Keith H. Campbell

(1954–2012)

Creator of Dolly, the first mammal cloned from an adult body cell.

Keith Campbell was the inspiration behind Dolly the sheep, the first mammal to be cloned from an adult body cell. He died on 5 October at the age of 58. A few days later, the Nobel committee recognized the importance of the field by awarding the 2012 medicine prize to John Gurdon and Shinya Yamanaka for their achievements in reprogramming cells.

In 1995, Campbell — then at the Roslin Institute near Edinburgh, UK — conceived of a method to generate a pair of cloned lambs, Morag and Megan, from a cell taken from a sheep embryo. In his opinion, these were "the first animals produced from differentiated cells because these cells had differentiated in culture". It took Dolly, however, to convince the scientific community that differentiated mammalian body cells — which had already become specialized for a particular function — could be reprogrammed to produce an entire organism.

In the mid-1990s, the consensus among cell biologists was that clones could not be produced from cells that had become specialized. Decades earlier, Gurdon, a British developmental biologist, had managed to produce adult frogs by transferring the nuclei of tadpole cells into eggs stripped of their own nuclei. But reprogramming differentiated mammalian embryonic cells or adult body cells was thought unlikely to work.

Campbell's breakthrough was realizing that he could reprogram the nuclear information in a donor cell if he coordinated the cell cycles of the donor embryo cell and the recipient egg. By depriving the cells in his laboratory cultures of nutrient-rich serum, he forced them to enter a quiescent state. When cell division was reactivated, the cell cycles were aligned. By transferring the nucleus of an embryo cell into an egg cell from which the chromatin had been removed, and then activating that nuclear material, he created Morag and Megan.

Wanting to track down exactly when the developmental potential of embryonic cells was lost, Campbell and Ian Wilmut, the Roslin Institute's group leader, asked their colleague James McWhir for some adult cells. McWhir gave them some sheep mammary-gland cells that happened to be in the freezer. The Edinburgh-based biotechnology company PPL Therapeutics, which was collaborating with the Roslin Institute, was using the sheep cells for experiments on drug development.

I always wonder who was most surprised when, after being transferred into a ewe, one of the embryos derived from the nucleus of a mammary-gland cell developed into an apparently normal lamb: the ewe, the farm hands or the research team? Wilmut certainly was surprised. I think Campbell was optimistic that even adult cells could be reprogrammed.

MURDO MACLEOD

Campbell was born in 1954 in Birmingham, UK, and grew up there and in the Scottish city of Perth. He graduated from Queen Elizabeth College, London, in 1978 with a bachelor's degree in microbiology. After various jobs, including a locum position as chief medical laboratory technologist in South Yemen, he started a PhD in 1980 at the University of Sussex, UK. It was at Queen Elizabeth College and as a postgraduate student studying frog-egg maturation that Campbell developed his interest in the control of cell division and in the factors that direct the behaviour of cell nuclei. After postdoctoral positions at the universities of Edinburgh and Dundee, Campbell joined the Roslin Institute in 1991.

Campbell left the institute in 1997 to become head of embryology at PPL Therapeutics, where he led work on cloning pigs. In 1999, he became professor of animal development at the University of Nottingham, UK, where he continued to work on nuclear reprogramming and cloning techniques. (PPL Therapeutics was sold when it ran into financial problems in 2003, largely because of the difficulty of using animal cloning to develop pharmaceutical products.)

Despite the tremendous media stir prompted by Dolly's birth, animal cloning has never really come of age as a commercially useful biotechnology. This is mainly because, in most species, epigenetic marks (experience-dependent molecular alterations that alter how genes behave, but not their sequence), carried over in the introduced chromatin, cause embryonic losses and postnatal abnormalities. Yet somatic cell cloning has proved a very useful tool in mouse developmental and cell biology, and has made significant contributions to stem-cell biology. In 2008, Campbell and Wilmut were jointly awarded half of the prestigious Shaw Prize in Life Science and Medicine, with Yamanaka winning the other half.

Keith was acutely aware that the cloning method he had pioneered drew strong opposition from some, including conservative religious groups and members of the Green Party. He defended his work, saying that it was important for the progress of biology and possibly medicine, but he was strongly opposed to human reproductive cloning.

A great companion and argumentative in a delightful way, Keith was a strong supporter of his colleagues and a proud father of his daughters Claire and Lauren. It was perfectly in keeping with his wry humour that he named Dolly the sheep after the singer Dolly Parton, and told *The New York Times* in 1997 that sex "will always be the preferred way of having children". Cloning, he said, is "far too expensive and a lot less fun than the original method". ■

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