6-2019-6716 | Generation of Human Induced Trophoblast Stem Cells for Modelling and Treating Placental Dysfunction Diseases

Buganim Yossi, HUJI, School of Medicine - IMRIC, Developmental Biology and Cancer Research

Background

Recurrent miscarriage, preeclampsia and intra-uterine growth restriction (IUGR) are three common implantation (placental)-related diseases and a major cause of mortality and morbidity for mother and child, complicating between 3 to 10 percent of pregnancies, with increasing rates in recent years.

- It is estimated that dysfunctional placental stem cells (i.e. trophoblast stem cells (TSCs)) or early differentiating trophoblastic cells are a major cause leading to these diseases.
- Regenerative medicine is a new and expanding area that aims to replace lost or damaged cells, tissues or organs in the human body through cellular transplantation.
- The conversion of fibroblasts into other cell types by the direct conversion approach opened an attractive avenue that resolves ethical issue and the immune rejection problem and the need for donor cells.

Our Innovation

- Placental dysfunction is associated with about 70% of all miscarriages. It is also a major cause of fetal growth restriction (FGR) that may lead to the birth of retarded children and death.
- Our lab developed a novel paradigm to convert human skin cells into human induced trophoblast stem cells (hiTSCs).
- When over expressing four TSC master regulators, we were able to successfully generate hiTSCs that exhibit similar morphology, transcriptome and methylome to their blastocyst-derived TSC counterparts and could grow stably in the absence of their exogenous factors for a long time.
- Moreover, hiTSCs are fully functional and can successfully differentiated into all trophoblast subtypes in vitro and in NOD/SCID mice.

Application

- Since isolating human TSCs from healthy individuals hold major ethical problems and might exhibit immune-rejection problems, hiTSCs are an excellent alternative source of cells that solve these limitations and holds great promise in regenerative medicine for the treatment of miscarriage and other placental dysfunction diseases.
- Since hiTSCs can be isolated at late stages of pregnancy, in contrast to hTSCs that can be isolated only during the first trimester, these cells can be used to model placental dysfunction diseases and offer a great platform for drug discovery.

Patent Status

Contact for more information:

Keren-Or Amar
VP, Business Development, Healthcare

Yissum Research Development Company of the Hebrew University of Jerusalem
Hi-Tech Park, Edmond J. Safra Campus, Givat-Ram, Jerusalem
P.O. Box 39135, Jerusalem 91390 Israel
Telephone: 972-2-658-6688, Fax: 972-2-658-6689