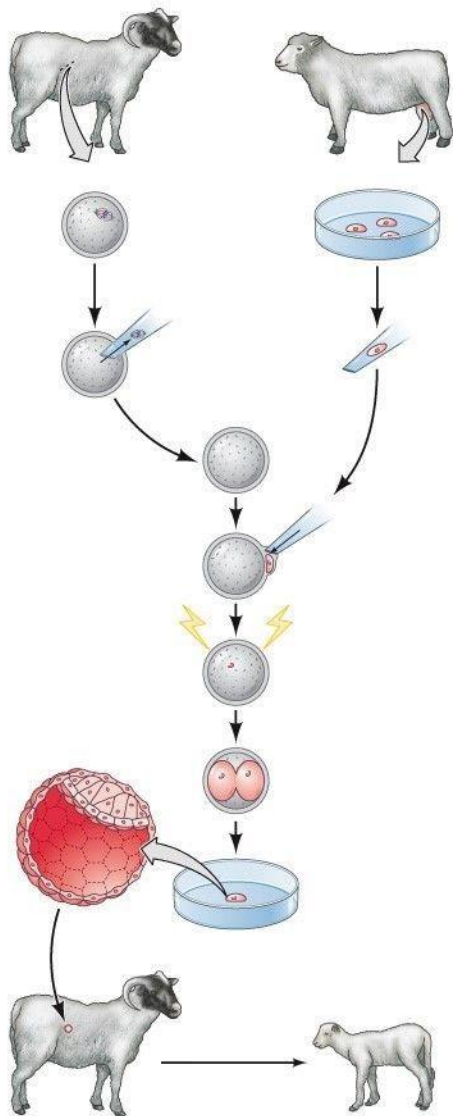


Genomic Equivalence and Cloning

Ian Wilmut and colleagues took cells from the mammary gland of a 6-year-old pregnant ewe and placed them in culture (Figure 1A; Wilmut et al. 1997). The culture medium was formulated to keep the cell nuclei at the intact diploid stage (G1) of the cell cycle; this cell-cycle stage turned out to be critical. The researchers then obtained oocytes from a different strain of sheep and removed their nuclei. These oocytes had to be in the second meiotic metaphase, the stage at which they are usually fertilized. The donor cell and the enucleated oocyte were brought together, and electric pulses were sent through them, thereby destabilizing the cell membranes and allowing the cells to fuse. The same electric pulses that fused the cells activated the egg to begin development. The resulting embryos were eventually transferred into the uteri of pregnant sheep.

Of the 434 sheep oocytes originally used in this experiment, and the 277 zygotes implanted, only 1 survived: Dollyⁱ (Figure 1B). DNA analysis confirmed that the nuclei of Dolly's cells were derived from the strain of sheep from which the donor nucleus was taken (Ashworth et al. 1998; Signer et al. 1998). Cloning of adult mammals using similar asexual reproduction techniques has now been accomplished in guinea pigs, rabbits, rats, mice, dogs, cats, horses, and cows, and the list keeps growing. In 2003, a cloned mule became the first sterile animal to be so reproduced (Woods et al. 2003). Thus, it appears that the nuclei of vertebrate adult somatic cells contain all the genes needed to generate an adult organism. No genes necessary for development have been lost or mutated in the somatic cells; *the DNA of their nuclei is equivalent*.

(A)



After I. Wilmut et al. 2000. *The Second Creation: Dolly and the Age of Biological Control*. Harvard University Press:Cambridge, MA.

(B)



Photograph by Roddy Field © Roslin Institute

Figure 1 Cloning a mammal using nuclei from adult somatic cells. (A) Procedure used for cloning sheep. (B) Dolly, the adult sheep on the left, was derived by fusing a mammary gland cell nucleus with an enucleated oocyte, which was then implanted in a surrogate mother (of a different breed of sheep) that gave birth to Dolly. Dolly later gave birth to a lamb (Bonnie, at right) by normal reproduction. (A after I. Wilmut et al. 2000. *The Second Creation: Dolly and the Age of Biological Control*. Harvard University Press:Cambridge, MA.)

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ⁱ The creation of Dolly was the result of a combination of scientific and social circumstances. These circumstances involved job security, people with different areas of expertise meeting one another, children's school holidays, international politics, and who sits near whom in a pub. The complex interconnections that gave rise to Dolly are told in *The Second Creation* (Wilmut et al. 2000), a book that should be read by anyone who wants to know how contemporary science actually works. As Wilmut acknowledged (p. 36), "The story may seem a bit messy, but that's because life is messy, and science is a slice of life."