BIOGRAPHICAL MEMOIRS

John Bertrand Gurdon

October 2, 1933–October 6, 2025
Elected to the NAS, 1980

A Biographical Memoir by Edward M. De Robertis and Douglas A. Melton

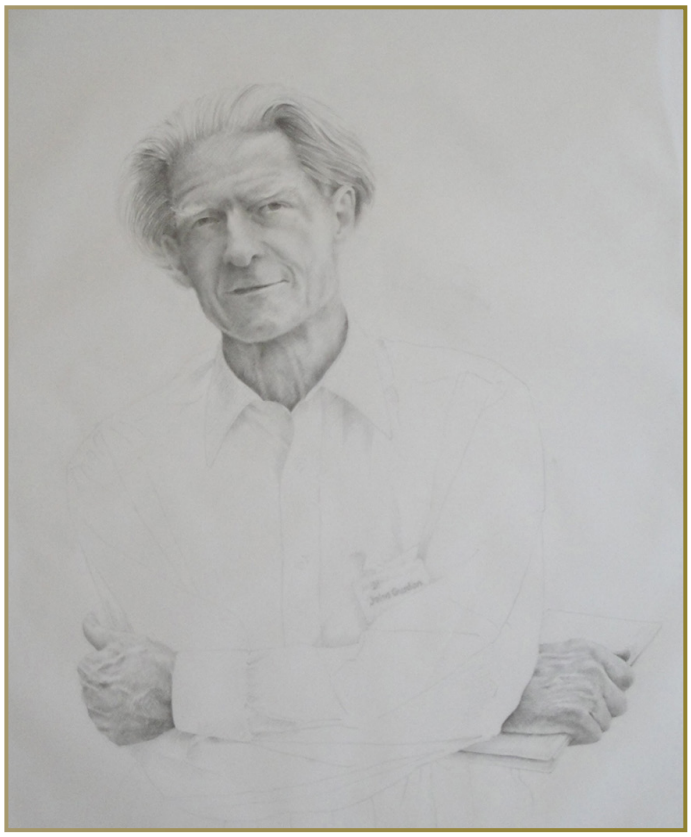

Figure 1 Portrait of Sir John Gurdon. *Courtesy of the artist, Prof. Nadia Rosenthal of the Jackson Laboratories.*

Sir John Gurdon was blessed with an important discovery at age twenty-five and used his good fortune for the common good of developmental biologists. As a graduate student, he demonstrated that differentiated cells retained the complete gene repertoire to form all cell types of the body. He developed the *Xenopus* oocyte as a living test tube for molecular biology. His oocyte microinjection studies provided the first vertebrate system to translate mRNA, transcribe DNA, and express cloned genes. He investigated the reprogramming of somatic nuclei to the gene expression pattern of oocytes for many decades. The discovery that differentiated cells could be reprogrammed to become pluripotent was recognized with the 2012 Nobel Prize for Medicine, shared with Shinya Yamanaka. He was the quintessential English gentleman, who taught by example and built new research institutions. His tireless support for scientific societies led him to deliver lectures throughout the world that were a model of clarity, inspiring generations of developmental biologists. His secret weapon was to never stop working at the bench with his beloved oocytes and embryos.

Early Life and Education

John Bertrand Gurdon came from a distinguished English family of Norman origin. A village named Gurdon still exists in Normandy, and his genealogical tree records the names John and Bertrand numerous times. A Bertrand (Bertram) de Gurdon was recorded in 1199, and a John (Jean) de Gurdon is listed circa 1400. Centuries of Gurdons rest in a graveyard in the village of Assington in Suffolk. Although several Gurdons were knighted, John's branch did not inherit a title. One of his second cousins, also named Gurdon, is currently a hereditary peer of the House of Lords. In 1995, Sir John received the title of Knigh Bachelor from the British Crown for his contributions to science, a well-deserved acknowledgement.

John's parents lived in India, and his banker father made his fortune before returning to the United Kingdom.John was born on October 2, 1933, in Surrey and was sent with his sister Catherine to the safety of the countryside during

World War II. Later in life, he was reluctant to discuss any penuries during this period.

Gurdon's early education is described in a beautiful autobiographical review.[1] Despite a childhood interest in butterflies, at Eton boarding school John was deemed unsuitable for science. In a now-famous report card, his biology Master wrote:

> I believe Gurdon has ideas about becoming a scientist. On present showing this is quite ridiculous. If he can't learn simple biological facts he would have no chance of doing the work of a specialist, and it would be a sheer waste of time both on his part and of those who would have to teach him.

Later, John had this report framed and kept it above his desk in the lab. Consequently, his education at Eton specialized in Latin and Greek. A competitive sportsman, he concentrated on becoming captain of the squash team, which he did. He was admitted to Oxford University after taking the entrance exam, but on the condition that he would not study Latin or Greek, as he was below standards. Wishing to study biology, he took a remedial year before entering a doctor of philosophy program. John was rejected by the Entomology Department but accepted by the Zoology Department. In a happy day for developmental biology, during his remedial year of study, John's embryology teacher was the Russian émigré Michaïl Fischberg, who asked if he would be interested in doing Ph.D. work with him. Fischberg proved to be an exceptional mentor.

Genetic Information Is Not Lost during Cell Differentiation

Fischberg worked with *Xenopus laevis*, a South African frog, that has the advantage of laying eggs throughout the year after stimulation with human chorionic gonadotropin. These frogs were widely used as a pregnancy test. Fischberg had trained with Ernst Hadorn in Zürich, who had studied with Fritz Baltzer in Bern, who had studied with Theodor Boveri (together with Hans Spemann) in Würzburg, altogether an impressive lineage of biologists. Thus, through John Gurdon, a multitude of current *Xenopus* researchers can trace their lineage to Boveri, the founder of European cell biology. Three months into John's Ph.D., Fischberg suggested repeating the nuclear transplantation experiments that Robert Briggs and Thomas King had recently performed in the frog *Rana pipiens*. The problem addressed was a classical one in embryology: is genetic potential lost during cell differentiation? This idea can be traced to August Weismann, who in the 1890s, inspired by the phenomenon of chromatin diminution in the nematode worm *Ascaris,* had proposed that genetic material was lost in differentiated somatic (body) cells but was kept intact in the germ line. Briggs and King found that transplanted nuclei from blastula stages kept their totipotency and gave rise to tadpoles. But when they took nuclei from older, tailbud tadpoles, the frequency went down to almost nothing.[2] They concluded that totipotency was lost in later development.

Using *Xenopus* embryos and an improved enucleation method with ultraviolet light, Gurdon found that in *Xenopus,* transplanted single nuclei could give rise to mature frogs even from neural plate and tailbud tadpole stages.[3] These experiments were enhanced by the foresight of Fischberg, who had a spontaneous mutant observed in the lab that had a single nucleolus rather than the usual two. The number of nucleoli served as a lineage tracer and was essential to demonstrate that the genetic material came from the transplanted nucleus and not from the host egg.

Gurdon published this landmark discovery at age twenty-five and continued to be driven by an unquenchable curiosity. He proceeded to show that nuclei of differentiated cells had a full developmental potential.[4] He chose endodermal cells from advanced feeding tadpoles that could be recognized as differentiated because of their cylindrical shape and brush border of microvilli for nutrient absorption. Improving the transplantation technique, he reached a frequency of 24 percent normal development. When John left for his postdoc at the California Institute of Technology (Caltech), Fischberg accepted a professorship in Switzerland and, most fortunately, took Gurdon's tadpoles with him to Geneva, where they were raised by his technician, Verena. , and shown to be fertile.[5] Michaïl Fischberg generously declined authorship. These experiments established that genetic information is not lost during cell differentiation. Differentiated somatic cells could be reprogrammed and maintained the complete set of genes required for development.

Like many important discoveries in science, Gurdon's nuclear transplantation results were initially met with skepticism, and it took him fifty years to receive the Nobel Prize. Some argued that he might have inadvertently picked germ cells instead of differentiated cells as the nuclear donor or that advanced feeding tadpoles are not really adults. John forged ahead and kept doing the experiment in various ways for the next decade. For example, he transplanted keratin-positive epidermal nuclear donors obtained from adult foot-web explants of 1-nucleolus frogs and obtained clones by serial nuclear transplantation.[6] All objections dissipated when Dolly the sheep was cloned in Scotland.[7] Named after country singer Dolly Parton, this sheep was obtained through the fusion of the nucleus of a cell from an adult mammary gland with an oocyte. The path was open for nuclear reprogramming in mammals. Shinya Yamanaka was

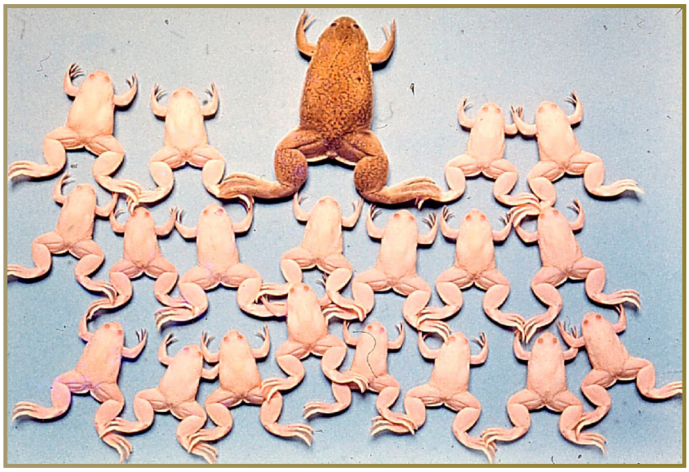

Figure 2 Clone of Xenopus laevis frogs derived by nuclear transplantation of nuclei originating from a single embryo. The donor nuclei were transplanted into the eggs of a wild-type pigmented female (shown at top center) and marked by both the 1-nu mutation and an albino mutation. All members of the clone were male. *Reprinted with permission from Gurdon, J. B. 2013. The egg and the nucleus: A battle for supremacy.* Development *140(12):2449–2456.*

able to reprogram fibroblasts into induced pluripotent stem cells (iPSC), dispensing with oocyte cytoplasm altogether by simply transfecting a cocktail of four transcription factors into mouse and later human fibroblasts.[8] The discovery of iPSCs opened the stem cell field to patient-derived iPSC disease models and tissue replacement therapies. The revolutionary Yamanaka reprogramming factors and the pioneering studies of Gurdon were a perfect match, recognized by the 2012 Nobel Prize in Physiology or Medicine for "the discovery that mature cells can be reprogrammed to become pluripotent."

A Living Biochemical Test Tube for Molecular Biology

In 1962, Gurdon undertook a one-year postdoctoral stay at Caltech to work on bacteriophage genetics. Although no publications resulted from this period, John met many interesting scientists at the famed Athenaeum Faculty Club, which he remembered fondly. Among these was James Ebert, director of the Carnegie Institute of Embryology in Baltimore, who introduced John to Donald D. Brown, a new staff member working with *Rana*.

Gurdon and Brown struck what would be an enduring friendship, cemented by a mutual love for tennis. John sent him the *1-nucleolus Xenopus* mutant, and it was found that *0-nucleolus* homozygous mutant tadpoles completely lacked synthesis of large ribosomal RNAs.[9] This was a momentous discovery that established the nucleolus as the site of ribosome biosynthesis. At Carnegie, Don Brown introduced his postdoc Igor Dawid to *Xenopus* eggs, which he later used to discover mitochondrial DNA. In this way, many scientists working on *Xenopus* in the United States today can trace their research back to a young John Gurdon.

The appointment of Fischberg as a professor in Geneva opened the way for Gurdon to return to Oxford, although to a junior position. There, he initiated investigations into nucleic acid synthesis, showing that (a) multiple brain nuclei introduced into fertilized eggs synthesized DNA, (b) oocytes matured with progesterone did not synthesize DNA but instead condensed the chromosomes, and (c) oocytes dissected from the ovary (where they are arrested in meiotic prophase) promoted RNA synthesis.[10] Using a modified saline solution, he could keep oocytes alive for many days and weeks. The cell cycle differences in nuclear activity among oocytes, maturing oocytes, and eggs provided the basis for the discovery of maturation promoting factor and cytostatic factor by Yoshio Masui in Canada and earned Tim Hunt a Nobel Prize.

During studies on nucleocytoplasmic interactions, Gurdon first recognized the potential of introducing purified molecules into living oocytes. He iodinated histone proteins and found that when injected into oocyte cytoplasm, they were transported into the giant oocyte nucleus, called the germinal vesicle. This meant that the signal sequence for nuclear transport resided in a mature nuclear protein and thereby opened an entire field of research. This work, introducing the first purified molecules into an oocyte, went mostly unrecognized because it was published within a review paper.[11]

Gurdon's introduction of the *Xenopus* oocyte as a test tube for molecular biology was worthy of a Nobel Prize in its own right. Previously, amphibian embryos had been used by embryologists to analyze the rapid succession of events occurring during development. Oocytes dissected from the abdomen of female frogs could be cultured for weeks without

Figure 3 John Gurdon returning to the famed Caltech Athenaeum sixty years after his postdoctoral studies. *Photo by Eddy De Robertis.*

dividing and were biochemically active, providing a powerful assay system for the emerging field of molecular biology. In 1971, a truly daring experiment was performed. The group of Jean Brachet in Belgium had purified a sedimentation peak of 9S from rabbit reticulocytes that was suspected to consist of globin mRNA. However, no system to translate mRNA into protein existed at the time. Gurdon and colleagues showed that microinjected purified mRNA was able to direct the abundant synthesis of rabbit globin in *Xenopus* oocytes.[12] This was a revolutionary assay system that has since been used in myriad experiments studying not only the synthesis of proteins, but also their cell trafficking, secretion, and function as neurotransmitter membrane receptors in living oocytes. Following the introduction of synthetic mRNA from cloned genes, *Xenopus* embryos became a very valuable test system.[13] The work on mRNA translation led to an invitation to join the Medical Research Council's Laboratory of Molecular Biology (LMB) in Cambridge, United Kingdom.

The LMB was at the very center of the rise of molecular biology. The chair at that time was Max Perutz, and one could not walk a corridor without seeing luminaries such as Francis Crick, Fred Sanger, Aaron Klug, Sydney Brenner, Cesar Milstein, and others who would go on to earn Nobel Prizes. It was a very exciting period, when Sanger was inventing DNA sequencing and Cesar Milstein was developing monoclonal antibodies. Discussions at lunch in the canteen looked after by Gisela Perutz were memorable, as were the coffee and tea breaks. There were no formal group meetings, but researchers discussed experiments at length in the canteen. The philosophy at the LMB was that no one was to be co-author in a paper to which he or she had not made a meaningful contribution, by which it was meant at least one figure. This stimulated the free exchange of ideas in the British scientific tradition of "measure twice, cut once". The Gurdon lab became a magnet for postdoctoral fellows. John would experiment alongside them while collaborateing on specific projects with only two, or at most three, at any one time.

Following the microinjection of mRNA, transcription of DNA was the next logical step. During experiments involving microinjecting multiple somatic nuclei into oocytes, John noticed that sometimes the injected material remained inside the large oocyte nucleus. By injecting into the animal (top) oocyte pole, it was possible to introduce SV40 DNA, which was then transcribed by RNA polymerase II in the germinal vesicle.[14] In a parallel transatlantic collaboration with his friend Don Brown, John showed that RNA Polymerase III could transcribe *Xenopus* 5S rDNA purified by density gradient centrifugation.[15] In follow-up studies, it was shown that cloned recombinant genes could be transcribed into mRNA and translated into protein.[16] At that time, recombinant DNA cloning was revolutionizing biology, but there were no efficient means of expressing the cloned sequences, with the oocyte system representing an exception.[16,17]

During these years, John received many more invitations to speak at conferences than he could possibly attend. With typical generosity, he sent the authors, Ronald Laskey, and others as his substitutes. We became far better known than deserved during those exciting days for molecular biology. His rising tide lifted all boats.

After Max Perutz retired as chair of the LMB in 1983, Gurdon and his longtime collaborator, Ron Laskey, started a new Cancer Research Campaign (CRC) institute as part of the Department of Zoology at the University of Cambridge. John became interested in how cells perceive small variations in concentration and duration of a gradient of Activin, a mesoderm-inducing factor discovered by James C. Smith. He found that muscle differentiation required the interaction of a few hundred induced cells interacting close to each other, leading to the proposal of a "community effect" during development to explain the formation of blocks of tissues in the embryo.[18,19]

Nuclear Reprogramming and the Battle for Supremacy between Nucleus and Cytoplasm

The leitmotif of Gurdon's research was his relentless pursuit of how nuclear reprogramming of somatic cells is achieved. Beginning with experiments using brain nuclei introduced into oocytes in 1968, he continued to pursue this line of research throughout his career. He devised methods to gently isolate nuclei from cultured mammalian cells and investigated the molecular changes after reprogramming of multiple injected somatic nuclei into oocytes.[20] Microinjection of nuclei from a *Xenopus* kidney cell line into oocytes of the newt *Pleurodeles waltlii* caused the reprogrammed nuclei to reactivate specifically the expression of oocyte-type proteins and, remarkably, this reprogramming took place in the complete absence of DNA replication.[21] This is unlike the case of iPSCs, which require extensive cell division. Later, the expression of stem cell factors such as Oct-4 was found to be reactivated in oocytes.[22]

There is a "battle for supremacy" between the oocyte cytoplasm and somatic nuclei.[23] Differentiated nuclei resist reprogramming through epigenetic modifications in DNA and histones that attempt to keep stem cell pluripotency genes turned off, but they are overwhelmed by the vast supply of oocyte cytoplasm.[24] Once a transcription complex is assembled in the oocyte, it is stable for hours and days, as revealed through DNA competition experiments.[25] Even at age ninety, Gurdon was reactivating pluripotency genes in mouse embryonic fibroblasts by treating them with extracts of manually isolated oocyte germinal vesicles after transient permeabilization of the plasma membrane.[26]

Figure 4 Sir John Gurdon. *Image credit: Wellcome Collection.*

A Lifetime of Dedication to Institutions for the Common Good

Gurdon embodied the principle that to whom much is given much is expected. Despite never ceasing work at the bench, he made time to serve the institutions that move the machinery of science forward. He served as Master of Magdalene College, Cambridge, and as Governor of the Wellcome Trust. He was an indefatigable supporter of scientific societies because, as he liked to say, they are built by scientists for other scientists. These efforts took him throughout the world giving lectures that were models of clarity. At meetings, he dutifully visited as many poster sessions as possible, asking incisive questions and bringing joy to many young students. He enjoyed traveling, especially to exotic locations in Asia and Latin America, where he could indulge his hobby of chasing butterflies. He was remarkably disciplined in his use of time: microinjection experiments on Tuesdays and all correspondence answered on Fridays. His knighthood and Nobel Prize were very well earned, for he was not only a remarkable scientist but also a builder of institutions.

Concluding Remarks

Sir John passed away peacefully at home surrounded by his family at age ninety-two. He was a generous gentleman who mentored generations of scientists through example. An unquenchable curiosity was his driving force. Through a deep sense of duty to the institutions that keep science running, his beneficial influence spread throughout developmental biology. A passion for science led him to tirelessly experiment with frog eggs and oocytes in a long and very interesting life. He was the archetypal English gentleman. He and his wonderful wife, Jean, created a welcoming atmosphere for his many trainees. John's example and wonderful smile will be remembered by those fortunate to know him. His long and interesting life epitomized the Golden Rule of Western Civilization—love your neighbor as yourself—to the great benefit of biology. In sum, John Gurdon was a good man.

Acknowledgments

This memoir is based on obituaries by Edward M. De Robertis,[27] Douglas A. Melton and Edward M. De Robertis,[28] and Gurdon's autobiographical review.[1]

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