Interspecies SCNT-derived Humanesque Blastocysts [1]

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Since the 1950s, scientists have developed interspecies blastocysts in laboratory settings, but not until the 1990s did proposals emerge to engineer interspecies blastocysts that contained human genetic or cellular material. Even if these embryos were not permitted to mature to fetal stages, their ethical and political status became debated within nations attempting to use them for research. To study cell differentiation [4] and embryonic development and causes of human diseases, interspecies-somatic-cell-nuclear-transfer -derived (iSCNT) humanesque blastocysts provided opportunities for research and therapy development. Such a technology also involved ethical debates.

During the early 1950s, Robert Briggs at the Institute for Cancer Center, which later became Fox Chase Cancer Center in Philadelphia, Pennsylvania, and Thomas Joseph King Jr. at the Lankenau Hospital Research Institute in Philadelphia, Pennsylvania, studied the developmental trajectory and potential of tadpole embryonic cells. Briggs and King developed a technique to transfer the nucleus [5], which is the organelle that contains nuclear DNA, of one cell into an enucleated cell, or a cell from which the nucleus [5] has been removed. In 1952 the two published their technique in the article "Transplantation of Living Nuclei from Blastula Cells into Enucleated Frogs' Eggs." The two scientists had transplanted the nucleus [5], and therefore genetic material, of an adult somatic cell [6] or a differentiated cell into an enucleated egg [7] cell for the first time. Briggs and Kind noted that the resultant blastocyst [8], or the stage of embryonic development characterized by an inner cell mass [9] surrounded by an outer cell layer, developed into a mature organism.

In the following decades, scientists practiced the procedure with varying degrees of success between different species of organisms, including sheep [10], goats, chicks, quails, cows, and rabbits. However, only in 1998 were human-derived cellular materials first used for interspecies blastocysts. Jose C. Cibelli at the University of Massachusetts in Amherst, Massachusetts, and his team fused the nucleus [5] of human white blood cells with enucleatedcow [11] oocytes. They published their results in the article "Transgenic bovine chimeric offspring produced from somatic cell [6]-derived stem-like cells." Of the fifty-six transplants conducted in their experiment, only one developed to the sixteen to four-hundred cell stage, and then growth terminated.

In November 2006, two research teams in the UK independently submitted applications to the UK Human Embryology and Fertilisation Authority (HFEA) in London, UK, to develop stem cell lines using animal oocytes and human nuclei. Although Cibelli's team had attempted to develop those cells, they did not plan in their 1998 experiment to keep the cell lines alive. The UK research teams included Lyle Armstrong at Newcastle University in Newcastle upon Tyne, UK, and Stephen Minger at King's College in London, UK. In response, the HFEA held a series of consultations, debates, and surveys with the public and with specialists to make an informed and representative decision about how to address research applications to engineer cross-species blastocyst [8] lines.

On October 1, 2007, the HFEA published its report titled "Hybrids and Chimeras: A report on the findings of the consultation," which described its final decisions. The report states that the HFEA found no reason to prohibit the development of blastocysts using human cellular or genetic material as long as the research is necessary, ethical, and adheres to a strict code of practice. In all cases, the report prohibited researchers to grow such embryos to birth. Additionally, the report states that violating those policies will result in imprisonment. Afterwards, Armstrong and Minger synthesized for the first time iSCNT humanesque-blastocysts (ISHBs).

To create ISHBs, the researchers first obtained an egg [7] cell or oocyte [12] from an animal such as a rabbit [13] or a cow [11]. They treated the female animal with a super-ovulation [14] drug, which helps ovaries release more oocytes compared to a typical ovulation [14] cycle. Then, the researchers extracted the oocytes and removed their nuclei with a pipette. Next, the researchers observed the oocytes under ultraviolet light to ensure that they lacked their nuclei. The researchers then inserted the nucleus [5] of a human somatic cell [6] into an enucleated oocyte [12] by placing it in a fusion chamber and stimulating it electrically or chemically, so that the two entities fused together and developmental began.

After several days of development, blastocysts formed. From a blastocyst [8], the researchers removed theinner cell mass [9] and cultured it, and then they placed it on a layer of feeder cells and supplied the inner cell mass [9] (ICM) with the nutrients required for survival and replication. After a few days, the researchers observed colonies of undifferentiated stem cells [15].

In normal embryos, stem cells [15] from the ICM are pluripotent, or can develop into many kinds of more specialized cells as the embryo develops. When scientists culture those ICM cells, the cultured cells are also pluripotent. But for cells cultured from the ICMs of ISHBs, researchers by 2015 had yet to establish that they were similarly pluripotent.

With their experiments, Armstrong and Minger inspired many scientists who aimed to explain aging and how diseases develop in the body, and to find therapies to improve human health. Other researchers addressed the ethical issues underlying the use of animals to model human disorders and diseases. Researchers have shown that some organisms, such as rats, lack the complex neural anatomy and psychology found in humans [16], and they are thus not good models to study some human diseases such as schizophrenia. Some researchers argued that iSCNT humanesque blastocysts may provide new models to study how a particular disease occurs, as well as the genetics of some pathogeneses.

Research on humanesque blastocysts often bypass the need for human oocytes. Obtaining human oocytes sometimes raised ethical issues because the process to obtain them from women typically poses a series of health risks to the donors at multiple stages of the procedure. For instance, to harvest oocytes, a super-ovulation [14] hormone [17] is administered to the woman for several days to release more oocytes than a normal ovulation [14] cycle. These hormones [18] have been linked to adverse effects on the health of the woman, including cancer or personality and mood shifts. The extraction itself poses risks common to other invasive procedures. In addition, some argue that using human oocytes solely for research purposes diminishes the value of human life. Using animal oocytes to create humanesque blastocyst [8] cell cultures bypasses the need to put women at risk in creating stem cell lines for research.

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Subject

Blastocyst [39] Diseases [40] Bioethics [41] Briggs, Robert [42] Fox Chase Cancer Center [43] King, Thomas J. (Thomas Joseph), 1921-2000 [44] Lankenau Hospital. Research Institute [45] Tadpole [46] Cell nuclei--Transplantation [47] DNA [48] Gene Transfer, Horizontal [49] Recombination, Interspecies [50]

Topic

Theories [51]

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