

Roundtable: Embryonic or adult stem cells: scientific and ethical considerations

Biological differences between embryonic and adult stem cells

Gerhard Gstraunthaler

Division of Physiology, Innsbruck Medical University (Innsbruck) (AT)

Characteristics of embryonic and adult stem cells. Stem cells are unique cell populations that retained the capability of either self-renewal in nearly infinite cell divisions or to differentiate into one or several cell types. Embryonic stem cells are pluripotent, i.e. they retained the potential to differentiate into one of the approx. 220 somatic cell types of the mesoderm, endoderm or ectoderm. In contrast, adult stem cells are multipotent, harbouring the ability to differentiate into specific cell types of the tissue of origin in which they reside. Thus, adult stem cells are the *in vivo* source for cell renewal during tissue turnover or in tissue repair. However, broad plasticity of adult stem cells have been described, allowing the cells to differentiate across tissue lineage boundaries to give rise to cell types of other lineages.

Source and origin of embryonic and adult stem cells. Embryonic stem cells are isolated from the inner cell mass of mouse or human blastocysts. The generation of human embryonic stem cell lines from preimplantation blastocysts and their use in basic research as well as in future therapeutic application has raised considerable ethical concerns. The source of a human blastocyst are exclusively fertilized eggs that have been grown *in vitro* for 5 to 6 days. Fertilized eggs may be provided from surplus zygotes after *in vitro* fertilization (IVF). However, the isolation and preparation of cells from the inner cell mass results in the destruction of the blastocysts and is thus considered an embryo-consuming technology, which by this reason is prohibited in many European countries. Alternative technologies, like somatic nuclear transfer, have been developed in order to avoid to waste fertilized human embryos, however, ethical concerns still exist, since enucleated human oocytes are needed. The latest development are induced pluripotent stem cells (iPS), obtained by direct reprogramming of somatic cells after retroviral transfection. Adult stem cells are easy to obtain, although they reside in low abundance in adult tissues and organs, so-called stem cell niches. Any ethical concerns about harvest and isolation of adult stem cells are neglectable. The sources for adult stem cells are manifold and include easily available human tissue, like blood, bone marrow or adipose tissue, or human material, which is normally unused or even discarded, like umbilical cord, placenta, or deciduous milk teeth. Also amniotic fluid has been recently described as potential source of stem cells.

Pitfalls and mistakes in culturing embryonic stem cells. When human embryonic stem cells (hESC) are expanded *in vitro* in tissue culture, it is critical to maintain their self-renewal and differentiation capacity. In present state-of-the-art culture protocols, hESC are cultured on mitotically inactivated mouse embryonic fibroblast feeder layers, which serve three important functions: (1) they support hESC growth, (2) prevent spontaneous differentiation of hESC during culture, and (3) maintain hESC pluripotency. Mouse embryonic stem cells can be maintained *in vitro* in undifferentiated state, when the culture medium is supplemented with leukemia inhibitory factor (LIF), or when LIF is secreted in sufficient amounts by mouse fibroblast feeder layers. LIF, however, does not act on hESC, which must be cultured in high amounts of fetal bovine serum (FBS) supplementation. The use of animal-derived feeder layers and culture medium supplements, like FBS, turned out to pose the risk of cross-species contamination of hESC with animal pathogens, thereby greatly limiting the future clinical application of the cells. Recent studies have indicated the expression of immunogenic nonhuman sialic acid residues by hESC, due to their culture in the presence of FBS, and cells would be rejected when transplanted for therapeutic purposes. Thus, great efforts have been undertaken to develop xeno-free and feeder-free culture conditions for hESC, however, with limited success.

Keywords: pluripotency, blastocyst inner cell mass, IVF, iPS, stem cell niches, stem cell culture