EDITORIAL

Stem Cells and Cloning: What's the Difference and Why the Fuss?

As a writer of embryology textbooks, I find myself regularly wishing that my latest book hadn't gone to press just a month before the most recent major breakthrough in embryotechnology. This year, the cause celebre was the twin announcements of the production of human embryonic stem cells derived from the inner cell mass of the blastocyst[6] or from primordial germ cells taken from 5-to-9-week-old human embryos.[4] These reports, coupled with the news account of an announcement that a private biotech company in Massachusetts (Advanced Cell Technology) claims to have produced embryonic stem cells by fusing a buccal epithelial cell of a human with the enucleated oocyte of a cow,[7] have spawned numerous articles and editorials that simultaneously extol the technological leaps and decry our collective inability to provide an ethical basis for such work.

For at least the next few years, the public image of cloning will continue to be the indelible imprint of Dolly, the impassive sheep that was generated by fusing a mammary epithelial cell with an enucleated egg. Dolly, by the way, has by now produced a normal offspring of her own in the old-fashioned way.

In the popular press, the distinction between stem cell technology and cloning is often blurred. Yet, despite superficial similarities in certain aspects of technique, the goals and processes are quite different. A fundamental biological unifying factor, however, is the fact that the nuclei of most cells in both embryos and adults contain a full complement of genetic information.

As normally understood, cloning consists of fusing the nucleus of a donor cell (or the whole cell in the case of Dolly) with an enucleated oocyte. The donor cell can come from either an embryo or an adult. In the case of mammals, the fused cell is allowed to divide a few times in vitro before being implanted into the specially primed uterus of a surrogate mother. One of the most difficult aspects of cloning has been matching the condition of the donor nucleus with that of the egg, so that cell division (embryonic cleavage) will occur.

What is often forgotten is that the first cloning was done 40 years ago on plants, when F.C. Steward of Cornell[5] was able to produce entire carrot plants from single somatic cells (the kind that we eat). Now in the agricultural world, cloning from somatic cells is routinely applied for the propagation of many types of plants. The vertebrate equivalent of cloning began with the nuclear transplantation experiments of Briggs and King in 1952,[1] and the first production of a vertebrate animal from an adult nucleus was accomplished by John Gurdon,[2] who inserted the nucleus from an intestinal epithelial cell of an adult *Xenopus* into an enucleated egg.

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Although initially cloning was used to demonstrate some very important scientific principles, the principal driving force behind cloning today is economic, a primary goal being the efficient propagation of rare or valuable species. At this stage of our technology, at least, the cloning of an individual or armies of humans from a single super donor in Hitleresque fashion is yet far away, but one learns "never to say never" in the world of technology. An unknown in present cloning techniques is the extent to which the mitochondrial DNA of the host oocyte affects the phenotype of the cloned individual. Almost invariably the advent of a major new technological advance, such as cloning, has preceded the establishment of an ethical framework for it, no matter how long beforehand that advance might have been anticipated.

Embryonic stem cell technology is based on older experimental embryological work showing that individual cells from the inner cell mass of the mammalian blastocyst are capable of forming any cell type in the body. As pointed out in the following article by O'Shea,[3] this technique involves the isolation of cells from the inner cell mass and their propagation in vitro under conditions that allow them to remain pluripotent and to reproduce themselves indefinitely. The goal of embryonic stem cell technology is to identify environmental conditions that will lead the stem cell to differentiate consistently into a uniform cell type.

At this time, the use of embryonic stem cells has been a boon to those who are trying to unravel the molecular pathways leading to the differentiation of specific cell types. As pure science, this is in itself a monumental goal and one that will require an immense amount of experimentation to attain. Beyond understanding mechanisms of normal cellular differentiation, stem cell technology can be used to uncover information about the development of genetic mutants or about

the developmental capabilities of cells that have been genetically engineered. The holy grail at the end of these lines of investigation is the production of non-immunogenic cells that can be used for the correction of genetic or pathological cellular deficiencies (e.g. pancreatic beta cells in diabetics) or for the replacement of injured or killed cells and tissues (e.g. necrotic myocardial cells in infarcted regions of the heart).

Goals such as those outlined in the previous paragraph are usually considered laudable by commentators, but the ultimate source of the embryonic stem cells is quite controversial, because they are derived from human embryonic material. By way of contrast, it is not the origin of the cellular materials but the end product that has caused the most concern among ethicists and others in cloning experiments. Especially when genetic manipulation is involved, in either of these techniques concerns mount, not so much when somatic cells are the target, but when the manipulation affects germ cells that could transmit the manipulations to succeeding generations.

LITERATURE CITED

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