GENERATION OF ARTIFICIAL GAMETES: ARE WE CLOSE?

R.A. Reijo Pera[1], S. Panula[1,2], J. V. Medrano[1,3], K. Kee[1], R. Bergström[2], C. Simon[3], O. Hovatta[2]

[1]Institute for Stem Cell Biology & Regenerative Medicine, Department of Obstetrics and Gynecology, Stanford University School of Medicine, Stanford University, Palo Alto, CA 94305, USA; [2]Department of Clinical Science, Intervention and Technology; Karolinska Institutet,Karolinska University Hospital Huddinge; SE-171 86 Stockholm, Sweden; [3]Centro de Investigación Principe Felipe & Instituto Valenciano de Infertilidad (IVI) Valencia University; Avda. Autopista del Saler 16-3, Valencia, Spain

Ten to fifteen percent of couples are infertile with the most common causes being linked to the production of few or no oocytes or sperm. Yet our understanding of human germ cell development is poor, at least in part due to inaccessibility of early developmental stages to molecular genetic studies. Pluripotent stem cells may provide the necessary human genetic system to study germ cell development and ultimately treat infertility associated with reproductive aging, premature ovarian failure, and/or poor oocyte and sperm quality. Human induced pluripotent stem cells (iPSCs) are particularly promising in this regard. However, the ability of iPSCs derived from human adult somatic cells to form the germ cell lineage has not been reported. Here, we compared the potential of human iPSCs derived from adult and fetal somatic cells to differentiate to primordial and meiotic germ cells relative to human embryonic stem cells (hESCs). We observed that iPSCs differentiated spontaneously to primordial germ cells (PGCs) and in response to overexpression of intrinsic regulators, also formed meiotic and post-meiotic cells. Indeed, iPSCs showed enhanced differentiation to PGCs, as well as to meiotic cells, even under conditions that promote the undifferentiated state. Results suggest that human iPSCs derived from reprogramming of adult somatic cells may provide a useful model for basic human molecular genetic studies and ultimately clinical studies of potential novel therapeutical applications.