Differentiation 88 (2014) 3–8

Contents lists available at ScienceDirect

Differentiation

journal homepage: www.elsevier.com/locate/diff

Lessons from a great developmental biologist

Edward M. De Robertis *

Howard Hughes Medical Institute and, Department of Biological Chemistry, University of California, Los Angeles, CA 90095-1662, United States

ARTICLE INFO

Keywords:
JB Gurdon
Xenopus
Nuclear reprogramming
Nuclear transplantation

ABSTRACT

The announcement that Sir John Gurdon had been awarded the 2012 Nobel Prize for Medicine or Physiology was received with great joy by developmental biologists. It was a very special occasion because of his total dedication to science and turning the Golden Rule of western civilization – love your neighbor as yourself – into a reality in our field. This essay attempts to explain how John became such a great scientific benefactor, and to review some of his discoveries that are less well known than the nuclear transplantation experiments. A few personal anecdotes are also included to illustrate the profound goodness of this unique man of science.

1. Introduction

John B. Gurdon is probably the most beloved developmental biologist of our times. What has been the secret of his success? One answer would be a life tirelessly dedicated to science that was then invested in the common good of others in the field. Here I would like to describe some of the Gurdon scientific landmarks that are not generally known, some of the service John has given all of us, and relate a few stories about my interactions with my scientific mentor.

John Bertrand Gurdon belongs to an ancient English family. His first and middle name have been used repeatedly by many of his ancestors. I once saw a Gurdon genealogical tree; it included a Bertrand de Gurdon recorded circa 1200 and a Jean de Gurdon ca. 1400. The French origin of the names is due to the fact that the "de Gurdon" were of Norman ancestry. Personally, I quite like the nobiliary "de" but this preposition was dropped along the centuries. Many of the Gurdon ancestors were knights but John's side of the family did not inherit the title (although even today his second cousin is a hereditary peer, or member of the House of Lords, and his children carry the Gurdon surname). In what must have been a great personal satisfaction, Sir John regained a knighthood on his own merits in 1995. His parents lived in India but returned to Britain where John and his sister Catherine were born. As children during the Second World War, they were sent to the countryside and shared in the generalized hardships of those times, which shaped a generation. John attended Eton and, famously against the recommendation of his biology teacher, studied Zoology at Oxford. An excellent personal historical account published in Annual Reviews of Cell and Developmental Biology details these early years (Gurdon, 2006). Gurdon's (1954) first paper was on the description of an insect new to Britain, and he has kept a keen interest in butterflies which has driven his travels to exotic places all over the world.

2. An early start

It was a happy day for developmental biology when young Gurdon found an excellent Ph.D. mentor at Oxford. Michaïl Fischberg had an interesting scientific lineage: he studied with Ernst Hadorn in Zurich, who had in turn studied with Fritz Baltzer in Bern, who had himself studied under Theodor Boveri in Wurzburg. Much of European cell biology can be traced to Boveri (including Hans Spemann among others). Three months into his Ph.D. studies, Fischberg asked young Gurdon to re-investigate the Briggs and King nuclear transplantation experiments using eggs of the frog *Xenopus*. This South African frog was used for pregnancy testing and had been recently introduced by Pieter Nieuwkoop in Holland and by Fischberg in Britain for embryological research (reviewed in Gurdon and Hopwood, 2000). Fischberg had had the foresight of keeping a strain of *Xenopus* carrying only one nucleolus (as compared to wild-type frogs which have two nucleoli) that had been found spontaneously in the lab and provided an invaluable nuclear marker. At age 25 Gurdon published a paper in Nature entitled "Sexually mature individuals of *Xenopus laevis* from the transplantation of single somatic nuclei" (Gurdon et al., 1958). Later on, fertile frogs were obtained from differentiated intestinal nuclei (Gurdon and Uehlinger, 1966). This work demonstrated that differentiated nuclei could be reprogrammed and that genetic information is not lost during cell differentiation (reviewed in Gurdon, 1974). This important discovery was not readily accepted and John spent many years reproducing the experiment in various

* Corresponding author. Tel.: +1 310 306 1463; fax: +1 310 206 2008.
E-mail address: ederobertis@mednet.ucla.edu

0301-4681/$ - see front matter © 2013 International Society of Differentiation. Published by Elsevier B.V. All rights reserved.
Join the International Society for Differentiation (www.isdifferentiation.org)
http://dx.doi.org/10.1016/j.diff.2013.12.004

settings. Finally, his perseverance was rewarded in 2012 with the Nobel Prize.

3. Service to others

The key to John Gurdon, I think, is that he interpreted the good fortune of making such an important discovery as a beginning graduate student as a call of duty to give back to others; noblesse oblige. To whom much is given, much is expected; this philosophy has rarely been followed so tirelessly. John's beneficial influence has been felt at many levels in our field of developmental biology. He has been an indefatigable supporter of scientific societies, in which scientists organize themselves for the common good of their field. He attends many of their large meetings and always makes it a priority to discuss as many posters as humanly possible with students. For decades John was the *éminence grise* behind the Company of Biologists (publishers of Development and Journal of Cell Science), who plow the journal profits back into the scientific community. He started, together with Igor Dawid, the *Xenopus* conferences that take place regularly every two years since 1984. In 1983 he founded a new institute in Cambridge, now aptly renamed the Gurdon Institute, the premier research center in our field. He served as Master of Magdalene College, Cambridge (a large job), and Governor of The Wellcome Trust, London. He was President of the International Society of Developmental Biologists, and served in many committees that keep the machinery of science running.

An early start, a good advisor, superb scientific publications, a record of selfless service for the common good, and finally his secret weapon: John is always working at his bench with his dissecting microscope, micromanipulator, and his beloved *Xenopus* oocytes. He has set the tone for the entire *Xenopus* field, one in which many principal investigators continue working with their own hands. Gurdon has trained many scientists (Figs. 1 and 2) and one can safely say the majority of the *Xenopus* development field is his F2–F4 progeny.

4. A lifetime of discovery

John Gurdon has made many important contributions to cell and developmental biology in addition to demonstrating the totipotency of single nuclei transplanted into eggs. These landmark studies are described here chronological order.

John Gurdon, together with his long-time friend Donald D. Brown of the Carnegie Institution, showed that when 1-nucleolus frogs were crossed, the resulting 25% of anucleolate tadpoles lacked ribosomal RNA synthesis (Brown and Gurdon, 1964). This key discovery led to the current realization that the function of the nucleolus is to produce large ribosomal RNA. In addition, this collaboration had the of introducing the frog *Xenopus* to American molecular biology.

John explored the effects of microinjecting multiple nuclei (initially from brain) instead of a single one. He found that in eggs laid by the frog DNA was replicated; that in progesterone-matured oocytes chromosomes condensed but did not replicate DNA; and finally that nuclei microinjected into oocytes enlarged and synthesized RNA, but did not replicate DNA (Gurdon, 1968). These observations were later pursued by Yoshio Masui in Canada and led to the discovery of maturation-promoting factor (MPF) which

Fig. 1. The Gurdon group at the Laboratory of Molecular Biology, Cambridge, circa 1980. Top row: Doug Melton (graduate student), Marvin Wickens (postdoc), William Earnshaw (Laskey's postdoc), Eddy De Robertis, Ruth Longthorne (Eddy's technician), Richard Harland (Laskey's graduate student), Kazuko Nishikura (Eddy's first postdoc), Laurence Korn (postdoc), Stewart Weisbrod (postdoc), John Gurdon (at age 46) and Julian Wells (sabbatical visitor from Australia). Lower row: Sue Whytock (John's technician), two young ladies, Barbara Rodbard (John's excellent secretary) and Jeff Partington (postdoc). Long-time colleague Ron Laskey is missing from this photo. Note that John was the most handsome gentleman, and kept only a small group working directly with him.