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Novel engineered physiological culture platform produces endoderm and hepatocytes uncontaminated with undifferentiated sourcehuman parthenogenetic stem cells

Nikolay Turovets[1], Larissa Agapova[1], Jeffrey Fair[2], Richard West[3], Alina Ostrowska[1], Vladimir Agapov[1],Irina Turovets[1], Andrey Semechkin[1], Marie Csete[4] and Nikolay Turovets[1]

[1]International Stem Cell Corporation, Grand Rapids, 4Organovo, USA
[2]Cedars-Sinai Medical Center, Grand Rapids, 4Organovo, USA
[3]West Labs Scientific, Grand Rapids, 4Organovo, USA

Human parthenogenetic stem cells (hpSC) are derived from the inner cell mass of blastocysts from unfertilized oocytes that have been parthenogenetically activated. These cells demonstrate markers, morphology and behavior characteristic of human embryonic stem cells (hESC), including extensive self-renewal and differentiation into cells of all three germ layers. Differentiated derivatives of HLA homozygous hpSC with common haplotypes may reduce the risk of immune rejection after transplantation, thus offering significant advantages over hESC for application in cell-based therapies due to reduced toxic alloimmune reactions. Moreover, derivation of hpSC does not require viable blastocyst destruction.

Derivation of differentiated cell products that are not contaminated with undifferentiated cells is a major technical roadblock for translation of all pluripotent stem cell-based therapies.

We report a novel method to derive a high-purity hepatocyte population from hpSC, based on reproducing features of the normal human embryonic microenvironment. The method mimics the developmental process of transition through a primitive streak of early hepatocyte progenitors, using a differentiation device that incorporates a three-dimensional extracellular matrix (ECM) combined with a porous membrane.

Treatment of undifferentiated hpSC above the membrane using signaling-directed differentiation results in an epithelial-to-mesenchymal transition, in which responsive cells acquire the ability to migrate through the membrane into the ECM, where they further differentiate into functional hepatocytes. The obtained populations of the differentiated cells are highly purified, segregated from and not contaminated with undifferentiated cells.

The method and data represent a significant step toward creation of pluripotent stem cell-derived cell products for use in regenerative medicine and drug discovery.

Biography

Nikolay Turovets, PhD, Director of Research and Therapeutic Development at International Stem Cell Corporation was instrumental in planning and implementing the research that led to the first intentional isolation of human parthenogenetic stem cells that form the basis of ISCO's core technology. Further work led to the creation of the first human HLA-homozygous stem cell line that has the potential to overcome immune rejection. Dr. Turovet's continues his scientific career at UC Irvine as a research scholar. Prior to joining ISCO Dr. Turovets earned a Ph.D. in cancer biology and held the position of the head of IVF department's embryology laboratory at the leading government hospital of Gynecology, Obstetrics and Perinatology in Russia. Dr. Turovets has published in the field of clinical and basic cell biology and is co-author of cell technology patents and patent applications.