Nuclear Transplantation [1]

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Nuclear transplantation is a method in which the nucleus [3] of a donor cell is relocated to a target cell that has had its nucleus [3] removed (enucleated). Nuclear transplantation has allowed experimental embryologists to manipulate the development of an organism and to study the potential of the nucleus [3] to direct development. Nuclear transplantation, as it was first called, was later referred to as somatic nuclear transfer or cloning [4].

Yves Delage [5] first wrote about nuclear transplantation [6] in 1895, speculating that if one were to replace an egg [7] nucleus [3] with another egg?s nucleus [3], full development would occur. Later in 1938, Hans Spemann [8] suggested an experiment whereby, using technologies not yet available to him, one could remove the nucleus [3] of an egg [7] and replace it with a different nucleus [3] extracted from a developed cell. Thomas King and Robert Briggs were the first to perform experimental nuclear transplantation [6]. The technique was soon after used by John Gurdon [9] and eventually led to the first clone of a mammal [10], ?Dolly? the sheep [11], by Ian Wilmut [12] in 1996.

Nearly fifteen years after Spemann wrote about the possibility of nuclear transplantation [6], Briggs and King, using northern leopard frogs (*Rana pipiens* [13]), performed the first nuclear transplantation [6] experiment. They transplanted the nucleus [3] from an early stage embryo to an unfertilized egg [7] that had been enucleated. The egg [7] cell was pricked with a clean glass needle in order to induce a fertilization [14]-like response. The faux activation of fertilization [14] allowed for extraction of the nuclear material inside while also activating the host egg [7] cell. Meanwhile, the nucleus [3] of a donor cell was extracted and then inserted into the newly enucleated and activated egg [7] cell. That process induced development of the host egg [7] according to the instructions of the newly inserted nucleus [3], resulting in the formation of an organism with the same genetic material as the donor cell, or a clone.

Briggs and King continued to examine the potential of differentiated cells throughout the 1950s. They found that if the donor nucleus [3] was extracted later in development, the potential of directing full development in the activated egg [7] cell was greatly reduced. After the Briggs and King experiments it was generally accepted that the nuclear material in developing cells slowly loses its potential for full development.

That view was challenged in 1958 when Gurdon's experiments with African claws frogs (*Xenopus laevis* [15]) produced fully developed frogs from the transferred nucleus [3] of cells much later in development. Gurdon allowed the cloned frogs to develop to sexual maturity and was then able to mate two sexually mature clones, suggesting that the donor nuclei were able to fully redirect development. Gurdon?s experiments were widely accepted by the scientific community but questions remained for several decades. Scientists were concerned about whether the nucleus [3] of the host egg [7] cell was truly enucleated. The question of whether remnants of the host egg [7] cell or the inserted nucleus [3] directed development remained unanswered from 1958 to 2002, despite many attempts by Gurdon to prove it was the inserted nucleus

[3].

In 2002, however, Konrad Hochedlinger [16] and Rudolf Jaenisch [17] published an experiment using nuclear transplantation [6] of mature white blood cells to generate mouse [18] clones. Hochedlinger and Jaenisch were able to show that the inserted nucleus [3] induced development in the host egg [7] cell.

Although experimental embryologists continued to use nuclear transplantation [6] to create clones of several species, Ian Wilmut?s cloning [4] experiment in 1996 was a controversial and widely publicized cloning [4] experiment. Dolly was cloned using the nucleus [3] of a mammary gland cell from an adult sheep [11] and transplanting it into an enucleated egg [7] cell from another sheep [11]. The activated egg [7] cell was then transferred into a third surrogate [19] sheep [11] that carried Dolly to term. Dolly died at the age of to six due to lung disease and severe arthritis, and although her death was not attributed to the fact that she was a clone, many believe that the relationship between telomeres and aging was the reason for her demise.

Nuclear transplantation may have begun as a subtle idea in the late 19th and early 20th centuries, but it evolved into a feasible and widely used process by experimental embryologists in the late 1990s. The cloning [4] of Dolly the sheep [11] worried many about the possibility of human cloning [4] and the moral boundaries of modern advances in science. In the context of the embryonic stem cell discourse of the late 1990s and early twenty-first century, somatic nuclear transfer has been contrived into moral arguments about rights of the human embryo. Furthermore, nuclear transplantation [6] has spurred ethical discussion on the value of a human life during all stages of development. Many scientists have abandoned the methods involved in nuclear transplantation [6] and have adopted methods set forth by Shinya Yamanaka [20] in his experiments involving induced pluripotent stem cells [21].

Sources

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