A chapter in , Vol. 5 pp.505-548, 2006.
Squire, L. R. (Ed.).. Burlington, MA: Society for Neuroscience, Elsevier Academic Press.

Montreal, Canada
January 15, 1938

McGill University, B.Sc. (1959)
McGill University, M.D.C.M. (1963)

baseball diamonds, tennis courts, a ski hill, and a hockey rink. It was also advantageous having an older brother with whom I could play sports. He also stimulated me to read books and listen to music, as my parents had little interest in either.

I did well in school, and although I took all of the math and science courses available, I was not a budding scientist. I took courses in physics, chemistry, algebra, trigonometry, and intermediate algebra, but there were no biology courses available: we were taught how to brush our teeth but that was all the biology taught during my twelve years in school. It was only many years later that I realized how strange that was. What was the education board thinking? I would still not know where my heart is located if I had not eventually studied medicine.

Another oddity about growing up in Montreal in those days was that, although the

Despite my less than noble motives for studying medicine, I greatly enjoyed my four years in medical school, partly because it was my first real exposure to biology. We spent an excessive amount of time studying anatomy, however, so that my brain is still cluttered with detailed and useless anatomical facts, which, unlike more useful information, I cannot seem to forget. There was an enormous amount of rote learning, but our teachers were excellent, and they prepared us well for practicing medicine. Medical school is probably not an optimal preparation for being a scientist. It trains you to look backward and compare the patient at hand with similar patients seen previously, whereas a scientist tries to see things in new ways,

classic case of poliomyelitis that had been sneakily pulled from the archives. None of us had ever seen a case of polio, but it was nonetheless humiliating to not have even mentioned it as a possibility.

We were able to switch visas because the change in the draft law was still several weeks away. The new visa, however, meant that I had to leave the US at the end of my training, which was just over a year away. Until I changed visas, I had been planning to stay in the US after my residency, possibly to do neuro-ophthalmology with David Cogan at the Massachusetts Eye and Ear. Now, I needed a new plan. I asked my friend Barry Arnason, a neurologist and neuroimmunologist at the MGH, if he had any suggestions. At a similar stage in his career, he had done experimental immunology with Guy Voisin at l'Hôpital St. Louis in Paris. He suggested that I do the same and offered to arrange it. I agreed, and a few hours later it was all fixed up.

Within weeks, however, a physicist friend in Boston sent an article to me entitled "Immunology at Mill Hill" that had just been published in

marrow-derived B cells. Because the two classes of cells look the same and occur together in the peripheral lymphoid organs such as the spleen and lymph nodes, there was an urgent need for ways to distinguish and separate them from each other. Av had recently heard the Boston immunologist Arnold Reif describe an alloantigen called (later called) that was present on the surface of mouse thymus lymphocytes. As thymus lymphocytes give rise to T cells, Av thought that Thy-1 might also be present on T cells but not B cells, in which case it could serve as a useful T cell marker.

Using an antibody- and complement-mediated cytotoxicity assay that I learned from my lab mate Marion Ruskowicz, I first showed that Thy-1 is present on peripheral lymphocytes as well as on thymus lymphocytes. I then examined lymphocytes from mice that Sandra Nehlsen (a Ph.D. student of Medawar who worked across the hall from me) had been chronically treating with anti-lymphocyte serum to deplete T cells. I found that the spleen and lymph nodes of these mice contained normal numbers of Thy-1-negative lymphocytes but very few Thy-1-positive lymphocytes, strongly suggesting that Thy-1 is present on T but not B cells, as Av had suspected [2]. I then used the antibodies to analyze a system that Av had developed to study the collaboration between lymphocytes from mice immunized with a carrier protein and lymphocytes from mice immunized with a hapten; when both lymphocyte populations were transferred into irradiated mice and immunized with the hapten coupled to the carrier protein, the mice produced large amounts of anti-hapten antibodies. Before transferring the cells, I treated one or other population with anti-Thy-1 antibodies and complement to kill the T cells and showed that the carrier-primed cells were T cells and the hapten-primed cells, which produced the

one of the first direct demonstrations of Ig molecules on the surface of lymphocytes, which immunologists had postulated would serve as receptors for antigens.

The finding of Ig on some lymphocytes but not on others raised the question of which class of lymphocyte expressed the Ig. To find out, I examined lymphocytes from mice depleted of T cells, either by chronic treatment with anti-lymphocyte serum or by thymectomy, irradiation, and bone marrow transplantation. I found that all the Ig-positive cells were B cells [7], which began a prolonged and frustrating search by many laboratories for the antigen receptors on T cells, which were only identified as Ig-like proteins years later, after many false leads. Surface Ig, however, rapidly became a standard marker for B cells in all vertebrates. Later, when we moved to UCL, for example, John Owen and I collaborated with Max Cooper, who was on sabbatical from Birmingham, Alabama, and used anti-Ig antibodies and tissue explant cultures to show directly that B cells develop in the fetal liver and adult bone marrow [8], rather than in the gut, as had been suggested by others (including Max), and that B cells arise from pre-B cells, which have already begun to make IgM heavy chains [9].

When I visualized Ig on the surface of B cells with fluorescent antibodies, a remarkable feature of the staining was that it was located at one pole of the cell, forming a fluorescent "cap" [7]. Göran Möller at the Karolinska Institute in Stockholm saw the same distribution almost ten years earlier [10]. To determine what was special about the pole of the cell where the Ig was located, I collaborated with Stefanello de Petris, an Italian scientist working at the NIMR. Nello was an expert in using ferritin-coupled antibodies to localize antigens in cells in an electron microscope. For reasons known only to him, he labelled lymphocytes with ferritin-coupled anti

Cancer Research Fund (ICRF, now Cancer Research UK) until Av left UCL for Berlin. Although we were not financially part of the Unit, the ICRF services were invaluable to us. Moreover, during this entire period, I had the wonderful privilege of sharing an office with Av, who was a protective patron and role model, as well as an inspiring and generous friend.

The research plan was to raise antibodies against cells of the nervous system and use them to distinguish and separate the different cell types so that we could study their development and interactions, mainly in a culture dish. This was before the monoclonal antibody revolution, and there were many formidable problems to overcome. Since neural cells are fixed in complex arrangements in the nervous system, they are much more difficult to isolate than are lymphocytes. Moreover, we would need relatively pure populations of cells for raising and testing antibodies, and so we might be defeated by the very problem we wanted to solve. To overcome this catch 22, we decided to start with cells from neural tumors; as each tumor initially arises from a single cell, its cells should be relatively homogeneous. We took advantage of the discovery by Hermann Druckrey and his colleagues at the University of Freiburg that one can induce tumors of the peripheral and central nervous systems in a high proportion of rats by injecting either newborns or their pregnant mothers with the chemical carcinogen ethylnitrosourea (ENU) [14].

Kay Fields, an American phage molecular biologist who had just finished a postdoc

My first graduate student, Peter Stern, had shown earlier that Thy-1 was present on rat and mouse fibroblasts [18]; Jeremy and Kay showed that anti-Ran-1 and anti-Thy-1 antibodies labelled non-overlapping populations of cells in cultures of newborn rat sciatic nerve cells: whereas anti-Ran-1 antibodies labelled the Schwann cells, anti-Thy-1 antibodies labelled most of the non-Schwann cells [16]. These findings allowed Jeremy to devise a strategy for purifying Schwann cells that depended on killing the contaminating non-Schwann cells with anti-Thy-1 antibodies and complement [19].

Jeremy and I went on to study some of the properties of purified rat Schwann cells. We found, for example, that either an increase in intracellular cyclic AMP [20] or an

Our initial studies on Ran-1 and Schwann cells provided a much-needed proof of principle that we could use antibodies to identify and purify a neural cell type. Our goal, however, was to use this approach to study cells of the CNS, which was much more challenging.

To begin to define markers for CNS cells, we turned to cultures of newborn rat optic nerve cells. The advantage of these cultures is that they do not contain neurons, and so they are not much more complex in terms of cell types than cultures of sciatic nerve. Fortunately, Amico Bignami and Larry Eng and their colleagues had already identified glial fibrillary acidic protein (GFAP), an intermediate filament protein expressed by astrocytes but not by oligodendrocytes, microglial cells, or neurons [27]. We obtained anti-GFAP antibodies from Bignami and found that they labelled two morphological types of astrocytes, which we later called type-1 and type-2 astrocytes; the former had a fibroblast-like morphology and the latter a process-bearing morphology [28]. Other cells in the culture had multiple branching processes and were GFAP-negative, and we assumed that they were oligodendrocytes. I then tested a number of lectins and antibodies, hoping that some would label these putative oligodendrocytes. I found one that did: antibodies against a major myelin glycolipid—galactocerebroside (GC)—labelled these cells and no others in optic nerve cell cultures [29].

By this time, George Kohler and Cesar Milstein had developed the monoclonal antibody technology that dramatically increased the power of the antibody approach. Perry Bartlett, an Australian postdoc from Johns Hopkins University, made our first monoclonal antibody by immunizing mice with cultured brain astrocytes. He called the cell-surface antigen that the antibody recogn

how the intrinsic mechanism operates. This seemed a worthwhile effort, because we suspected that similar mechanisms probably operate in many types of precursor cells.

An important advance in understanding the intrinsic mechanism came from Ben Barres (who was Barbara Barres at the time). He joined us as a postdoc from Harvard Medical School, where, as a Ph.D. student, he did important work on the physiology of glial cells. He made two critical contributions to the analysis of the intrinsic counting or timing mechanism in OPCs. First, he developed a sequential immunopanning method to purify OPCs from neonatal rat optic nerves [53]. He

The first clue about the molecular nature of the intrinsic timer came from Béa Durand, a postdoc from Strasbourg. She showed that the amount of the cyclin-dependent protein kinase inhibitor $p27^{Kip1}$ progressively increases in the nucleus of purified OPCs as they proliferate in the presence of PDGF and the absence of thyroid hormone [64]. The amount of the protein reaches a plateau at the time when most of the cells would have stopped dividing if thyroid hormone had been present; without the hormone, the cells continue to proliferate, despite the high levels of $p27^{Kip1}$. Béa then collaborated with Jim Roberts in Seattle to show that, in cultures containing PDGF and thyroid hormone, mouse OPCs that are deficient in $p27^{Kip1}$ divide for a day or two longer than wild-type OPCs before they differentiate, suggesting that $p27^{Kip1}$ is one component of the timer [65]. Jim Apperly, a Ph.D. student, showed that over-expression of $p27^{Kip1}$ accelerates the timer, providing further support for a role of $p27^{Kip1}$ in the timing process [66]. As most of the organs in $p27^{Kip1}$-deficient mice contain more cells than normal, it seems likely that $p27^{Kip1}$-dependent timers operate in many types of precursor cells. Yasu Tokumoto went on to show that mRNA levels remain constant as the protein increases in proliferating OPCs, suggesting that the increase in the protein over time depends on post-transcriptional mechanisms that remain to be identified [66].

Toru Kondo showed that the inhibitor of differentiation (Id) protein Id4 is also a component of the timer, although it works in the opposite way from $p27^{Kip1}$ [67]. Id proteins inhibit basic helix-loop-helix gene regulatory proteins that are required for differentiation in many types of precursor cells; in this way, they promote proliferation and inhibit differentiation of the precursors. Toru found that Id4 protein decreases as purified OPCs proliferate in the presence of PDGF and the absence of thyroid hormone and that, in this case, the mRNA and protein decrease in parallel, suggesting that a transcriptional mechanism is probably responsible for the progressive decrease in Id4 protein. Over-expression of Id4 prolongs proliferation and inhibits differentiation, consistent with the idea that the normal fall in Id4 helps determine when OPCs stop dividing and differentiate.

The OPC timer, like other intracellular timers, is still poorly understood. It is clear that it is complex and depends on the progressive increase of some intracellular proteins like $p27^{Kip1}$ and the progressive decrease of others like Id4. Both transcriptional and post-transcriptional controls have roles, but how these controls operate remains a mystery.

Charles ffrench-Constant, a medically trained Ph.D. student, found that there are small numbers of OPCs in cell suspensions prepared from adult rat optic nerves [68]. Like their neonatal counterparts, these adult OPCs are A2B5-positive and develop into type-2 astrocytes when cultured in 10% FCS and into oligodendrocytes when cultured in serum-free conditions, although they differentiate more slowly than do neonatal OPCs. Mark Noble and his colleagues independently found these cells and characterized them in more detail; most important, they showed by time-lapse recording that adult OPCs can develop from neonatal OPCs in culture [69].

We had great difficulty using immunocytochemistry to identify OPCs in the intact developing and adult optic nerve. Julia Burne, a technician turned Ph.D. student, in

collaboration with Barbara Fulton, used a technique developed by Becky Pruss (after she had left London) to label cells, including OPCs, that have Ca^{2+} (and cobalt)-permeable glutamate-activated ion channels [70]. The method used the glutamate agonist quisqualate to stimulate such cells to take up cobalt, which could then be precipitated, enhanced with silver, and visualized by either light or electron microscopy. In this way, Julia and Barbara could specifically label OPCs in the intact rat optic nerve. They found that OPCs acquire progressively more complex cell processes as the nerve matures and that they constitute about five to ten per cent of the cells in the adult optic nerve [71]. They also found that the processes of these cells end on nodes of Ranvier. Previously, Bob Miller and Barbara had injected horseradish peroxidase into individual cells in the adult optic nerve and found that some cells extend processes exclusively to nodes [72]; we originally thought that these cells were type-2 astrocytes, but it is now clear that they are OPCs, as was later confirmed by Arthur Butt and his colleagues at King's College London [73].

Adult OPCs are among the most interesting cells in the mammalian CNS. They are among the few cell types that Cajal missed, although they are 5–10% of the cells throughout the CNS (excepting the retina), as assessed by staining with antibodies against the NG-2 proteoglycan, which Joel Levine and Bill Stallcup at the Salk Institute originally showed recognize OPCs [74]. In white matter, OPCs send their processes to nodes of Ranvier, and in both white and grey matter, they receive excitatory synapses, as convincingly shown by Dwight Bergles and his colleagues at Johns Hopkins Medical School [75]. They proliferate in response to injury and can produce new oligodendrocytes in response to myelin damage [76]. Given their abundance in both white and grey matter, their complex morphology, and the low rate of oligodendrocyte turnover in the normal CNS, it seems unlikely that the normal function of adult OPCs is simply to replace lost oligodendroctytes, but their other functions remain a mystery. There is a pressing need to study the consequences of eliminating these cells in the adult CNS.

Why do OPCs become progressively more complex during development? Is it because their environment changes, because they intrinsically mature over time, or both? Fen-Biao Gao showed that perinatal OPCs have an intrinsic developmental program that changes many aspects of the cell over time [59]. He first compared the

his colleagues at Stanford showed earlier that OPCs in the rat optic nerve start to express GC after many months [78]. It seems that the intrinsic OPC maturation program continues to change the cells for months, which is remarkable. Intracellular programs that change developing cells over time are among the most mysterious processes in development and deserve much more attention than they have received.

We were surprised to find that OPCs did not undergo replicative cell senescence and permanently stop dividing, even after more than a year of proliferation in culture. The cells remain diploid, and unlike genetically immortalized cells, they maintain p53-dependent and Rb-dependent cell-cycle checkpoint mechanisms [79]. Dean could rapidly induce them to acquire a senescent phenotype by culturing them in FCS or by treating them with DNA-damaging drugs. At the same time, Alison Lloyd and her colleagues had obtained very similar results with purified rat Schwann cells [80]. Together, these studies showed that, unlike human cells, some normal rodent cells can apparently proliferate indefinitely in culture: they continue to express telomerase and therefore do not undergo progressive telomere shortening and uncapping, which cause normal human cells to stop dividing after a limited number of divisions, a process logically called replicative cell senescence. So-called replicative senescence in rodent cells, by contrast, results from "culture shock" caused by high concentrations of serum and/or oxygen or by other stresses, rather than from a telomere-dependent cell-division counting mechanism [81].

The isolation of human embryonic stem (ES) cell lines and embryonic germ (EG) cell lines in 1998 triggered a cascade of hope, hype, and hysteria that continues to amplify to this day. A surprising observation by Toru Kondo dropped us into the middle of this stem cell madness. We had supposed that OPCs were committed to becoming oligodendrocytes (and possibly type-2 astrocytes), but Toru showed that this was not the case: they could be reprogrammed by extracellular signals to become multipotential cells that can produce both neurons and glia [82]. He found that, if he treated purified OPCs with BMPs for two to three days and then with basic fibroblast growth factor (FGF-2), the OPCs convert to a phenotype that closely resembles CNS neural stem cells. They can proliferate indefinitely in FGF-2, and depending on the signal proteins in the culture medium, they are able to give rise to type-1 astrocytes and neurons, as well as to oligodendrocytes and type-2 astrocytes, just as CNS neural stem cells. Thus, OPCs are specified to become oligodendrocytes, but they are clearly not irreversibly committed to do so.

As mentioned earlier, the BMPs induce OPCs to become type-2 astrocytes, and Toru showed that this step is required for the conversion of purified OPCs to stem-like

extracellular signals to avoid apoptosis in culture. For these cells, the signals are autocrine factors secreted by other lens epithelial cells or chondocytes, respectively. Miguel Weil, a postdoc from Israel, Mike Jacobson, a postdoc from UCSF, Harriet Coles, a Ph.D. student from Oxford, and my daughter Kim, who spent time in the lab while at university, together showed that all of the nucleated cells in various explanted mouse organs can be induced to undergo apoptosis if they are treated with a high concentration of the protein kinase inhibitor staurosporine in the presence of the protein synthesis inhibitor cycloheximide [91]. These findings suggested that all nucleated mammalian cells can undergo apoptosis and that they constitutively express all the proteins required to do so.

Ben Barres studied the role and regulation of apoptosis during oligodendrocyte development . Many years earlier, Sam David, a postdoc from Montreal, obtained indirect evidence that axons may promote the survival of oligodendrocytes and/or their precursors in the developing optic nerve. He found that transection of the neonatal rat optic nerve results in a dramatic decrease in both oligodendrocytes and OPCs [92]. Ben now showed that fifty per cent or more of the oligodendrocytes produced in the normal developing rat optic nerve die by apoptosis, apparently in a competition for limiting amounts of survival signals provided by the axons [53]. He showed that transection of the rat optic nerve at the end of the first week of postnatal life causes most of the newly formed oligodendrocytes in the nerve to die by apoptosis, as expected if these cells require signals from axons to survive [93]. Julia Burne then studied transgenic mice made by Jean-Claude Martinou in Geneva that over-express the gene in neurons, including retinal ganglion cells (RGCs). Because Bcl-2 suppresses apoptosis, it decreases the RGC death that occurs during normal retinal development and thereby increases the number of axons in the transgenic optic nerve. She showed that, as a consequence of the increase in axons, oligodendrocyte cell death in the developing transgenic optic nerve is greatly reduced, so that the number of oligodendrocytes is increased to match the increase in axon numbers [94]. (Julia later showed that the increase in axons is also associated with an increase in astrocyte numbers in the nerve, but in this case it is because the axons stimulate astrocyte proliferation rather than astrocyte survival during development [95].) Some years later, Pierre-Alain Fernandez, a French postdoc, showed that our old friend GGF is an important axon-associated survival signal for oligodendrocytes in the developing optic nerve [96].

Earlier, Ben had found that axons in the developing optic nerve also stimulate OPC proliferation or survival [97]. Thus, his work indicated that axons increase oligodendrocyte numbers by promoting both oligodendrocyte survival and the proliferation or survival of their precursors. He showed that the proliferation or survival effect on OPCs depends on electrical activity in the axons [97], whereas the survival effect on oligodendrocytes does not [53].

When we first started working on cell death, very little was known about the nature of the intracellular apoptotic program. In addition to showing that the death machinery is ubiquitously and constitutively expressed, our contributions to understanding the nature of the program were largely to show what is not required. Mike Jacobson showed that it does not require the presence of a nucleus [98], which was surprising at the time, given that nuclear condensation and fragmentation are central features of apoptosis. Others had reported that the Bcl-2 protein is located in the inner mitochondrial membrane, raising the possibility that both apoptosis and its inhibition by Bcl-2 might depend on oxidative phosphorylation. Mike excluded

these possibilities by showing that cells without mitochondrial DNA, which are incapable of oxidative phosphorylation, can still undergo apoptosis and that Bcl-2 can still protect them [99]. Similarly, it had been suggested that the apoptotic program depends on the generation of reactive oxygen species and that Bcl-2

Axonal “dying back", for example, occurs in many neurodegenerative diseases. In this process, there is a progressive degeneration of the axon over weeks or months, beginning distally and spreading toward the cell body. The selective degeneration of an axon, without the death of the parent neuron, can also occur in response to local injury and to a variety of metabolic, toxic, and inflammatory disorders, as well as during normal neuronal development. Some forms of axonal degeneration,

rise to the photoreceptors, neurons, and Müller glial cells of the retina, but not to the astrocytes. These landmark lineage studies, performed independently by Turner and Cepko [110], Holt and Harris and their colleagues [111], and Wetts and Fraser [112], identified the central question in retinal cell diversification: how do the multipotential precursors decide what type of retinal cell to become?

Takashi began to address this question by studying the timing of rod development. Using anti-rhodopsin antibodies to unambiguously identify rods, he found that the first rods appear in small numbers in the rat retina at E20 and then increase rapidly for the next week or so. Although rhodopsin-positive rods failed to develop in dissociated-cell cultures of E15 retina, they did develop right on schedule if the E15 cells were centrifuged into a pellet that was then cultured on a floating polycarbonate filter. The pellet culture system allowed him to mix cells from different developmental ages. He labelled the DNA in proliferating E15 cells with bromodeoxyuridine (BrdU) and mixed the labelled cells with a fifty-fold excess of unlabelled newborn retinal cells. The surprising finding was that the labelled E15 cells did not give rise to rods until the equivalent of E20, just as they did when cultured alone [113]. Thus, the presence of the newborn cells, which were producing large numbers of rods from the start of the culture, did not affect the timing of rod development by the E15 cells. The result was unexpected because all three laboratories that had done the lineage tracing studies had concluded that retinal precursor cells remain uncommitted until around the last cell division, when extracellular signals dictate what the daughter cells become. (They came to this conclusion largely because they found two-cell clones of mixed cell type.) Takashi's

FCS indirectly arrests rod development. Interestingly, FCS, for unknown reasons, does not stimulate Müller cell proliferation in pellet cultures, which is why rhodopsin-positive rods develop in these cultures even in the presence of FCS. Costas's findings corrected earlier findings that were interpreted to show that CNTF and LIF re-

feedback we received, as well as from the many reagents we obtained from other scientists.

I also learned from Av the value of reporting back on the scientific meetings I attended. I attended many meetings and felt guilty being away so much. The most compelling justification was that I sometimes learned things at a meeting that saved us months or years of work. Thus, whenever I turned down an invitation to a meeting, I had nightmares that I would miss something of overwhelming

2. **Raff M. (1969) Theta isoantigen as a marker of thymus-derived lymphocytes in mice. Nature, 224, 378-9.**
3. **Raff MC. (1970) Role of thymus-derived lymphocytes in the secondary humoral immune response in mice. Nature, 226, 1257-8.**
4. **Owen JJ, Raff MC. (1970) Studies on the differentiation of thymus-derived lymphocytes. J Exp Med, 132, 1216-32.**
5. **Raff MC, Owen JJ. (1971) Thymus-derived lymphocytes: their distribution and role in the development of peripheral lymphoid tissues of the mouse. Eur J Immunol, 1, 27-30.**
6. **Raff MC, Sternberg M, Taylor RB. (1970) Immunoglobulin determinants on the surface of mouse lymphoid cells. Nature, 225, 553-4.**
7. **Raff MC. (1970) Two distinct populations of peripheral lymphocytes in mice distinguishable by immunofluorescence. Immunology, 19, 637**

32. **Klymkowsky MW. (1981) Intermediate filaments in 3T3 cells collapse after intracellular injection of a monoclonal anti-intermediate filament antibody. Nature, 291, 249-51.**

33. **Eisenbarth GS, Walsh FS, Nirenberg M. (1979) Monoclonal antibody to a plasma membrane antigen of neurons. Proc Natl Acad Sci U S A, 76, 4913-7.**

34. **Raff MC, Miller RH, Noble M. (1983) A glial progenitor cell that develops in vitro into an astrocyte or an oligodendrocyte depending on culture medium. Nature, 303, 390-6.**

35. **Mirsky R, Wendon LM, Black P, Stolkin C, Bray D. (1978) Tetanus toxin: a cell surface marker for neurones in culture. Brain Res, 148, 251-9.**

36. **Raff MC, Abney ER, Miller RH. (1984) Two glial cell lineages diverge prenatally in rat optic nerve. Dev Biol, 106, 53-60.**

59. **Gao FB, Raff M. (1997) Cell size control and a cell-intrinsic maturation program in proliferating oligodendrocyte precursor cells. J Cell Biol, 138, 1367-77.**

60. **Gao FB, Durand B, Raff M. (1997) Oligodendrocyte precursor cells count time but not cell divisions before differentiation. Curr Biol, 7, 152-5.**

61. **Hart IK, Richardson WD, Heldin CH, Westermark B, Raff MC. (1989) PDGF receptors on cells of the oligodendrocyte-type-2 astrocyte (O-2A) cell lineage. Development, 105, 595-603.**

62. **Hart IK, Richardson WD, Bolsover SR, Raff MC. (1989) PDGF and intracellular signaling in the timing of oligodendrocyte differentiation. J Cell Biol, 109, 3411-7.**

63. **Hart IK, Richardson WD, Raff MC. (1992) PDGF increases the expression of Fos and Jun in newly formed oligodendrocytes that have become resistant to the mitogenic effect of PDGF. Glia, 6, 310-3.**

64. **Durand B, Gao FB, Raff M. (1997) Accumulation of the cyclin-dependent kinase inhibitor p27/Kip1 and the timing of oligodendrocyte differentiation. Embo J, 16, 306-17.**

65. **Durand B, Fero ML, Roberts JM, Raff MC. (1998) p27Kip1 alters the response of cells to mitogen and is part of a cell-intrinsic timer that arrests the cell cycle and initiates differentiation. Curr Biol, 8, 431-40.**

66. **Tokumoto YM, Apperly JA, Gao FB, Raff MC. (2002) Posttranscriptional regulation of p18 and p27 Cdk inhibitor proteins and the timing of oligodendrocyte differentiation. Dev Biol, 245, 224-34.**

67. **Kondo T, Raff M. (2000) The Id4 HLH protein and the timing of oligodendrocyte differentiation. Embo J, 19, 1998-2007.**

118. **Jensen AM, Raff MC. (1997) Continuous observation of multipotential retinal progenitor cells in clonal density culture. Dev Biol, 188, 267-79.**

119. **Neophytou C, Vernallis AB, Smith A, Raff MC. (1997) Muller-cell-derived leukaemia inhibitory factor arrests rod photoreceptor differentiation at a postmitotic pre-rod stage of development. Development, 124, 2345-54.**

120.

(ammended Jan. 2018)

Mike Klymkowsky	80–82	UCSF	University Colorado, Boulder

Miguel Weil	94–98	Hebrew U.	Tel-Aviv University.
Béa Durand	94–97	Inst. de Chimie Biol., Strasbourg	Institut Curie, Paris
Fen-Biao Gao	95–97	Duke U.	University Massachussets Med
John Finn	97–99	Johns Hopkins	US Dept. Homeland Security
Yasu Tokumoto	97–02	Tsokuba U.	Saitama Medical University

Erica Abney	77–82	U. Mexico	Homeopathic practitioner, London
Jim Cohen	78–85	Open U., UK	Retired, London
Rhona Mirsky	79–81	Dartmouth Med.	Emeritus, UCL
Anne Mudge	81–95	Harvard Med.	Retired
Bob Miller	85–87	Case Western Reserve U.	George Washington U. Med, D.C.
Steve Moss	91–93	Johns Hopkins Med.	Tufts University
Research Assistants			
Mary Megson	72–76	USA	USA
Anne Hornsby-Smith	76–78	South Africa	South Africa
Jelena Gravilovic	78–81	UCL	U. East Anglia, UK
Julia Burne	85–98	St. Thomas's Hospital, London	Retired, London
Michele Binder	99–02	Melbourne U.	Florey Institute, Australia
Christine Jolicoeur	99–02	Laval U., Quebec	Montréal Clinical Research Institute
Sabbatical Visitors			
David Samuel	74–75	Weizmann Inst.	Deceased

Murray Freedman

[redacted]

Jerry Gross	76	Harvard Med.	Deceased