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

The use of stem cells in toxicology

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Embryonic and adult stem cells (eSC & aSC) have the potential to differentiate in culture into many different cells and tissues depending on the conditions of culture. For ethical and scientific reasons predominantly culture conditions for rodent SC have been established. However, as outlined by other participants in the round table discussion, increasingly interest is focusing on human stem cells (hSC), consequently methods for applying hSC to safety studies are emerging.

SC are capable of renewing themselves; that is, they can be continuously cultured in an undifferentiated state, giving rise to more specialized cells of the human body such as heart, liver, bone marrow, blood vessel, pancreatic islet, and nerve cells.

Therefore, SC are an important new tool for developing unique, *in vitro* model systems to test drugs and chemicals and a potential to predict or anticipate toxicity in humans. An overview of the applications of SC technology will be given in the area of toxicology. Specifically, core technologies will be addressed that are emerging in the field and how they could fulfill critical safety issues such as QT prolongation and hepatotoxicity, two leading causes of failures in preclinical development of new therapeutic drugs. aSC derived from various sources, such as human bone marrow and placenta, can potentially generate suitable models for cardiotoxicity, hepatotoxicity, genotoxicity/epigenetic and reproductive toxicology screens.

For embryotoxicity testing the embryonic stem cell test (EST) has been developed in our lab during the past 20 years applying mouse ESC. The meSt have successfully been validated in an ECVAM validation study and molecular endpoints have been established in addition to morphological ones as well as reporter gene assays. Currently several groups are implementing the basic principles of the EST to hESC and the first encouraging results have been published on applying the heSt.

From a more general perspective, the most likely immediate uses of hESC will be *in vitro* test systems and disease models. Major and minor pharmaceutical companies have entered this field, and the European Union is sponsoring academic research into hESC-based innovative test systems. This is perfectly in line with approaches on both sides of the Atlantic, to use human cell-based *in vitro* systems for safety evaluations, and to shift the focus of toxicology away from classical animal experiments and more towards a mechanistic understanding.

Keywords: stem cells, embryonic stem cells, adult stem cells, human stem cells, mouse stem cells, toxicity testing, safety testing, embryonic stem cell test, EST