John Bertrand Gurdon (1933–)

Sir John Bertrand Gurdon further developed nuclear transplantation, the technique used to clone organisms and to create stem cells, while working in Britain in the second half of the twentieth century. Gurdon's research built on the work of Thomas King and Robert Briggs in the United States, who in 1952 published findings that indicated that scientists could take a nucleus from an early embryonic cell and successfully transfer it into an unfertilized and enucleated egg cell. Briggs and King also concluded that a nucleus taken from an adult cell and similarly inserted into an unfertilized enucleated egg cell could not produce normal development. In 1962, however, Gurdon published results that indicated otherwise. While Briggs and King worked with Rana pipiens frogs, Gurdon used the faster-growing species Xenopus laevis to show that nuclei from specialized cells still held the potential to be any cell despite its specialization. In 2012, the Nobel Prize Committee awarded Gurdon and Shinya Yamanaka its prize in physiology or medicine for for their work on cloning and pluripotent stem cells.

Gurdon was born 2 October 1933, in Hampshire, England. From a young age animals interested him, and he later recalled raising thousands of caterpillars during his childhood. Gurdon's parents believed in the importance of education, and so he attended Eton College, a prestigious boys' school near Windsor, England. At the age of fifteen, after completing his first semester of science education at Eton, Gurdon's schoolmaster reported that Gurdon was the worst pupil he had ever taught and that it would be a waste of time for him to pursue science. Following this report, Gurdon instead studied classics, though he remained interested in the life sciences, serving as secretary of the Natural History Society at Eton.

After Eaton, Gurdon attended Christ Church College at Oxford University, in Oxford, England. Though he intended to continue to study classics, his admittance was dependent on studying zoology, as the University had a shortage of science majors. Gurdon worked with Sir Alister Hardy at Oxford, and he graduated with First Class Honors. In 1956, Gurdon applied to the zoology department to begin his doctorate, originally intending to work with an entomologist. However, the entomology professor rejected Gurdon. Instead, he worked with the embryologist Michael Fischberg.

With the direction of Fischberg, Gurdon began to work with the new techniques of nuclear transplantation, applying them to a species of African frogs, Xenopus laevis. Gurdon's dissertation argued that adult cells maintained their totipotency, or their ability to become any cell type. Gurdon's first attempts at nuclear transplantation failed, as the Xenopus eggs prevented the insertion of the micropipette necessary to manipulate the nucleus. This problem was solved when Fischberg procured an ultraviolet light for his microscope. To his surprise, when Gurdon subjected Xenopus eggs to the proper frequency of UV light, the tough gel coating of the egg softened, allowing him to insert a foreign nucleus using a micropipette. The UV light also effectively enucleated the egg by irrevocably damaging the native DNA and allowing the inserted nucleus to initiate development. Gurdon soon succeeded in replicating the results of Briggs and King, and he poduced normal tadpoles from nuclear transplanted embryos that had nuclei from early blastula and gastrula cells. However, despite this success, Gurdon was unsure about the accuracy of his results.

Gurdon devised another experiment to verify that the tadpoles were a product of the transplanted genetic material and not of the deactivated resident nucleus of the egg. Another student of Fischberg's, Sheila Smith, had recently found a mutation in the number of nucleolus in Xenopus. The mutation eliminated a nucleolus, a small organelle located within the nucleus, leaving only one. Gurdon transplanted nuclei that exhibited the mutation into normal oocytes and found that the

resulting tadpoles exhibited the traits associated with the mutated nuclei, proving that the frogs developed using the donor nucleus, not the irradiated host DNA.

After Gurdon succeeded using nuclei from the same stages that Briggs and King had used, he began to use nuclei from more specialized cells. In 1956, Briggs and King had concluded that the nucleus of a fully differentiated somatic cell, such as a liver cell or an intestinal cell, could not guide the development of a new organism. In other words, Briggs and King believed that something physically occurred to the DNA of cells as they moved from the undifferentiated cells of an early embryo to the specialized cells that make up mature organisms. However, by 1962, Gurdon successfully produced tadpoles using nuclei taken from gut cells of swimming tadpoles by using the same procedures. Gurdon reported the findings in "Adult Frogs Derived from the Nuclei of Single Somatic Cells," refuting Briggs and King's argument that no adult cells could ever produce viable clones. Despite the skepticism from many scientists, including those of his advisor Fischberg and especially from the laboratory of Briggs and King, Gurdon continued to advocate his conclusions.

After he was awarded his doctorate from Oxford in 1960, Gurdon accepted a postdoctoral position at the California Institute of Technology in Pasadena, California. He worked with Robert Edgar on bacteriophage, using the then most recent molecular biology techniques. However, Gurdon said that he had trouble working with bacteriophage. Still, Gurdon said he learned much, and for the rest of his career, he integrated molecular analysis into his nuclear transplantation work.

In 1962, Gurdon returned to Oxford, replacing his advisor in the Department of Zoology after Fischberg had left for a position in Geneva. Gurdon worked at Oxford until 1971, when he moved to the University of Cambridge in Cambridge, England and joined the Medical Research Council's (MRC) Laboratory of Molecular Biology. While at the MRC, Gurdon mentored a number of post-doctoral students, including Edward De Robertis. Gurdon eventually became the head of the Cell Biology Division at the MRC, before he moved to the University of Cambridge's Zoology Department to accept the John Humphrey Plummer Professorship of Cell Biology in 1983.

From 1983 to 2000, Gurdon served as a research professor in the Department of Zoology. He was also a founding member of the Cancer Research Campaign Unit of Molecular Embryology at Cambridge along with Ron Laskey. Between 1990 and 2001, he chaired the Wellcome CRC Institute of Cancer and Developmental Biology at Cambridge, and from 1995 to 2000 he served as Governor of the Wellcome Trust. He also was the Master of Magdalene College at Cambridge from 1995-2002. In 2004, the Wellcome Institute was renamed the Gurdon Institute in his honor.

Gurdon's discovery, that an adult nucleus could successfully be transferred to an enucleated cell and reinitiate normal development, wasn't conclusively confirmed for nearly five decades. No one could demonstrate whether the donated nucleus was obtained from a differentiated cell or from one of the few stem cell residing within specialized tissues. Even the cloning of a sheep named Dolly in 1997 by Ian Wilmut and Keith Campbell suffered from the inability to provide conclusive proof. However, in 2002 Konrad Hochedlinger at the University of Vienna in Austria and Rudolf Jaenisch at the Massachusetts Institute of Technology in Cambridge, Massachusetts published the results of a nuclear transplantation experiment that used mature white blood cells, or lymphocytes, which contained distinct genetic patterns that they could detect in a cloned organism. Using their method, Hochedlinger and Jaenisch showed that nuclear transplanted mice contained the distinct genetic patterning of the specialized nuclei, eliminating the unlikely possibility that successful nuclear transplantations relied on undifferentiated cells imbedded in mature tissues. Gurdon's early work, supplemented by the work of Hochedlinger and Jaenisch, showed that a differentiated adult nucleus could fully reinitiate development when transplanted into an enucleated egg.

Gurdon received several awards for his early work in embryology, including the Scientific Medal of the Zoological Society in 1968. In 1971, he became a Fellow of the Royal Society. He was awarded the Emperor Hirohito International Prize for Biology in 1987. In June 1995, he was Knighted Sir John Bertrand Gurdon. He earned the Edwin Grant Conklin Medal from the Society for Developmental Biology in 2001, and he received the Albert Lasker Basic Medical Research Award in 2009 alongside Shinya Yamanaka, who had discovered a method to induce cells into pluripotency in 2002. In 2012, Gurdon and Yamanaka shared the Nobel Prize in Physiology or Medicine for their work on cloning and pluripotent stem cells.

As of 2012, Gurdon's research focuses on the mechanisms by which the egg reprograms the transplanted nucleus, sometimes allowing it to dedifferentiate and direct the formation of an entire functional organism. He continues to use nuclear transplantation techniques. His research has sparked some controversy as to the future of cloning. Gurdon says that cloning of cells for therapeutic purposes, once the method has been appropriately perfected, should pose no moral issues.

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