Glycoproteins to Other Sites

In neurons, pioneering work by Leblond and Bernard Droz in 1963 showed that labelled proteins migrated continuously away from the cell body, and along axons to the nerve terminals in a 'slow axoplasmic flow'. These pulse-chase studies with radioautography were the very first to visualize axonal flow.

Radiographic studies by Leblond and Bennett in 1971 examined animals killed at later times after injection of ^3H -fucose, and provided the first documentation for the migration of glycoproteins from the Golgi apparatus to lysosomes. Similarly, studies by Leblond with Bennett and Haddad 1970 and 1974 showed migration to different regions of the cell-surface membrane. The presence of carbohydrate in the plasma membrane of all surfaces of cells had not generally been realized at that time, and it was first revealed in the light and electron microscope by the periodic acid-Schiff and periodic acid-silver techniques by Rambourg and Neutra in 1966, and by Rambourg in 1967. The nature of the plasma membrane was not yet fully understood, and the carbohydrate was thought to be present in a 'cell coat' located at the external surface of the cells. Formal proof that the label resided in glycoprotein molecules of the plasma membrane itself was lacking because, in these radioautographic studies, the labelled molecules had not been characterized biochemically. Elegant proof was subsequently provided by John Bergeron and his colleagues in 1982 which examined fibroblasts infected with vesicular stomatitis virus. In these cells, only the viral G membrane protein is produced, and radioautography similarly showed the passage of ^3H -mannose label from the rough endoplasmic reticulum through the Golgi apparatus to the plasma membrane.

Leblond as Chair

During the years 1957-74, Leblond was the Chair of our Department of Anatomy, and under his tenure the Department became one of the world's top research facilities in cell biology and microscopy.

Leblond was known and fondly remembered by generations of medical students as a superb teacher. He trained 120 graduate students, including a long list of Ph.D. students, many of whom went on to distinguished academic careers in their own right. Leblond paid special attention to fostering a collegial and social atmosphere, and all members of the Department were frequently welcomed in his home by his wife and four children for both social and scientific activities. His wife would regularly accompany Leblond to scientific meetings all over the world, where she was frequently observed making notes during the

presentations. At home, he and Gertrude maintained a European lifestyle, with formal dinner hours at which all the children attended, and French was the sole language of communication. Perhaps reflective of his original interest in film-making, Charles Leblond loved to tell a good story, and this was the basis of much of his excellence in teaching—an example set for the whole department.



During the Leblond era, the department always held a Christmas Party. These parties were originally held in the Leblond's Westmount home! Subsequently, they were transferred to our Strathcona building. Faculty and students provided the food and the department provided the liquor. Not surprisingly, these events sometimes tended to become inebriated! When the parties were translocated to the McIntyre building cafeteria and later to Thompson House, all liquor had to be purchased at the facility's bar, and drinking became more moderate. Nonetheless, the evening's activities continued to include humorous skits performed by both faculty and students, as well as excellent Christmas singing by the "professorial choir".

A romantic with a passion for the classics, Charles Leblond was fascinated by language. One continuing interest was his endeavour to ensure the use of the correct name for the technique that he had spent a lifetime developing. In a review chapter written in 1987, entitled 'Radioautography: the role played by anatomists in the development and application of the technique', he writes:

"The reasons why the term 'radioautography' is preferred to 'autoradiography' for the detection of radioactive elements by photographic emulsion are as follows. The term 'autoradiography' is a compound word including the term 'radiography'. This term is defined as a picture produced by an x-ray beam that has passed through an object. Since this object, for instance a bone examined after a fracture, is located between the source of radiation and the emulsion, it appears white in the emulsion; that is, it is seen as a negative image. In contrast, when radioactive elements are seen in sections, the object under study is itself the source of the radiation that influences the emulsion. The black image thus produced is a photographic positive. It may be referred to as an autograph, i.e. 'the reproduction of form or outline of anything by an impression from the thing itself' (*Oxford English Dictionary*, 1975). Hence, the author called it initially a 'radioactive autograph'. Later, on the advice of an editor, he condensed these two words into

‘radioautograph’. The procedure is often called ‘autoradiography’, but ‘radioautography’ is the correct term.”

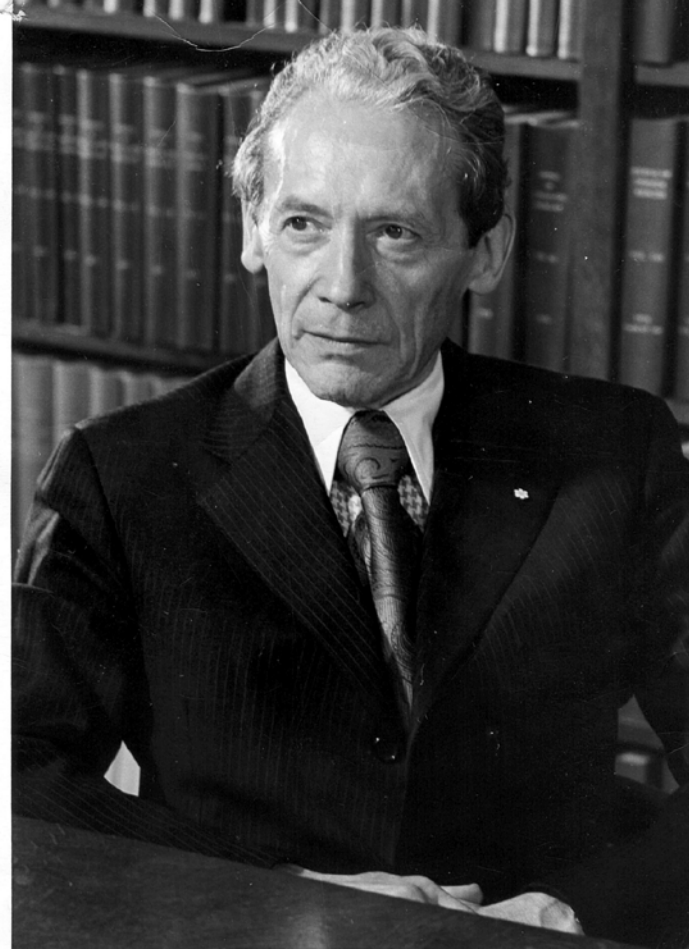
Leblond’s infectious enthusiasm for research was reflected by his glee in examining histological sections with the light microscope that he perpetually kept beside his office desk.



Above his desk he kept a clock showing the stages of spermiogenesis (the development of spermatids into mature sperm cells), which he had elegantly worked out and published with Yves Clermont in the early 1950s. A photograph of this clock appears in a review article published in 1965, “The Time Dimension in Histology”, which was Leblond’s presidential address to the diamond jubilee of the American Association of Anatomists. On the face of this clock, he depicts the young spermatid appearing at 1:00 p.m., the spermatid with its head cap at 5:00 p.m., and at midnight the full-fledged sperm “raring to go”. For this study, Leblond and Clermont had applied the periodic acid–Schiff stain to demonstrate the carbohydrate nature of the Golgi elements involved in the formation of the acrosome. With whimsical humor, Leblond adopted the purple colour of this stain, whose use he had pioneered, as his personal trademark, and adopted its use in his clothing, home furnishings, and even in the name of his country house, “Val Mauve”.

Later Years

The year 1975 marked Leblond’s sixty-fifth birthday, and the University regulations at this time made retirement obligatory at this age. Leblond had no desire to retire and arranged with the University to change to a post-retirement status but to remain as a full-time member of the Department. Having stepped down as Chair, he temporarily vacated the Department to become a Fogarty Scholar at the National Institutes of Health, thus providing a period of absence to allow his successor, Yves Clermont, to establish himself as the new Chair. After this hiatus, Leblond returned to continue his active research for three more decades at McGill.



C.P. Leblond

In more recent studies, Leblond and associates combined electron-microscopic morphology and radioautography to correct a long-standing misconception about the site of collagen formation, which had been thought to take place in the extracellular matrix. In a study of odontoblasts with Melvin Weinstock in 1974 and of fibroblasts with Fausto Marchi in 1984, ^3H -proline label was observed to behave in a fashion similar to that in pancreatic acinar cells, namely passing from the rough endoplasmic reticulum to the Golgi apparatus. At this site, the label was seen to be associated with fine parallel filaments within vesicles (representing α chains). Later the filaments fused into parallel bundles (procollagen formation), which then lost their individuality when the vesicles became secretory granules. Hence, in either odontoblasts or fibroblasts, collagen formation takes place inside the cell.

Other pioneering studies were performed on basement membranes, and used immunostaining to identify four molecules, namely heparan sulphate proteoglycan, type IV collagen, laminin and fibronectin. In a study by Leblond and colleagues in 1989, it was found that the incubation of the first three of these molecules together at 35 °C yielded an artificial basement membrane that was indistinguishable in the electron microscope from natural basement membranes. Thus a biological structure, the basement membrane, had been artificially made *in vitro* for the first time.

Leblond also maintained his long-standing interest in adult stem cells of the gastrointestinal tract. Detailed studies with colleagues in 1985 and 1993 showed the various cell populations of stomach cells were derived from adult stem cells.

Finally, with his last Ph.D. student, Elaine Davis, Leblond took on a new interest in elastic lamina formation during vascular wall development. Electron-microscopic studies published by Davis in 1993 showed an elaborate and important connection of endothelial and smooth muscle cells to the elastic laminae. Radioautography demonstrated that the turnover rate of elastin in the mouse aorta was a remarkable 27 years!

The radioautographic method developed by Leblond was instrumental in many other studies conducted in our Department. In a study by Dennis Osmond in 1980, B lymphocytes were identified by the localization of labelled anti-IgM antibodies attached to their surface immunoglobulin molecules. Finally, a study by John Bergeron and colleagues in 1985 showed that ¹²⁵I-labeled insulin receptors were localized both at the cell surface and within the endosomal apparatus of target cells.

In recent years, radioautographic procedure has been largely superceded by other techniques such as immunocytochemistry. It continues to be used today by molecular biologists to study the localization of genes and DNA sequences and to detect RNA molecules *in situ*.

Leblond's research career continued into the third millennium. His total contributions resulted in the publication of 430 scientific papers, many of them still frequently cited. His last two large review publications in 1991 and 1995 dealt with the time dimension in cell biology. After the latter date he was an author of eleven more peer reviewed articles, including a final paper in 2006, published with Eunice Lee.

Leblond continued to attend all weekly departmental seminars well into his nineties, and inevitably addressed incisive questions to all the speakers. He gave a final presentation to an internal conference in 2004 at the age of 94. The presentation was brought on a USB stick, and maintaining his trademark wit, he remarked that "Until a month ago, I thought that Powerpoint was a tool for sharpening pencils!"

On a personal level, he continued to live life to the fullest. His wife Gertrude died in 2000, after a very happy marriage of 64 years, and his dedication to her during her last years was moving. After her death, Leblond continued to have room for commitment and a need for companionship. At the age of 91 years, he married for a second time to a childhood friend, Odette, from Lille, with whom he and Gertrude had frequently communicated over the years. Odette passed away in 2004 at the age of 94 years. During his final years, Leblond suffered from a tremor that made handwriting difficult, and from bouts of trigeminal neuralgia that were intrusive. Neither, however, prevented him from maintaining an active lifestyle. He continued to live in the Westmount home that he and Gertrude had occupied since moving to Montreal some 60 years earlier. On 10 April 2007, Leblond died at the age of 97 years, surrounded by the love and constant attention of his devoted children, all of whom lived in Montreal and took regular turns in providing care in the evenings. Until the very end, he continued to work at home on his computer, with the attitude that it was an essential part of living to keep productive for as long as possible.

In recognition of his achievements, Leblond received many honorary degrees (Acadia University 1972, McGill University 1982, Université de Montréal 1985, York University 1986, Université de Sherbrooke 1988), as well as numerous awards, including Rockefeller Fellow (1935), Fellow of the Royal Society of Canada (1951), the Flavelle Medal (1961), the Medal Leo Pariseau (1965), the International Gairdner

Foundation Award (1965), Fellow of the Royal Society of London (1965), honorary member of the American Academy of Arts and Sciences (1970), National Institutes of Health Fogarty Scholar (1975), Officer of the Order of Canada (1977), the American Association of Anatomy's Henry Gray Award (1978), the Wilson medal from the American Society of Cell Biology (1982), the McLaughlin Medal (1983), the Quebec Government's Prix Marie-Victorin (1992) induction into the Canadian Medical Hall of Fame (1995), the prestigious Companion of the Order of Canada (1999), and Grand Officer of the National Order of Quebec (2001). As mentioned above, based on his historic discovery of adult stem cells with Yves Clermont, Leblond was nominated on two more occasions for a Nobel Prize in the two years prior to his death.

C. P. Leblond will be remembered as a pioneer who, contrary to all current dogma, provided dramatic evidence for the continuous dynamic turnover of cells in many tissues, as well as the first recognition of the dynamism present in the components of all cells. He was one of the very first to introduce the dimension of time into the previously static concepts of histology and cell biology. Finally, he will be remembered personally as an extraordinary individual who generously shared his journey with many trainees, collaborators and employees - all of whom held him in the highest esteem and were changed by the extraordinary opportunity to have worked with him.

During Leblond's tenure at McGill, the Department truly occupied a "place in the sun". This remained for many years after Leblond's retirement from the Chairmanship.

48. The C.P. Leblond Celebratory Symposium (2011)

In 2006, the idea was proposed by the author (as well as independently by Dr. Phil Gold) that Dr. Leblond's outstanding achievements as an educator and biomedical researcher be commemorated for posterity by changing the name of our historic M1 amphitheater in the Strathcona building to the "C.P. LEBLOND AMPHITHEATER". This was the room in which Leblond had given so many of his classic lectures over the decades! Dr. Leblond was informed of the intention to make this proposal in the months before his death and was very pleased.

Our Departmental Chair, John Bergeron, enthusiastically put forward the idea to Dean Levin, along with the support of Dr. Abe Fuks. At the time, the university rules stated that no such action could be carried out while the nominated individual was still living. After Dr. Leblond's death the idea was proposed again, and finally was approved by the University. To celebrate the occasion of the renaming, an International Symposium was held on October 14, 2011. Distinguished speakers from around the world were invited to describe their work which was related to various aspects of the original pioneering research of C.P. Leblond. A large number of guests from the department, university, scientific community, and Dr. Leblond's family were invited to attend.

The symposium was an all-day event, followed by a formal cocktail party in the amphitheater. This was then followed by a celebratory dinner for the speakers and guests at the Mount Royal Club.

The symposium was opened by Vice Principal Levin, and the welcome address was by the Provost, Anthony C. Masi. The speakers were:

Dr. Alain Beaudet, President, Canadian Institutes of Health Research;

Dr. Hans Clevers, Department of Molecular Genetics, Hubrecht Institute, Utrecht;

Dr. Martin Dym, Department of Biology, Georgetown University;

Dr. Stuart Kornfeld, Professor of Medicine, Hematology Division, Washington University in St. Louis;

Dr. Marilyn Farquhar, Department of Cellular and Molecular Medicine, University of California San Diego;

Dr. Alberto Luini, TIGEM-Telethon Institute of Genetics and Medicine, Naples, Italy;

and

Dr. Jennifer Lippincott-Schwartz, Cell Biology and Metabolism Branch, National Institutes of Health Bethesda, MD.

John Bergeron was instrumental in holding organizational meetings and in raising money for every step of the event, and it was his enthusiasm and hard work that was largely responsible for its success.

49. The Second World War (1939-1945)

Over 5,500 McGill faculty and graduates enrolled in the armed forces during the Second World War. However, in contrast to the First World War, students were encouraged to complete their university studies rather than enrolling in military service.

Certain of faculty members of our Anatomy Department were actively involved in the war theatre. Leblond left McGill to serve with the Free French forces in North Africa. Martin Banfill was a military prisoner in a Japanese war camp, and Dennis Osmond, as a teenager, lived through the London blitz.

By the end of the war, some 300 McGill men and women had lost their lives and had their names inscribed on the university's memorial ^{Frost 2:222}.

Professors who stayed at their posts carried a heavy burden of teaching ^{Hanaway 2:202}. Laboratory equipment and supplies were hard to come by ^{Frost 2:221}. Scientists in every discipline reviewed their fields of expertise to see if they might make a contribution to the war effort. Leblond carried out research studies on anoxia as experienced in high altitudes by war-time pilots. As mentioned previously, the productivity of Selye during this period was impressive, and the concept of stress was an important factor for the military.

Financial problems at the end of the war were immense. The great depression during the 1930's and all suspension of development during the war had left buildings and equipment in urgent need of repair. Academic salaries were low, with a professor earning an average of \$3,000 per year - less than a skilled mechanic ^{Pasztor: 60}.

Following the Second World War, however, there was an enormous expansion in biomedical science and technology ^{Hanaway 2:202}. In the 12 years from 1943-56, the Department of Biology acquired 20 new faculty, Bacteriology 16, Physiology 8, Anatomy 6, and Biochemistry 2 ^{Johnstone:54}.

50. Stanley Martin Banfill (McGill: 1946-1971)



Martin Banfil

Martin Banfill came to our Department as a teaching fellow in 1946. A doctor's son, he was born in 1907 in East Angus, Quebec. After his B.A. from Bishop's, he took his medical degree at McGill, graduating in 1933. Following this he became a general practitioner in the small town of Cookshire, Quebec (where his patients included the family of the author of this work). He was also attached to the Royal Rifles of the Canadian Medical corps. During the Second World War, this regiment was shipped to the British Colony of Hong Kong in November 1941, where Banfill was the officer in charge of 40 men at a medical centre. Less than three weeks later, on December 8, the Japanese attacked, over-running the British defences on the mainland in a week and then crossing to the Island of Hong Kong where the Canadians held out for two weeks. Of the 1,900 Canadian defenders, 292 died and the rest were taken prisoner. When the Japanese captured the city, Banfill was forced to witness the execution of many of his men. On that infamous "Black Christmas" day, he was informed that he would also be beheaded immediately after interrogation, but his life was spared by a Christian-educated Japanese officer. He became a prisoner of war for four years in a Japanese camp where another 267 Canadians would die of disease, starvation, physical abuse or execution. Here Banfill was one of the few detainees to live through a diphtheria epidemic. He managed to survive the horrific conditions of the camp by eating rats, etc. Liberated in 1945,

Banfill was made an Officer of the Order of the British Empire POW survived Black, Christmas, National Post, May 30, 2007
www.canada.com/story_print.html; Blair Crawford, Ottawa Citizen, Nov. 10, 2015: "Author (Terry Meagher) tells story of the fall of Hong Kong".

During his time in the prison camp, Banfill had found an Anatomy textbook and maintained his sanity by devoting himself to memorizing the book from cover to cover. After the war, with this accumulated knowledge, he decided to become a professional Anatomist!

He returned to our Department at McGill as a Lecturer in 1947, but then went back to Hong Kong to serve as a witness in a war crimes trial. He testified that the Japanese had executed 21 British and Canadian soldiers for which the Major-General in charge was sentenced to 20 years in prison. After the trial, Banfill accepted an appointment as Dean of Medicine at the University of Hong Kong until 1952. Upon his return to McGill, he was promoted to Associate Professor, and then to Full Professor in 1962. He was also appointed to the important role of Associate Dean (Admissions) of Medicine in 1964.

Martin Banfill was highly respected as a teacher of Gross Anatomy, and he co-authored, with C.P. Martin, a famous "red book" entitled: "Workbook of Anatomy". Every word of this book tended to be memorized, cover to cover, by all of the medical students. He had a whimsical sense of humor, and his lectures were often enlivened by tales of battle-field surgery.

During the turbulent days of the late 1960s and early 1970s, Banfill, like many other professors, was subjected to the disrespectful behavior of militant students. After one such episode he decided that this was enough and submitted his resignation in 1971 after a long career of service.

After his retirement, he lived in Montreal's West Island for many years, returning once to our Department to be honored with a plaque-naming ceremony. He died in his 100th year in 2007.

51. Yves Wilfrid Clermont (McGill: 1953-1998)

Yves Clermont first joined our Department as a graduate student in 1950. Working with C.P. Leblond, he accepted the difficult challenge of deciphering the meaning of the associations of germ cells involved in spermatogenesis. He had received a classical French education, obtaining his B.Sc. from the Université de Montréal.



Yves Clermont 1960

Clermont obtained his PhD after only three years in 1953, and was appointed a Lecturer in our department during the same year. This was followed by a post-doctoral fellowship in Paris at the College de France. He came back to the Department as an Assistant Professor in 1956 and was promoted to full Professor in 1963.

In his research career, Yves Clermont acquired a world-wide reputation as a specialist in male reproduction. As mentioned previously (see C.P. Leblond) Yves Clermont was the other principal player in the monumental discovery of adult stem cells in the seminiferous epithelium. Understanding the association of germ cells in this epithelium was a complex problem, and required the identification of the maturation stage of all of the germ cells involved (i.e. spermatogonia, spermatocytes, spermatids and spermatozoa). The key to solving this complex problem lay in using a histochemical technique, the periodic acid-Schiff (PAS) technique which selectively stained the Golgi complex and acrosomic system of the cells. By observing the morphological changes occurring in these organelles, it was possible to identify the different generations of germ cells. This led to a seminal publication of Leblond and Clermont which precisely defined the 14 different stages of the adult rat seminiferous epithelium.

Analysis of these stages then brought these authors to their second seminal finding, i.e. the discovery of stem cells in the seminiferous epithelium. Their publication thus stated that: "At each cycle, there is the reappearance of a new dormant cell which acts as the stem cell of spermatocytes ... This is described as the "Stem Cell Renewal Theory". This article is the first in which nests of cells dividing in an adult organ were designated as 'stem cells'. The significance of this discovery was not fully appreciated at the time, but over the years its monumental importance has come to be understood. In addition to morphological analysis, Clermont also carried out dynamic studies in which he used radioautography to determine the time line of spermatogenesis.

Clermont, spent many years clarifying the structure of cells in the human testis and epididymus. A superb microscopist, he described the full sequence of events that give rise to mature sperm cells, as well as describing the acrosomic system and cytoskeletal elements such as the perforatorium. His first love was light microscopy and he did not particularly working on the Electron Microscope. Thus most of his ultrastructural studies were carried out with his graduate students or with collaborators such as Louis Hermo and Alain Rambourg. Over this same period, Clermont played a key role in revealing the structure

of the Golgi apparatus and secretory pathway, not only in male reproductive cells (e.g. spermatogonia, Sertoli and epididymal cells) but also in cells of many other systems. His resulting articles on Golgi morphology were classics. A special feature was the very first three-dimensional analysis of Golgi structure, using thick sections and stereo techniques at the resolution of the million-volt electron microscope. It was these studies that emphasized the structure of the Golgi apparatus not as simple stacks of cisternae but as complex ribbons extending throughout the cytoplasm. This correlated the ultrastructural appearance of the Golgi apparatus with the original network described by Camillo Golgi at the light microscope level.

Clermont's early electron microscope investigations of both sperm formation and Golgi structure were carried out in the early 1960's, and were amongst the very first EM studies performed on these structures. They utilized one of the Department's first electron microscopes and were truly pioneering efforts. Clermont's morphological drawings were magnificent works of art, and his publications were renowned for their illustrations. These were done in collaboration with Margo Oeltzschner, who joined our Department as a technician in 1957, and subsequently became our departmental artist. Several of his 150 publications were designated as "Citation Classics" by the Institute for Scientific Information. He served on several granting agencies, including the MRC (now CIHR), NIH, Ford Foundation, FRSC and FCAR. In graduate teaching, he supervised 15 graduate students and 14 postdocs, many of whom went on to occupy high-ranking positions in universities around the world.

As an educator, Clermont was an outstanding teacher of Histology. His blackboard lectures were legendary and enchanted a whole generation of medical and dental students. He created a unique sense of excitement and enthusiasm for the subject of histology. His lectures were both thought-provoking and entertaining, and he is remembered by countless classes of students (perhaps 5000 in all) as a thrilling lecturer. In an age when there were fewer teaching awards than at present, Clermont won the Osler award. This award, the most prestigious in Medicine, was presented by the final year medical class to the teacher thought to have had the greatest influence on their medical career. This was perhaps the first time the award was presented to teacher of first year medicine whom most students would not have seen since four years previously!

Yves Clermont as Chair (1975-1985)

In 1975, Dr. Leblond had reached the age of sixty-five and was obliged by University regulations to retire as Chair of the Department. This left some very large shoes to fill! In the tradition of the McGill medical school, the position of departmental chair was not viewed simply as an administrative appointment to be rotated periodically among departmental members. Rather the chairperson needed to be a senior person at the Full Professor level who had achieved distinguished international status in terms of their research in addition to being an excellent teacher.

Our Department was fortunate in having not one but two such candidates, i.e. Yves Clermont and Dennis Osmond. Both men were at the pinnacle of their careers and either could easily have assumed the chair.

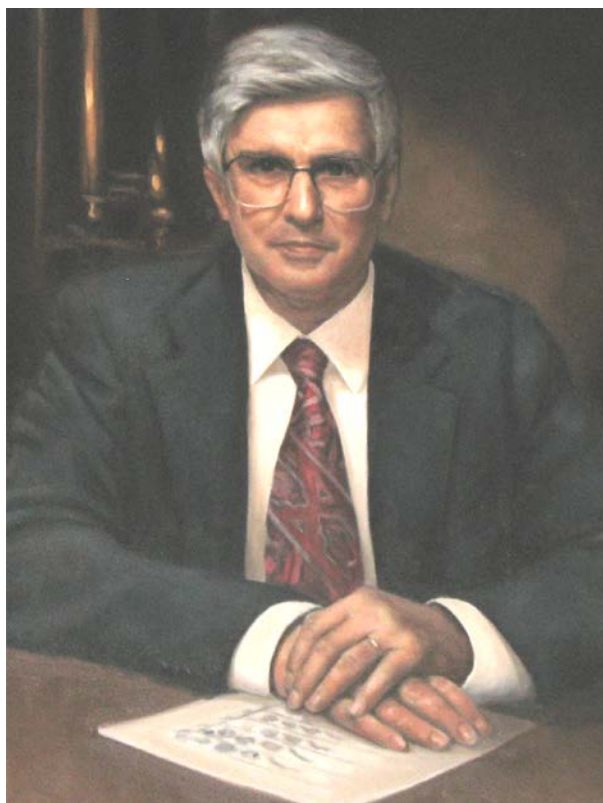
In the end, it was Yves Clermont who was chosen, based mainly on his seniority in the department. It was envisioned by everyone that, ten years later, at the end of Clermont's tenure as chair, Dennis Osmond would be chosen as the new chair.

Thus Yves Clermont took over as chair in 1975. During the period of transition, Dr. Leblond discretely vacated the department, and took a one year sabbatical leave at the N.I.H. in Washington, D.C. Clermont made an excellent chair and in 1980, his appointment was renewed for a second five year term. During this period, the Department thrived under his leadership.

The decade of the 1980's was a time of recession in Canada ^{Hanaway 2:204}. Yet research funding of our departmental members remained high. Enrollment of students in the undergraduate B.Sc. program increased from 322 students in 1977 to 513 in 1981, and new courses were being continually added. Limited funding, however, caused problems with infrastructure and aging equipment, as well as with attracting high quality graduate students.

Over the course of his career, Clermont was awarded many research honors. He was awarded the Ortho Prize of the Canadian Society for the Study of Fertility (1958), the J.C.B. Grant Award from the Canadian Association of Anatomists (1986), the Prix Scientifique of the Province of Quebec (1963), and the Serano Award of the American Society of Andrology (1992). He became a Fellow of the Royal Society of Canada in 1972,

Clermont retired from our Department in 1998, and was awarded an Emeritus Professorship. He continued for several years to work with Michael Lalli on a superb Atlas of Histology which has now been made available to our medical/dental students on line. In 2013, our Departmental histology laboratory was named the "Yves Clermont Histology Laboratory" in his honor.



Portrait of Yves Clermont

52. Norman J. Nadler (McGill: 1953-1997)



Norman Nadler -

1993

Norman Nadler became a Lecturer in our Department 1953. He had obtained his M.D. degree from McGill and became a graduate student of C.P. Leblond from 1952-1955. He became Assistant Professor in 1961, and was Associate Professor from 1966 until his retirement in 1997. Along with his academic career, he maintained a medical practice, becoming a noted specialist in Endocrinology.

Norman Nadler was our Department's resident mathematician! Over the years, he performed several studies pertaining to the mathematical interpretation of results obtained from radioautographic investigations, and he gained an international reputation for this work. His main scientific interest was in the production of thyroglobulin by cells of the thyroid gland. He was instrumental in establishing the computer facilities of our Department.

A gifted lecturer, Nadler was appreciated by generations of students. In our graduate program he was the main lecturer in our Experimental Morphology course his lectures on Statistics were memorable. As a witty speaker, he could always be counted on to enliven any Departmental gathering.

53. Beatrix Kopriwa (McGill: 1958-1978) and the Radioautography Facility



Beatrix Kopriwa

Beatrix Kopriwa came to our Department a research technician in 1958. She had obtained a Ph.D. degree in chemistry in Austria. She was promoted to Research Associate in 1963, Lecturer in 1964, Assistant Professor in 1966, and was Associate Professor from 1969 until her retirement in 1978 (or later).

During her whole period at McGill, Beatrix Kopriwa devoted her energy to improving the technique of radioautography, a tool used in a large part of our Department's research investigations. In mastering this difficult technique, our Anatomy Department was one of the world's most successful research centers, resulting in a great many publications. Beatrix Kopriwa was instrumental in this success, and she became an international authority on the subject. One of the biggest challenges was in maintaining the quality of emulsion which we received from companies such as Kodak. The radioautography facility, run by Kopriwa and her technician, Fernando Evaristo, was, along with the electron microscope lab, the life-blood of the department. In 1978, Beatrix Kopriwa retired and was replaced by Mohammed El Alfy.

54. Hershey Warshawsky (McGill: 1959-2013)



Hershey Warshawsky - 1960

Hershey Warshawsky joined our department as a graduate student in 1959, after having obtained a B.Sc. in Biology at Sir George Williams University. Working under the supervision of Dr. C.P. Leblond, he obtained his M.Sc. in 1961 and then his Ph.D. in 1966. He became a Lecturer in our Department in 1963 while completing his Ph.D. degree. This was followed by a Fellowship year (1966-67) in the Orthopedic Research Laboratories at Harvard University.

Upon his return to McGill, Warshawsky became an Assistant Professor in 1967, was promoted to Associate Professor in 1970, and then to Full Professor in 1977. He was an Associate member of the Faculty of Dentistry. He was a visiting professor in the Departamento de Morfologia, Universidade de Sao Paulo, Brazil in 1971, the Department of Anatomy, Royal College of Dentistry, Aarhus, Denmark in 1980, the Faculdade de Odontologia de Piracicaba, Universidade Estadual de Campinas, Brazil in 1987, and the department of Oral Biology and Surgery, University of Queensland, Australia in 1988.

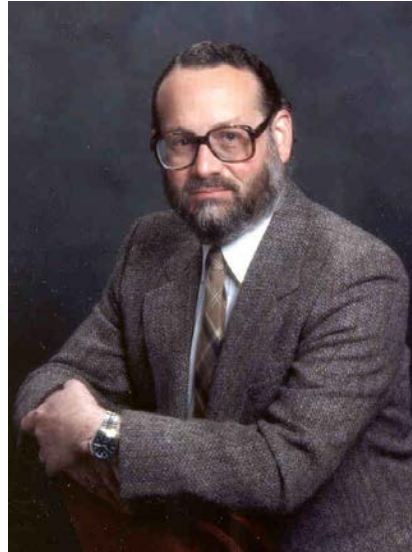
As administrator, Hershey Warshawsky played a multitude of important roles at all levels of the University as well as in External bodies. He was: Director of our Electron Microscopy Laboratory, member of the University Senate, Chair of the Senate Committee on Student Grievances, Chair of the Senate Appeals Committee for Student Discipline and Grievances, and was the first elected member of the Royal Institution for the Advancement of Learning, and Governor of McGill College and University. Outside of the University administration, he was President of the McGill Association of University Teachers (MAUT), Chief Advisor of MAUT, and a Council member of the Canadian Association of Anatomists.

In 1995, upon the Retirement of Dennis Osmond from the position of Chair of the Department of Anatomy and Cell Biology, Hershey Warshawsky served as Acting Chair during the period from 1995-1996.

In his research career Warshawsky initially investigated the trafficking of newly synthesized protein molecules in pancreatic exocrine cells, He then began to focus on calcified tissues, and went on to become

a world authority on the structure of enamel and the renewal processes of tooth ameloblasts and odontoblasts *and the* secretion of their matrix. To facilitate these studies, he developed a classic technique for the decalcification of hard tissues which is used world-wide today. In addition, he carried out investigations on the formation of bone and cartilage and the localization of receptors for calcitonin, insulin, parathyroid hormone, epidermal growth factor, and TGF beta in a variety of tissues.

Warshawsky authored over 91 peer-reviewed articles, 65 abstracts of oral presentations and 4 book chapters, served on grants panels of the Medical Research Council, and was a Guest Editor for the *Anatomical Record*.



Hershey Warshawsky - 1994

Throughout his career, Hershey Warshawsky was a superb and beloved teacher, both to our undergraduate B.Sc. students and to our medical and dental students. His unique contribution has been recognized in his being the only McGill faculty member to have been awarded both the Yaffe teaching award of the Faculty of Sciences and the Osler award of the Faculty of Medicine.

In the Medical Faculty, he was the primary teacher along, with Yves Clermont, of Histology to first year medical and dental students. In the Faculty of Science, he was instrumental in establishing our Anatomy B.Sc. program. His course in Dynamic Histology became one of the most popular and prestigious courses in McGill's undergraduate curriculum. The term "Dynamic" was included in the name to emphasize the concept that both cells and molecules in histologic tissues were not static as visualized in a fixed section but were in a state of constant dynamic activity. He also developed the specialized upper level course in Calcified Tissues and taught a graduate course in Histology in our M.Sc. and Ph.D. programs.

In collaboration with other departments, Hershey Warshawsky was one of the pioneer teachers of the Core Biology curriculum program, lecturing in Cell Biology to classes of over 1000 students in the York

Theatre. When the New Medical Curriculum was introduced in 1995, Warshawsky became Coordinator of the important Unit 1, which initiated the program.

In graduate teaching, Warshawsky supervised the research projects of 5 M.Sc. and 11 Ph.D. students. The latter included students who have gone on to prestigious university careers of their own, such as Antonio Nanci of the Université de Montréal, and both Mark McKee and Charles Smith of our own department.

In recognition of his scientific achievements, he received the following awards: a Doctorem Odontologiae, honoris causa in 1991 from the Royal Dental College in Aarhus, Denmark, a Research in Oral Biology Award in 1992 from the International Association for Dental Research, and an Honorary Fellowship in the Royal College of Dentists of Canada in 1996.

Hershey Warshawsky retired from a full-time appointment in 2000 and was awarded the position of Professor Emeritus. During the subsequent thirteen years, he maintained an active part-time teaching contribution in our Department, fulfilling a crucial role as chief instructor of all of the first-year Medical and Dental Histology laboratory program as well as delivering several lectures. A scholarship for Anatomy undergraduate students was created in his honor, and his achievements were celebrated in a Faculty of Medicine ceremony in 2014.

55. Dennis G. Osmond (McGill: 1965-)



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Dennis Osmond joined our McGill Anatomy Department as an Associate Professor in 1965. He had received his scientific and medical training from the University of Bristol, England, where he graduated in Physiology (First Class Honors, 1951) and Medicine (M.B., Ch.B., 1954). Following hospital internships in internal medicine and general surgery, he served for two years as a medical officer in the Royal Army Medical Corps. From 1957 to 1964, Osmond was a Demonstrator and then Lecturer in Bristol University's

Department of Anatomy. During this period he spent one year (1960-61) in the U.S.A. at the University of Washington, Seattle, as a Fulbright Scholar.

At McGill, Osmond was promoted to Full Professor in 1967, and to the Robert Reford Professorial Chair in 1974. Osmond's research led to Visiting Scientist awards held at the Walter and Eliza Hall Institute for Medical Research, Melbourne, Australia (1972-73), the University of Birmingham, England (1979), the Basel Institute for Immunology, Switzerland (1980, 1996), and as a Gaylord Scholar at the Oklahoma Medical Research Foundation (1995).

Administratively, Osmond served on a large variety of committees at the Medical Faculty and University levels. He was Chair of our Department from 1985 to 1995 (see later).

Osmond's pioneering work as a researcher in the field of immunology established the central role of the bone marrow as a primary site of B lymphocyte (B cell) production and quality control. This was an important contribution to our understanding of the normal immune defenses of the body since little had previously been known about the life history and function of lymphocytes as a whole. Using radioautography with newly available radioactive tracer molecules, Osmond was able to identify B cells in bone marrow of laboratory animals and to show that these cells were being continuously produced in massive numbers within the bone marrow itself, rather than entering this site from the blood stream, as previously had been thought. B cells were identified by their newly recognized property of displaying antibody molecules (immunoglobulins) at their cell surface. Anti-IgM antibodies labeled with radioiodine became bound to the surface of B cells. Such IgM-binding B cells could be identified in radioautographs since they exhibited a widely scattered radioautographic reaction due to the high energy of the beta and gamma rays from the radioiodine.

An ingenious double-labeling experiment allowed Osmond to follow the development of B cells in the bone marrow. The age of the cells was evaluated by giving repeated injections of ³H-thymidine. Cells labeled by this procedure over a period of time were identified by a radioautographic reaction that was strictly localized over their nuclei due to the low energy of the beta rays from tritium. This work led to the conclusion that IgM molecules are not displayed by newly formed B cells, but they appear and increase progressively in density as these cells mature. Osmond showed that the mature B cells were then disseminated through the blood stream to other lymphoid organs throughout postnatal life. B cells play an important role in the body's immune defenses by producing and releasing antibodies to neutralize harmful microorganisms and other foreign agents (antigens). Thus, the production of B lineage cells in bone marrow was shown to provide a continuous supply of new B cells to maintain the ability of the immune system to deal with novel antigens throughout life.

Incorporating other cellular markers, Osmond's work developed a widely accepted dynamic model of B cell development in bone marrow which defined and quantitated the rates of production of successive cell generations, representing stages in the differentiation, proliferation, and selection of precursor B cells. He also studied factors controlling the rate of B cell production and the selective removal of aberrant B cells by apoptotic cell death and macrophage deletion.

Using electron microscope radioautography, a technique pioneered in our department, Osmond was the first to demonstrate the localization of B lineage cells within intact bone marrow, leading to a model of the micro-environmental organization and the cellular and molecular interactions of B cells *in situ*.

In genetically modified mice, Osmond investigated genetic influences promoting either the apoptotic cell death or survival of B lineage cells in bone marrow. As models of human disease, the results help to understand mechanisms that may lead to B cell neoplasia (leukemia, lymphoma), autoimmunity and immunodeficiency.

Osmond published over 140 peer-reviewed articles, was an editor of two journals (Cell and Tissue Res., Amer. J. Anat.) and co-editor of two books. He served on various grants panels. He was an invited speaker at innumerable meetings all over the world and he organized and chaired several symposia and workshops.

He supervised the research projects of many graduate students, including F. Brahim, S.C. Miller, W.A. Kammerer, M.D. Rahal, S. Carson, M.T.E. Fahlman, G.M Fulop, N. Shenouda, C. Pietrangeli, G. Reid, A. Xenocostas, K. Jacobsen, S.J. Batten, S.R. Rico-Vargas, H. Valenzona, R. Janani, L. Liu, L. Fauteux and L. Lu. and postdoctoral fellows, Y. Yoshida, T. Nakatsui, W.C. Yang, F.P.H. Chan, V. Santer, D. Opstelten, Y.H. Park, L. Lu and Q. Yu.

In addition to his scientific career, Dennis Osmond has played major roles in Medical Education. He has taught gross anatomy, clinical anatomy, embryology and even neuroanatomy to generations of first year medical and dental students. He also administered the departmental Gross Anatomy facility. He was instrumental in bringing closed-circuit television to our Department, and also in creating our new anatomical museum in the mid-1970s. To generate many new reference specimens, he hired Dr. Calalb a surgeon. He also created a computer self-study facility for students in the north bay of the museum. This system, using laser-read optical disks provided active interaction with students and self-evaluation.

Until 1986, Osmond taught an excellent tutorial course in applied anatomy to surgical residents who were also acting as demonstrators in the first year Anatomy course.

In his own scientific field, Osmond, along with Sandra Miller, initiated and developed an excellent course on Cellular Immunology and Hematology. For graduate students he taught in courses in Experimental Morphology and the interdisciplinary course in Advanced Immunology.

In 1977, Dennis Osmond created the "Anatomy for Surgeons" course, one of the most popular and prestigious elective courses for fourth year students in the Faculty of Medicine. This course, featuring extensive dissection, daily student seminars, and clinical-anatomical conferences, is seen as a vital component of the "longitudinal training" in anatomy whereby students (especially those in the surgical and radiological specialties) receive additional instruction in anatomy in their later undergraduate or postgraduate years. Graduates of this course have acknowledged that it contributed greatly to their confidence and competence both in diagnosis and in the operating room.

In 1985, Osmond inaugurated the first Annual Commemorative Service for body donors and their families. He was convinced that the experience of working with bodies donated by local individuals not only provided essential anatomical instruction, but also played a powerful humanistic role in helping students prepare themselves to become caring and effective physicians. The commemorative service, held in June at the end of each academic year, allows students in the health professions, who have benefited from the donors' gift to medical education, to pay tribute and express their gratitude, as well as to interact with donors' families and other members of the broader community.

Prior to this time, the remains of the donated bodies used in the anatomy laboratory had been buried in an unmarked grave in a Montreal east end cemetery. Osmond felt that changes were necessary and overdue. He made arrangements with the Mount Royal Cemetery who donated a commemorative site for the interment of remains, where he was also instrumental in establishing a dignified monument. This compassion and respect is symbolic of the human element that Osmond has striven to bring to medical education.

Dennis Osmond as Chair

Dennis Osmond served as the chair of the Department of Anatomy from 1985 to 1995. This was a responsibility which he cherished and was the culmination of his administrative career. He served with dedication, not only as a leader but as a role model for all members of the department. He had great respect for the traditions of the Department and worked to maintain a social atmosphere.

He instituted new committees for graduate and undergraduate student affairs. He made arrangements for the funding of various facilities (i.e. the EM laboratory, radioautography, animal care, graphics, and photography) from the operating grants of the users. Whereas much of the previous research had been carried out in the department's centralized facilities, new research directions required more use of specialized personal laboratories equipped to carry out a variety of cellular, biochemical, immunological and molecular techniques.

Under Osmond's leadership, the name of our Department changed to Anatomy and Cell Biology in 1993, reflecting the fact that virtually all of the departmental research and all but two of our B.Sc. teaching courses were in aspects of Cell Biology. It was felt that the new name would give students a more realistic impression of the departmental mission and activities.

Administratively, most of Osmond's tenure as chair in the 1980's was carried out during lean years in which there were successive challenging cuts to the operating budget. This was a time of recession in Canada. There was not enough money for new labs, infrastructure repairs for our old building, upgrading ventilation of major teaching labs and support of new graduate students. The gross anatomy technical staff was cut from two positions to one, at a time when teaching classes were actually increasing. To save money, the university initiated a summer four day work week for research technicians in lieu of a salary

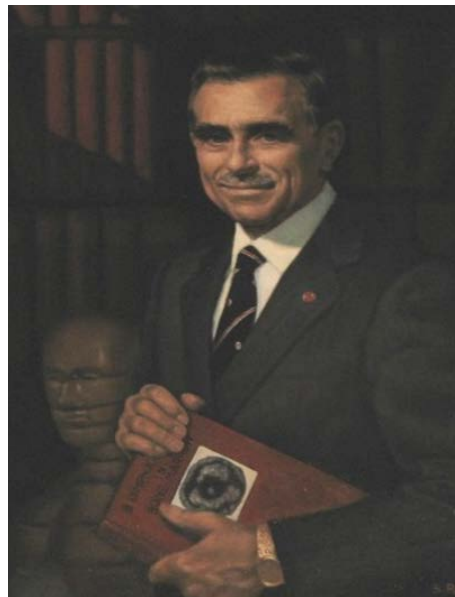
increase. This made life particularly difficult for faculty investigators, competing for funds on a national level.

Dennis Osmond retired from full-time service in our department in 2000, and was awarded an Emeritus Professorship. Since that time, he has continued to come to McGill in the spring of each year to run our prestigious Anatomy for Surgeons course, a task that requires many additional hours of organization throughout the year – this, at over the age of 85! In the fall of 2015, Osmond and his wife, Anne, travelled to Hong Kong where he was invited to give a retrospective seminar on his immunological research career to the Medical Faculty of the University of Hong Kong.

Osmond's scholarship has been recognized by a D.Sc. degree from the University of Bristol (1975), Fellowship in the Royal Society of Canada (1984), the John S. Latta Centennial Lecturer at the University of Nebraska (1985), the J.C.B. Grant Award of the Canadian Association of Anatomists (1989), and the Bernhard Cnader Award of the Canadian Society for Immunology (1995). He has served as President of the Canadian Association of Anatomists, Executive Committee member of the American Association of Anatomists, overseas member of the Council of the Anatomical Association of Great Britain and Ireland, and member of the Board of Directors of the International Society of Experimental Hematology.

For his excellent teaching contributions, Osmond was named to the Faculty of Medicine's Honor List for Educational Excellence in 2000. Subsequently, he was awarded the prestigious Osler Award for Outstanding Teaching in 2007.

Finally, In recognition of his contributions to health care in research and medical education, Dennis Osmond was appointed as a Member of the Order of Canada in 2006



Portrait of Dennis Osmond as Department Chair

56. S. Carl Harvey (McGill: 1966-1973)



Carl Harvey

Carl Harvey joined our department as a graduate student in 1960. He worked under the supervision of Yves Clermont and completed his Ph.D. in 1966. He became a Lecturer in the department in 1966 and was promoted to Assistant Professor in 1971. As supervisor of the Gross Anatomy Laboratory, Carl became a legend with the McGill medical and dental students, with whom he developed an extraordinary relationship. At all hours of the day, students could be seen filling his office adjacent to the laboratory.

Also, under the supervision of Dennis Osmond, Carl prepared many of the prosections which have been preserved as specimens in our museum. Osmond and Harvey were true pioneers at McGill in the use of closed-circuit television at McGill. Carl produced extensive televised live lab talks as well as video review tapes. He produced these tapes with no external technical assistance, using first generation T.V. equipment. He used no written script but simply spoke spontaneously, describing the specimen as the camera recorded the video and sound. These recorded reviews of all parts of the body, i.e. trunk, limbs, head and neck, resulted in the famous "Harvey Tapes". Although lacking some of the sophistication of professionally-produced tapes, they were outstanding in quality and a priceless teaching resource.

Carl Harvey decided that his love was gross anatomy teaching rather than research, and he applied to the chair, C.P. Leblond, for a permanent position as Anatomy Instructor and Curator of the Anatomy Museum. With McGill's emphasis on research in its tenure policy, Leblond could not offer this possibility. As a result, Carl moved to Baylor University in 1973 where he was offered such a position. He went on to a distinguished career at this institution where he achieved equal fame with the students. After becoming established at Baylor, Carl produced a whole new set of review tapes in color. He generously provided these, with no copyright restrictions to our department, and as a result the Harvey tapes with his distinctive voice could be heard for many years thereafter in the halls of the Strathcona building.

57. Peyush Lala (McGill: 1969-1984)



Peyush K. Lala

Peyush Lala was born and educated in India where he received an M.D. and Ph.D. degree from the University of Calcutta. He came to Canada to the Chalk River Nuclear Laboratories in 1967 and one year later was invited by Charles Leblond to join our Department of Anatomy at McGill as an Assistant Professor. He was promoted to Associate professor in 1975 and Full professor in 1979.

Leblond, who was an academic role model for Lala, had assigned him to teach human embryology to the medical students. This was something that Lala, with no previous experience, reluctantly accepted to do. In fact it turned out to be a career changing event. Lala became intrigued by the fact that the fetus and placenta, while foreign to the mother, were not rejected by the mother's immune system. Unsatisfied by current theories of explanation, he turned his research interests to placental cell biology and the rest is history Convocation Address by Peyush Lala at University of Western Ontario, June 13, 2013

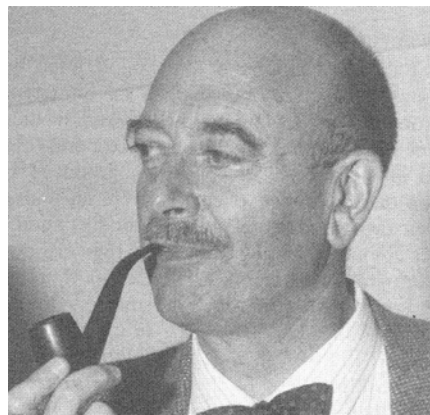
Lala became a beloved and accomplished teacher of embryology at McGill. On one occasion, the entire medical class took up the chant of "coloboma" in recognition of one of his teaching anecdotes. In 1984, he moved to University of Western Ontario in 1984 to become Chair of the Anatomy Department. For the following 30 years he pursued an illustrious career at Western until his retirement in 2013.

Lala's research career focused on the cellular and molecular mechanisms at the fetal-maternal interface. Certain placental cells, the extravillous trophoblast cells were known to invade the uterus and its arteries to derive adequate nutrients for the fetus. Lala's research identified many molecules which regulate the growth, migration and invasiveness of these cells. These include prostaglandin E(PGE)₂, an invasion-promoting molecule, and decorin, an invasion-inhibitory molecule, both produced by the decidual cells of the pregnant uterus.

Lala's other research interest was on the mechanisms of cancer growth and spread in human breast cancer, and this has led to new protocols for successfully treating certain human cancers. It has been shown that aberrant expression of Cyclooxygenase (COX)-2, an enzyme responsible for high PGE2 production by cancer cells, promotes breast cancer progression and metastasis by multiple cellular events. These include inactivation of cancer-fighting immune cells, stimulation of cancer cell migration and invasiveness, and stimulation of tumor-associated angiogenesis and lymphangiogenesis.

58. Brenard Droz, Alain Rambourg, and he French Connection

For many years our department maintained collaborations with a well-known laboratory in France, the Centre d'Etudes Nucléaires, located in the town of Saclay outside of Paris. In the 1960's, Bernard Droz came to McGill from Saclay in order to do his classic work with Leblond on axonal flow. Subsequently Gary Bennett went to Droz's laboratory in 1971, for a post-doctoral year to work with Droz on axonal flow.



Bernard Droz

Alain Rambourg came from Saclay to our department to work with Yves Clermont on the structure of the Golgi apparatus, using a variety of cell types as models. As part of this work, Louis Hermo travelled to Saclay for a post-doctoral year to work with Rambourg. These outstanding studies were carried out over a period of many years and contributed greatly to our understanding of this organelle. Alain Rambourg came to Montreal so often that he seemed like a member of our Departmental family!



Alain Rambourg

59. Antonio Haddad and the Brazilian Connection



Antonio Haddad

Antonio Haddad arrived in our department in 1968 from the Department of Morphology at the University of Sao Paulo in Brazil. He came as a visiting scientist to do work with C.P. Leblond on the synthesis of glycoproteins in the Golgi apparatus, using radioautography. This study used the thyroid gland as a model organ, and was carried out after injection of ^3H -fucose into rats. Collaborators in this project were Norman Nadler and Annette Herscovics. Subsequent excellent work carried out by Antonio Haddad as a visiting scientist in our Department resulted in several important publications, one of which (with Gary Bennett and C.P. Leblond in 1974), was designated a "Citation Classic" by the Institute for Scientific Information in 1989.

Upon his return to Brazil, Antonio Haddad arranged for the visits of several members of our Department including Hershey Warshawsky, Beatrix Kopriwa, Tony Graham, and Gary Bennett. These visits, along with return visits to McGill by Haddad resulted in several more collaborative papers with Gary Bennett.

Prior to the visit of Antonio Haddad, five other Brazilians had come to work in our Department, namely José Carneiro, Paulo Pinheiro, Joao Pedro Marques-Perera, José Merzel, and Renato Goncalves. During the following years, a number of other Brazilians also came to our Department, including Cassio Odney Garcia Munhoz, Ithamar Vugman, Fausto Marchi, and Valder Rodrigues de Melo. Nearly all of the visits of these scientists led to significant publications. Upon return to Brazil, however, only certain individuals, especially Antonio Haddad, went on to prestigious research careers. Nonetheless, the overall experience was undoubtedly worthwhile in terms of international relations, forging of international friendships, and teaching the English language and modern cell biological skills to individuals trying to make a scientific career in what was, at that time, a developing country.

60. Annette Herscovics (McGill: 1969-1974)



Annette Herscovics

Annette Herscovics became Lecturer in our department in 1969. She was promoted to Assistant Professor in 1970. Annette came to work with C.P. Leblond on the role of the Golgi apparatus using the thyroid follicular cell as a model. As described previously, Leblond and Marian Neutra had carried out radioautographic experiments with ³H-glucose and ³H-galactose, and they had come to the conclusion that the cellular site of addition of sugar residues to glycoprotein side chains in intestinal goblet cells was the Golgi apparatus. Subsequent work with Herscovics examined thyroid follicular cells, after incubation with ³H-mannose or ³H-galactose.

Preliminary results of this latter study, on the other hand, suggested that mannose (a core sugar in N-linked side chains) was added to these side chains in the endoplasmic reticulum, while galactose (a more

peripheral sugar in these N-linked side chains) was added in the Golgi apparatus. Leblond was shocked by, and at first unaccepting of these findings in spite of the fact that they had been predicted by a biochemical study published by Herscovics earlier in the same year. Only after repetition of the radioautographic studies with the same results did Leblond become convinced.

In 1974, Herscovics moved from McGill to the Mass General Hospital in Boston, where she continued her work on carbohydrate side chain synthesis. She returned some years later to the Cancer Centre at McGill and achieved an international reputation as an authority on glycoprotein synthesis.

61. Gary Bennett (McGill: 1970-2014)



Gary Bennett

Gary Bennett joined our Department as a graduate student in 1965. He had obtained a B.A. in History and a B.Sc. in Biology from Sir George Williams University. In our department, he obtained his M.Sc. and Ph.D. degrees in Anatomy in 1967 and 1971 under the supervision of C.P. Leblond. From 1970-1971, Bennett was a Faculty Lecturer in our Department. In 1971, he went to the Centre d'Études Nucléaires in Saclay, France, as a Postdoctoral Fellow working in collaboration with Bernard Droz on axonal flow. He returned to our Department as an Assistant Professor in 1972, became an Associate Professor with tenure in 1984 and was promoted to a full professor in 1997. In 1982 and 1983, Bennett was a Visiting Professor in the Departamento de Morphologia, Faculdade de Medicina de Ribeirao Preto, University de Sao Paulo, Brasil, working with Antonio Haddad. In 1986, he spent a sabbatical year as a visiting professor in the Department of Cell Biology at the University of Basel in Switzerland, working with Jurgen Roth.

Administratively, Bennett chaired or served on a variety of Departmental and Faculty committees including the Medical Library and the Senate University Library Advisory committees. For several years (2002-2009) he administered the Departmental Gross Anatomy facility and the Body Donor program. In this latter capacity, he interacted with the Quebec Government, Funeral homes, various hospitals, and

the general public. He was also the Chief Academic Advisor of our undergraduate B.Sc. program for many years.

Over the course of his career, Bennett's research interests centered on the synthesis of glycoproteins and the intracellular pathways followed by these molecules in a variety of cell types. Pioneering work with Charles Leblond and Antonio Haddad resulted in a Science Citation Index award (1989) for an article published in 1974 on the migration of glycoprotein from the Golgi apparatus to the surface of various cell types as shown by radioautography after labeled fucose injection into rats. This work was featured in a cover article of *Molecular Biology of the Cell* in 2001.

Bennett gave keynote addresses at the Royal Histochemistry Meeting on secretory processes in London in 1976 and the Falk symposium on liver carbohydrates in Basel, Switzerland in 1982, and he gave the Robert Feulgen lecture at the European Histochemical Society in Gargellen, Austria in 1986.

Throughout the forty years of his career, Bennett was noted as a teacher of Gross Anatomy to students in Medicine, Dentistry, and Physical and Occupational therapy. In our B.Sc. undergraduate program, he taught and co-administered the "Cell Biology of Secretion" course with John Bergeron, along other Cell Biology and Anatomy courses. In recognition of his teaching achievements, he was awarded membership in the Academic Honor List of the Faculty of Medicine in 1999 and was awarded the Osler prize by the medical class of 2006.

He retired as Emeritus Professor in 2010 and continued to teach on a part-time basis, lecturing and demonstrating to medical/dental students in the Gross Anatomy laboratory, until 2014.

62. Eugene Daniels (McGill: 1971-)



Eugene Daniels

Eugene Daniels joined our Department as a Lecturer in 1971. Daniels had obtained his B.Sc. in Zoology and Botany in 1963 at the University of South Africa. He completed his M.Sc. in Experimental Embryology in 1964 at the University of Manitoba and his Ph.D. in the same field in 1970 at the University of Manitoba. He carried out a post-doctoral year in Hematology at McGill in 1971.

At McGill, Daniels was promoted to Assistant Professor in 1974, and Associate Professor with tenure in 1979. Eugene Daniels administered our Gross Anatomy Teaching facility from 1974-1995 as Curator of Anatomy. In addition to supervising the two laboratory technicians, he was in charge of our Body Donation program, interacting with the Quebec Government, the Blythe Bernier Funeral home, various hospitals, and the general public.

Dr. Daniels' research has involved various aspects of mouse embryogenesis. It emphasizes the identification of gene expression throughout all stages of development, i.e. embryo, fetus, neonate, and adult, as a prelude to gene functional studies. The recording of normal expression patterns in interacting tissues forms a database for detailed analytic studies of the spatio-temporal functions of various genes. These include genes of the carcino-embryonic gene family, *bgp*; *hox* genes; planar cell polarity genes, *vang-1*; and PTP-PEST genes. Transgenic and knockout animals, generated by collaborators, are used to study the effects of these genes in developing tissues. This systemic holistic approach has allowed Dr. Daniels to contribute to identifying mechanisms involved in prenatal hemopoiesis, neurulation, and gut embryogenesis. It has also allowed investigation of the role of growth factors (such as progranulin) in the complex embryonic processes of vasculogenesis, angiogenesis, and neurogenesis. Integration of a detailed expression database with analytic embryogenesis protocols in the Daniels laboratory provides further tools for systems analysis in embryology. From 1991-1995, Daniels carried out collaborative studies in the McGill Cancer Centre in molecular embryology, using molecular techniques of RNA isolation, reverse transcriptase polymerase chain reaction, cloning, sequencing, preparation of RNA probes and in situ hybridization. Daniels has supervised five undergraduate student research projects, two M.Sc. graduate students, and co-supervised one Ph.D. student with A. Bateman.

In terms of teaching, Eugene Daniels has been in charge for many years of the Med-Dent teaching program in embryology. He has given all of the lectures and laboratory demonstrations in all Units (1-6) of the Curriculum of recent years. He has introduced a teaching innovation in this area by creating interactive embryology studies for medical and dental students. Daniels has also supervised many McGill residents in special laboratory dissections.

Daniels also introduced our exciting new Thiel procedure for embalming cadavers such that the tissues do not harden and remain more lifelike. This is of great value since it facilitates simulations of surgical procedures. These cadavers are used extensively by the new McGill simulation centre.

In addition to teaching in the first year Medical-Dental class and the fourth year Medical Anatomy for Surgeons course, Eugene Daniels has developed many programs for post graduate teaching. These include coordination and consultation for residency training programs in surgery in Université de Montréal

hospitals, general surgery for residents using the new embalming technique described above, invasive procedures for Emergency Medicine Residents, and organization of resident-surgeon training workshops.

A superb teacher, Eugene Daniels was awarded the Osler Teaching award in 1993, the Royal Bank Teaching Innovation Award in 1998, the Federation of Quebec Medical Students Society Lecture Award in 2002, the Canadian Association of Medical Education Certificate of Merit in 2001, as well as other teaching awards. The express wish of students in one medical class was that Dr. Daniels could be “cloned” in order to provide McGill with more teachers of such exceptional ability.

63. Michael F. Lalli (McGill: 1971-)



Mike Lalli

Michael Lalli became a Lecturer in our Department in 1971. He came to McGill after an early career as a pilot in the United States Air Force. In our Department, he carried out a Ph.D. from 1967-1972, studying spermatogenesis under the supervision of Yves Clermont. He was promoted to Assistant Professor in 1973 and Associate Professor in 1981.

For many years Michael Lalli was supervisor of our Electron Microscope laboratory, and he was instrumental in obtaining our new generation of electron microscopes, travelling to Japan for this purpose. As an administrator, he played a key role along with the Chair, Yves Clermont, in managing the affairs of our Department as well as being Building Manager of our Strathcona Anatomy and Dentistry Building.

In his teaching career, Lalli was greatly appreciated by many years of Dental classes for his excellent teaching and administration of their Head and Neck Gross Anatomy course. Mike Lalli retired in 2000 but continued to teach Gross Anatomy to the Medical and Dental students on a part time basis until 2015. He

also worked with Yves Clermont on a superb Atlas of Histology which has now been made available to our medical/dental students on line.

64. Charles E. Smith (McGill: 1971-)



**Charli
e
Smith**

Charles Smith joined our Department as a Lecturer in 1970 after obtaining his D.D.S. degree from McGill in 1970. He obtained his Ph.D. degree in Anatomy in 1975 under the supervision of Hershey Warshawsky. In 1976, he became an Assistant Professor in our Anatomy Department as well as in the Faculty of Dentistry. He was promoted to Associate Professor (with tenure) in our department in 1980 and to Full Professor in 1993.

From 1980-1986, he was Chair of the Department of Oral Biology in the Faculty of Dentistry, and from 1986-1994 he was Associate Dean for Graduate Studies and Research in the same Faculty. In 2004, Smith took early retirement and left McGill to join the Department of Stomatology at the Université de Montréal as a Senior Scientist. He returned to McGill in 2011, and since that time, has been a full-time Associate Member of our Department. In 2009, Smith became Professor Emeritus in the McGill Faculty of Dentistry. From 2009-present he has held a joint appointment (on staff) as Visiting Research Scientist and Adjunct Research Scientist in Department of Biologic and Materials Sciences, University of Michigan School of Dentistry, Ann Arbor, MI.

At McGill, Smith has served on a variety of committees both in the Faculty of Dentistry (over 23) and in our Department (over 8). Over his research career, Smith's interests have been very diverse, including

tooth development; structure of enamel; secretion and degradation of enamel matrix proteins; cytochemical localizations of phosphatases and proteinases; immunolocalization of carbonic anhydrase and solute carrier proteins in enamel organ cells; computer reconstruction of serial sections; computer simulation of cell function; image analysis; quantitative biology; morphometry; in vitro modeling of mineral induction processes and HA crystal growth; expression of matrix proteins in the male reproductive tract; programmed cell death; inter-relationships of the Golgi apparatus, trans Golgi network and lysosomes; male fertility; differentiation of germ cells; and development of spermatozoa. A prolific researcher, Smith has over 122 peer-reviewed publications. During the last 10 years, he has given 11 invited presentations.

He has co-organized two meetings and co-edited a special edition of the Anatomical Record as well as serving as a reviewer for over 50 scientific journals and granting agencies. In terms of teaching, Smith has taught in our Basis of Medicine Histology course along with several courses in second year Dentistry. He has supervised the research of 12 undergraduate, and 5 graduate students. In recognition of his teaching in the Faculty of Dentistry, he was awarded the Howard Katz Excellence in Teaching Award in 2002.

65. A Brief History of Electron Microscopy

Huge breakthroughs in new knowledge often come with the availability of new technologies, and this was certainly the case when electron microscopy was introduced. Just as the invention of the light microscope had revolutionized the science of Biology in the 1600's, the electron microscope brought about a similar dramatic change in the latter half of the twentieth century. By the early years of this century, the light microscope appeared to have yielded as much as it could in terms of revealing the detailed structure of the interior of cells. Further progress awaited the development of the electron microscope in the 1930's, which began to reveal the world of the infinitely small. Frost 2:255, Hanaway 2:202

The theoretical background for electron microscopes dates from 1924 when de Broglie, a French physicist, postulated that electrons had wave properties and that the wavelength was inversely proportional to the electron velocity.

A transmission electron microscope (TEM) is similar in design to a large upside-down light microscope. The source of radiation is a filament which emits electrons at the top of a cylindrical column about 2 m high. The column must contain a vacuum since electrons would be scattered by air particles. The electrons are attracted by a nearby anode and allowed to pass through a tiny hole to form an electron beam that travels down the column. Magnetic coils at intervals focus the electron beam just as glass lenses focus the light in a light microscope. The specimen is placed into the vacuum, through an airlock, in the path of the electron beam. Any electron-dense portions of the specimen scatter the electrons which hit them. The remainder of the electrons pass through the specimen and form an image on a phosphorescent screen, a photographic plate, or digital camera.

In an electron microscope with an accelerating voltage of 100,000 volts, the wave length of an electron is 0.004 nm. This would provide a theoretical resolution of 0.002 nm which is 100,000 times greater than that of a light microscope (200 nm). However, due to the aberrations of the electron lens and a small

numerical aperture, along with problems of specimen preparation, the normal effective resolution for biological objects is about 1nm. Nonetheless, this is still 200 times better than that of the light microscope

Alberts: 554

A scanning electron microscope (SEM) produces an image of the three-dimensional structure of the surface of a specimen. Whereas the TEM uses the electrons which have passed through the specimen to form an image, the SEM uses electrons that are emitted from the specimen's surface. The specimen is fixed, dried, and coated with a thin layer of metal, and then scanned with a very narrow beam of electrons. The quantity of electrons emitted as this beam of electrons bombards each successive point of the metallic surface is measured to control the intensity of a second beam which moves in synchrony with the primary beam and forms an image on a computer screen. Since the amount of electrons emitted depends on the angle of the surface relative to the beam, the image has highlights and shadows that give it a three-dimensional appearance. The resolution is not very high (about 10 nm) so that the technique is usually used to study whole cells and tissues

Alberts: 558

The first transmission electron microscope (TEM) was built by E. Ruska in Nazi Germany in 1933. With the Siemens Company, he designed a commercially produced microscope which became available in 1939, and was called the "SuperScope". The Second World War started immediately after this date, however, and the Germans limited the sale of these instruments to their own countrymen and other Axis powers

Pauly: 44

In North America, E.F. Burton, at the University of Toronto built a successful electron microscope in 1939. His student, James Hillier, subsequently joined The Radio Corporation of America (RCA) in 1940 and quickly developed the first commercial instrument in the Western Hemisphere. Sixty of these RCA EM-B microscopes were made during the Second World War. Their availability for biological studies was limited, however, since most usage was reserved for research into war-related materials.

While the electron microscope offered great possibilities, the problems of specimen preparation at first seemed formidable. One problem was that the fixation used for light microscopy was much too crude for high resolution work. It was subsequently found that fixation in osmium tetra-oxide vapors was satisfactory for electron microscope work. A second, perhaps more important problem, was that the beam of electrons could only penetrate a thickness of 0.1 μm , while the thinnest light-microscope tissue sections were 1-2 μm . Finally, the sections needed to be stable under the high vacuum essential within electron microscopes and also needed to be able to withstand the electron beam itself. Metal grids and films of various materials were developed to support these sections, but the problem of obtaining sufficiently thin sections remained.

The first successful biological studies came in 1944 when Keith Porter and Albert Claude of the Rockefeller Institute managed to obtain access to an RCA EM-B microscope at the Interchemical Corporation and then used this instrument to examine cultured cells. In these cultures the cells were grown on supporting film, and they had flattened themselves to such an extent that they were extremely thin at their periphery. Porter and Claude found, to their delight, that the cells exhibited considerable electron transparency in

these areas, and they were able to observe cell ultrastructure for the first time. These observations revealed the presence of a new cytoplasmic organelle, the endoplasmic reticulum ^{Pauly: 45, 60}.

To examine the interior of cell types in tissues, however, it was necessary to produce thin sections of tissue specimens. A major advance came with the embedding of tissues with the plastic methacrylate; this was infiltrated into cells as a liquid monomer and then polymerized to hardness. This plasticized medium could be cut into thin sections which were durable enough to withstand the conditions of electron microscopy.

Another huge problem involved the heavy steel microtome knives used for cutting sections. These were obviously unsatisfactory and not very sharp. At first, dry sections produced by the knives were picked up with a hair and laboriously transferred by hand to electron microscope grids, where they flattened and stuck down by pressure. A much better method of gathering newly-cut sections was developed when the newly-cut sections were floated from the knife edge onto a water surface. This flattened them and permitted an easy transfer to grids with a wire loop. A new problem arose, however, since the water caused rapid rusting of the metal knife edge. Surprisingly, a simple and effective solution came with the introduction of glass knives. These knives, which were produced by fracturing small squares of pane glass, were extremely sharp, and being quite inexpensive, could be disposed after each use. These glass knives were only surpassed by diamond knives in more recent times. The combined use of osmium tetroxide fixation of tissues, methacrylate embedding, glass or diamond knives, the Porter-Blum microtome, and the RCA EMU microscope set the stage for the veritable explosion of the key cytological discoveries in the early and mid-1950's.

One of these discoveries was the ultrastructure of the Golgi apparatus. As mentioned previously, Camillo Golgi, using the light microscope in 1896, had observed a network of threads in the cytoplasm around the nucleus of nerve cells and called the organelle the "reticular apparatus". Over the next 40 years, over 2,200 light microscopic papers described the Golgi apparatus in the majority of all cell types as a network of plates and threads. There was no understanding of its true nature, however, and there was, in fact, considerable debate as to whether or not the apparatus was real or just an artifact of the preparation methods. As late as 1949, Palade and Claude contended that the fixed impregnated Golgi apparatus of all cells was an artifact based on unspecific staining of various cell components ^{Bennett: Cell Biology of the Secretory Process.}

Karger, Basel 1984

The reality of the Golgi apparatus was finally established in the 1950's by electron microscopic studies. Thus Dalton and others showed that the Golgi complex consisted of stacks of flattened saccules with associated vesicles. Other studies such as those of Yves Clermont in our department quickly followed in the early 1960's.

In subsequent years, a multitude of other subcellular organelles has been revealed by electron microscopy. In recent times, cryo-electron microscopy and other techniques have permitted the investigation of the structure of individual macromolecular complexes and other nanometer-scale structures at near-atomic resolution. In cryo-electron microscopy, a very thin film of an aqueous

suspension of macromolecular complexes (or viruses) is prepared on a microscope grid and then is rapidly frozen to form vitreous ice in a coolant. A special sample holder keeps the hydrated specimen at minus 160 degrees C. in the vacuum of the microscope where it can be viewed directly without fixation, staining or drying. Because the image contrast is very low, special image-processing techniques must be used ^{Alberts:}
560.

66. Our Departmental Electron Microscope Laboratory

The history of electron microscopy in our Anatomy department begins in the 1940's with the purchase of an ancient RCA EMU-28 microscope. For the first few years, this instrument was housed, not in our department, but rather in the Eaton Electronics laboratory down the hill. The first electron microscope installed in our Anatomy EM laboratory in the Strathcona Building was purchased in 1958. This was a, and it was used until 1972 at which time it was sold to the Montreal General Hospital. In 1964, a electron microscope was purchased from Laval University. In spite of a bad reputation, this instrument was used for 21 years, becoming the longest serving microscope in the department.

Soon after obtaining the instrument from Laval, the RCA microscope was transferred from the Eaton Electronics laboratory to our EM laboratory where it functioned (after a fashion) until 1967. This microscope remains as a "museum piece" in the hallway of our current Facility of EM Research (FEMR).

In the mid-1960's, we obtained two Hitachi microscopes. These served for 10-13 years before one was sold to the Royal Victoria Hospital and the other to an art restorer.

The EM laboratory was initially administered by a chief technician, Deiter Curlis. He was succeeded by Ed Sandborn and his technician Pat Coen. After leaving McGill for the University of Montreal, Sandborn was succeeded by Berty Van Heyningen. She was in turn succeeded by Hershey Warshawsky, our first long-term director of the EM lab (from 1965 to 1973). Warshawsky played an instrumental role in obtaining all five of our first departmental microscopes. The technicians in the lab at that time were Julius Batky, succeeded by Ingrid Simons. After Hershey Warshawsky, the directors of the EM laboratory included Michael Lalli and Louis Hermo.



Julius
Batke

Mike
Lalli

Lenny
Volkov

Connie
Goodberry

Hershey
Warshawsky

Electron Microscope Laboratory in 1960's

The early electron microscopes were manual and crude by today's standards. This was particularly true of the old RCA microscope which was used in the pioneering ultrastructural studies of Yves Clermont on the perforatorium of the rat spermatozoon (1955) and the spermatid Golgi apparatus (1956). It was not uncommon for discharges to occur in the electron gun area, and sitting there in the dark with bolts of lightning and claps of thunder evoked the feeling in Hershey Warshawsky that "ten new commandments would soon come down from the mountain". Yves Clermont, in fact, did not like using the electron microscopes, and his images, taken on the old RCA and Elmiscope 1, were taken mainly by the chief technician Deiter Curlis.

In 1972, the Siemens Company offered the department a demonstrator model of the Elmiscope 1A Microscope and this was purchased for \$ 25,000. This microscope was in service for many years and was used to train all new researchers in the laboratory.

The work in the EM laboratory (i.e. preparing tissue samples, embedding the material, trimming blocks, cutting sections, scanning and taking photographs on the microscope, developing negatives, and producing positive prints) was very time consuming. A standard joke was that "EM" time was at least double ordinary time, and in the words of Antonio Haddad, "no matter what the hour, the lights of the EM laboratory were very seldom off".

During this exciting age, the deluge of new discoveries coming from electron microscopic investigation was exhilarating. Since the scientific research of almost all departmental members utilized this instrument, the EM laboratory was the life blood of the Department.

A new generation of instruments came in 1980's when electron microscopes with moving parts were replaced by those with integrated circuits in the new age of computers. With help from the Medical faculty, our department acquired both a Philips 301 and a Philips 400T electron microscope. These were used until 200 and 2004.

In 1986, a \$ 600,000 MRC Major Equipment grant enabled our department to purchase a JEOL JEM-2000FX STEM microscope with an X-ray micro-analytical system. In addition to Transmission electron microscopy, this instrument allowed for a Scanning function (thus the term "STEM"). The X-ray micro-analytical system permitted the identification and localization of virtually any element present in biological tissues. On the occasion of the inauguration of this "state of the art" instrument, Hershey Warshawsky wrote a brief history of our electron microscope facility in the McGill Reporter (Feb 13, 1986). For a description of more recent developments in our E.M. laboratory, see "73. The Facility for Electron Microscope Research (FEMR) in chapter 7.

67. John J. M. Bergeron (McGill: 1974-2010)



John Bergeron 1993

John Bergeron joined our department as an Assistant Professor in 1974. He had obtained a B.Sc. at McGill in Honors Biochemistry in 1966, and then went to Oxford as a Rhodes Scholar where he obtained a D.Phil. in 1969 under the supervision Dr. C.A. Pasternak. He then did post-doctoral work from 1969-1971 with Drs. P. Siekevitz and George Palade at the Rockefeller Institute in New York. With his strong background in Biochemistry and Cell Biology obtained at world-class institutions, Bergeron represented a valuable addition to our Departmental research team.

At McGill, he was promoted to Associate Professor (with tenure) in 1978, and to Full Professor in 1982. He became an Associate Member of the Department of Medicine in 1982. He was a Medical Research Scholar from 1974-1979 and a Chercheur Boursier from 1979-1985. He was Robert Reford Professor and Chair of our Department from 1996-2010.

In his research over the years of his career, John Bergeron became recognized internationally as one of Canada's outstanding cell biologists. His primary interest centered on the concept that cells must target proteins correctly in order for the physiological functions of these proteins to be realized. His research over the years spanned three major areas:

1. Signal transduction in the endosomal apparatus:

In the first phase of his career, Bergeron pioneered the study of the intracellular structures involved in ligand-induced internalization of cell surface receptors such as epidermal growth factor (EGF) and insulin receptors from the cell surface of hepatocytes. This work led to the hypothesis and demonstration of endosomal signaling that he elaborated with Dr. Barry Posner.

2. Protein transport in the endoplasmic reticulum.

Bergeron investigated the role of membrane phosphoproteins in the exocytic transport of proteins out of the endoplasmic reticulum (ER). Molecular cloning led to the discovery of calnexin, the major molecular chaperone for newly synthesized membrane and secretory glycoproteins. With Dr. David Thomas experimental evidence for the calnexin cycle and its relevance to quality control was defined.

3. The molecular anatomy of the Golgi apparatus.

Bergeron pioneered the development and use of quantitative proteomics in cell biology. He was President of the Human proteome Organization that he headquartered in the Innovation Centre that he cofounded with Dr. Tom Hudson adjacent to the Department of Anatomy and Cell Biology. Using this new technology Bergeron discovered GPP34 now known as Golp3 the first Golgi apparatus located oncogene responsible for Golgi structure and trafficking. Using quantitative proteomics with Dr. Tommy Nilsson he also established conclusively the maturation hypothesis for Golgi apparatus identity during protein secretion.

Bergeron authored over 225 peer-reviewed scientific articles and over 7 patents. He has been an invited speaker at over 155 scientific meetings, and has given over 59 seminars at McGill and elsewhere (since 1996). He was on the grants panel of over 35 agencies, on the editorial board of several journals, and organized over 15 conferences.

In terms of teaching, he taught in several Departmental courses including "Cell Biology of Secretion" and our graduate course in Cell Biology, as well as courses in the Biochemistry Department. He supervised the research projects of over 9 M.Sc. students, 19 Ph.D. students, and 25 Post-Doctoral students, as well as hosting visiting scientists.

John Bergeron as Chair (1996-2009)

In 1996, John Bergeron became the Chair of our Department of Anatomy and Cell Biology. He was taking charge of a world class department with an international reputation in both research and teaching, but there were certain major challenges. Our small department had traditionally heavy teaching responsibilities and, at the same time, there was a shortage of young cell biology researchers who could work with and inspire one another. Due to continued lean years of government funding, no appointments were available to hire new faculty members. Research funding had been lost for several faculty members as well as our Electron Microscope Centre.

In that same year (1996), at Bergeron's request, a committee consisting of R. Murphy, M. Chrétian, A.C. Cuello, M.S. Du Bow, R. Michel and A. Shrier prepared a report addressing the overall academic priorities of the Department of Anatomy as well as the future of the Electron Microscope Centre. Reflecting an earlier external evaluation of the Department in 1981 by Michael Gershon of Columbia University (described later in this work), the committee recognized that the academic future of the Department lay in research and teaching of the expanding field of Molecular Cell Biology. It recommended cross appointing a number of hospital cell biologists who could contribute to teaching of Histology and Cell Biology. It was observed that many of the research labs were closed evenings and weekends, suggesting a lack of productivity. Could a more critical mass of Cell Biology be created in one area of the building? Finally, it was felt that the Department should position itself as the center of strength for Cell Biology in the Medical Faculty, perhaps by creating cross-departmental programs with other Departments. The committee also recommended that the departmental EM Laboratory be turned into a University Core Facility which would generate extra operating support and create interactions with scientists outside.

The situation improved in 2001 when Bergeron obtained a CIHR maintenance grant as well as a Canadian Foundation for Innovation (CFI) grant for the EM Centre. With Tom Hudson, he obtained a very large CFI grant to create and fund the Genome Centre as well as a grant from Genome Canada/Quebec to establish the Proteomics division.

In the following years, it became possible to recruit several new faculty members, all of whom met the criteria of obtaining both peer-reviewed funding and salary support from national funding agencies within three years of their appointment. These included Chantal Autexier, Nathalie Lamarche-Vane, Martin Latterich, John Presley, Craig Mandato, Fiona Bedford, Elaine Davis, Dieter Reinhardt, and Isabelle Rouiller. At a more senior level, Marc McKee was also recruited as a joint appointment with the Faculty of Dentistry.

In the following years, CFI grants for the EM Centre and the Genome Centre were renewed (the only successful CFI applications at McGill that year). Operating grants from CIHR, CFI, and the National Cancer Institute (NCI) were also renewed. Bergeron at this time also cofounded the proteomics division of a biotech company, Caprion Technology, Inc., for which he was the Chief Scientific Officer.

In line with the committee recommendations mentioned above, it was recognized that there was an obvious need for increased collaboration between our Department and scientists carrying out Cell and Molecular Biology research in other McGill Departments. To facilitate this exchange, Bergeron greatly increased expanded the number of cross appointments, especially in Biology, Biochemistry, Pharmacology, and the Montreal Neurological Institute. Scientists from all of these Departments have made valuable collaborations with our departmental members and have sometimes trained their graduate students in our graduate program. An especially important contribution has been their willingness to teach in our various undergraduate courses.

As chair, Bergeron showed a supportive interest in all aspects of Departmental life. An important initiative was the holding of Department retreats. Held at a variety of resorts outside of Montreal, these retreats have concentrated on both our research and teaching programs.

In 2010, Bergeron left our department to become a Medical Scientist/Professor in the Division of Endocrinology at the McGill University Health Centre Research Institute. He was Co-Director of the Laboratory of Systems Medicine and Cell Biology in the Department of Medicine. He also remained an Associate Member of the Department of Anatomy and Cell Biology.

As Chair of Anatomy and Cell Biology, Dr. Bergeron lobbied effectively with MPs and cabinet members to help create CFI and Genome Canada. He has been effective through his work on several grants panels and committees overseeing the Medical research Canada of Canada as it transitioned to the CIHR. Additionally, he was on ACOR, the committee overseeing the NCI of the Canadian Cancer society, and has worked and chaired several of its grants panels. In recognition of his research accomplishments, he was awarded the Murray J. Barr Award of the Canadian Association of Anatomists in 1980, membership in the Royal Society of Canada in 1995, and then the prestigious McLaughlin medal from the Royal Society in 2004. He was subsequently elected president of the Human Proteome Organization (HUPO), an international body headquartered in Montreal. In 2010, he was honored with the both the Human Proteome Organization Discovery Award and the Canadian National Proteomics Network Award as well as the QEII Diamond Jubilee Medal.

In 2015, John Bergeron retired from McGill as Emeritus Professor. Over the years, he has been an effective and unstinting advocate for health research in Canada. In recognition of this effort, he was awarded (also in 2015) the Research Canada Distinguished Leadership Award for “sharing his knowledge and passion for health research with others through speaking and writing, and his lead role in growing community, provincial and national awareness related to health research”.

68. Sandra Miller (McGill: 1975-2014)



Sandra Miller - 1993

Sandra Miller joined our department as a graduate student in 1969 after having obtained a B.Sc. from Sir George Williams University in 1968. She completed her M.Sc. in with Dennis Osmond in 1971 and her Ph.D. in 1975. She became a Lecturer in our Department in 1975. She then left McGill to become a Post-Doctoral Fellow from 1976-1978 in the Division of Experimental Biology at Baylor College of Medicine in Houston, Texas.

At McGill, Miller was promoted to Assistant Professor in 1978, to Associate Professor with tenure in 1983, and to Full Professor in 1998. In 1991, she was a Visiting Scientist at the Howard Hughes Medical Institute at the Stanford University School of Medicine in California.

For the past 17 years, Sandra Miller has also directed our Annual Commemorative Service for Body Donors. This important service is attended by 340-400 hundred people, including students, the families of the donors, and as well as faculty and senior university administrators. It has brought Miller into frequent contact with the general public and the media (TV, press and radio at the city, national and even international levels. She has given numerous interviews and has been an exemplary spokesperson for the Department. It is thanks to her work that our body donor program is thriving.

In her research career, Sandra Miller's work concentrated on the cell and tissue biology of the immune system and tumor resistance, coupled in more recent times with the rapidly expanding field of medicinally important phytochemical factors such as those in Echinacea and North American ginseng.

Her early work was on the following topics: small lymphocyte production and lymphoid cell proliferation in mouse bone marrow (1977), production and renewal of murine natural killer (NK) cells in the spleen and bone marrow (1982), life history of cells mediating natural resistance to tumor cells and bone marrow

transplants (1984), the effect of bearing tumors on the ability of mice to reject bone marrow transplants (1987), and the decline in natural killer cell-mediated immune-surveillance in aged mice: a consequence of reduced cell production and tumor binding capacity (1994).

Her later work included the following topics: the rejuvenation of natural killer cells from aging mice treated with extracts from *Echinacea purpurea* (2000), the augmentation of natural killer cells and prolongation of life span in leukemic mice treated with *E. purpurea* and melatonin (2001), *Echinacea: A miracle herb against aging and cancer?* (2005), the role of melatonin in immune-enhancement: a potential application in cancer treatment (2006), and stimulation of spontaneous immunity in infant mice by an extract of North American ginseng (*Panax quinquefolius*): sustained, augmented immunity in adulthood long after withdrawal of the extract (2008).

In Miller's own words: "We wanted to find a treatment for cancer that was not as harmful as chemotherapy. We investigated the effects of Interleukin-2 and produced mice free of their leukemia, but this substance caused vascular leak syndrome and fever. By chance, I found out about new herb, *Echinacea*, and bought some at the drug store. After a few months we found that the number of leukemia cells went way down and the number of NK cells went way up. I have lived by the principle of never being closed-minded even to the most trivial things that may cross my path and sometimes they have turned out to be the solution to what I was looking for."

Research in the Miller lab during the first half of her career, resulted in developing an elucidation of the features of a specific, unique immune cell – the Natural Killer (NK) cell, whose central function is to act at the first line of defense against neoplasms *in vivo*. Just over 35 years ago when this cell, novel at that time was first identified in Sweden, Miller's lab made great strides in elucidating its immune-surveillance capacity, life cycle, organ of central origin, vascular and intra-organ (bone marrow, spleen, lymph nodes) transit time, and life span. They then used this information for the next 25 years to manipulate these cells *in vivo*, in both normal and tumor bearing mice, of three age groups (infancy, young adult and elderly) in attempts to ultimately abate cancer. Currently working with pharmaceutical and phytoceutical companies, they have manipulated NK cells such that the corporate world now has their research in patent status and in human trials with human cancer patients.

Miller has authored 69 peer-reviewed publications, and has given 17 invited seminars at McGill and at the national and international level. She has given plenary addresses at meetings of a variety of societies.

Sandra Miller also had an impressive career as an educator. She was one of the most popular and best-loved teachers in the basic medical sciences program. Her major contributions were in the Respiratory and Cardiology Section (Unit 2) and the Musculo-Skeletal Section (Unit 5), which she taught with a significant slant towards sports medicine and orthopedic problems. In her small group classes in Living Anatomy she taught the fundamental procedures of percussion, auscultation, palpation and use of the stethoscope, providing an anatomical basis for the students' future training. Miller also taught in our B.Sc. program and was joint organizer of the course on the Hemopoietic and Immune system. Even during the

last two years of her Ph.D. program, she had organized and taught a full course in Musculoskeletal Anatomy to students in Science, Dentistry and Physical and Occupational Therapy.

Miller described herself as “effervescent” and “queen bee of the laboratory”. She has a unique and enthusiastic style of teaching, consistently using overheads and self-drawn diagrams, avoiding power-point presentations which she felt constituted too passive a method of teaching.

At the Graduate Level, she has been sole supervisor of nine M.Sc. and two Ph.D. students, and co-supervised a third Ph.D student. She has been the Canadian representative on the Site Visit Team assessing the Faculty of Medicine at the National University of Singapore in 2008 and was Chair and Internal Member on the Site Visit team for the Department of Psychology at McGill University in 2013. In appreciation of her research, Miller has been honored with several awards, including the Murray L. Barr Junior Scientist Award by the Canadian Association of Anatomists (1985), and the J.C.B. Grant Senior Scientist Award from the Canadian Association of Anatomy, Neurobiology, and Cell Biology (2008).

The excellence of her teaching has resulted her appointment to the McGill University Faculty Honors List for Educational Excellence (1999), the Certificate of Merit Award of the Canadian Association of Medical Educators (2006), and the Osler award in 2013. Sandra Miller retired as Professor Emerita in 2014, but continues to produce research publications and is directing our Annual Commemorative Service for Body Donors for one more year.

69. Louis Hermo (McGill: 1977-)



Louis Hermo joined our Department as a graduate student in 1970. He had obtained a B.A. in Biology and Chemistry in 1967 from Loyola University, followed by a B.Ed. in Education from St. Josephs College in 1969. In our Department, he obtained his M.Sc. and Ph.D. degrees in Anatomy in 1972 and 1975 under the supervision of Yves Clermont. From 1976-1977, Hermo was a Postdoctoral Fellow at the Centre d’Études Nucléaires in Saclay, France, working in collaboration with Alain Rambourg on the Golgi apparatus.

Hermo returned to our department as an Assistant Professor in 1977. He became an Associate Professor with tenure in 1984 and was promoted to Full Professor in 1997. Administratively, Louis Hermo was director of our EM Facility, a member of various departmental and faculty committees, and an undergraduate student advisor. In the Faculty of Medicine, he was Chair of the foreign/US cohort of the Medical Admissions Committee from 1998-2008.

Over the course of his research career, Hermo's interests have related to the structure and function of the male reproductive system with particular interest in the testis and epididymis. He has used electron microscopy, immunocytochemistry, radioautography, and various tracers to study the movements of proteins in the secretory and endocytic pathways of various cell types lining the reproductive tract. A particular interest has been the functional role of the reproductive tract in sperm maturation. A second main interest of Louis Hermo has been the structure of the Golgi apparatus, particularly its three dimensional aspects. This has been studied in a variety of cell types, including those of the reproductive system.

In subsequent years, Hermo has investigated a great variety of topics related to the male reproductive tract, spermatogenesis and fertility. Recent attention has focused on the cytoplasmic droplet (CD)/Hermes Body found in epididymal sperm cells. The overall hypothesis is that sperm maturation is partly acquired by functional components of the CD. An integrated combination of ultrastructural and proteomic approaches has been used, and proteomic analysis has revealed that over 2,900 proteins are associated with the CD. The Hermo lab has selected some of them for further in-depth functional analysis.

Hermo has authored over 120 peer-reviewed articles and 130 abstracts, has given over 15 invited seminars. He has been an editor for two scientific journals and a reviewer for several others, and has served on three grants panels.

Louis Hermo has been a renowned teacher in our Department. Even as a final year Ph.D. student, he developed and taught the entire Limbs and Back Gross Anatomy course for the School of Physical and Occupational Therapy. After his return from France, he continued to give this course for five more years. Hermo then assumed responsibility for Systemic Gross Anatomy (ANAT 214), a course constantly rated as one of the most popular courses in all of McGill. For many years the course operated at well over its optimal capacity of 250 students, and even then many Anatomy and Physiology students had to be turned away. Hermo was able to successfully manage this huge course partly by recruiting large numbers of enthusiastic demonstrators from students in the more senior years of the B.Sc. program. One noted feature of this course was the annual bake sale which benefitted local charities. Students would prepare cakes with "anatomical" features, and these would be sold in combination with volunteered tuition time on the part of the demonstrators.

Louis Hermo also played a large role in our undergraduate research project course, both administering the course and supervising 130 undergraduate students! At the graduate teaching level, he supervised twenty-eight M.Sc. students and published 153 peer reviewed articles!

In 2007, Louis Hermo was awarded the J.C.B. Grant award by the Canadian Association of Anatomy, Neurobiology and Cell Biology. His teaching excellence was recognized by his receiving the Leo Yaffe award of the Faculty of Science.