

Human germ cell differentiation from fetal- and adult-derived induced pluripotent stem cells.

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Authors: Sarita Panula, Jose V Medrano, Kehkooi Kee, Rosita Bergstrom, Ha Nam Nguyen, Blake Byers, Kitchener D Wilson, Joseph C Wu, Carlos Simon, Outi Hovatta, Renee A Reijo Pera

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Public Summary:

This manuscript was the first to report the differentiation of human induced pluripotent stem cells, derived from adults, to form human germ cells. Moreover, the report shows that the germ cells can be differentiated to haploid progeny. This suggests the ability to use this system to understand human infertility and to understand birth defects due to errors of chromosome segregation in germ cells.

Scientific Abstract:

Historically, our understanding of molecular genetic aspects of human germ cell development has been limited, at least in part due to inaccessibility of early stages of human development to experimentation. However, the derivation of pluripotent stem cells may provide the necessary human genetic system to study germ cell development. In this study, we compared the potential of human induced pluripotent stem cells (iPSCs), derived from adult and fetal somatic cells to form primordial and meiotic germ cells, relative to human embryonic stem cells. We found that approximately 5% of human iPSCs differentiated to primordial germ cells (PGCs) following induction with bone morphogenetic proteins. Furthermore, we observed that PGCs expressed green fluorescent protein from a germ cell-specific reporter and were enriched for the expression of endogenous germ cell-specific proteins and mRNAs. In response to the overexpression of intrinsic regulators, we also observed that iPSCs formed meiotic cells with extensive synaptonemal complexes and post-meiotic haploid cells with a similar pattern of ACROSIN staining as observed in human spermatids. These results indicate that human iPSCs derived from reprogramming of adult somatic cells can form germline cells. This system may provide a useful model for molecular genetic studies of human germline formation and pathology and a novel platform for clinical studies and potential therapeutical applications.

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