Frank Edenhofer, J Cell Sci Ther 2011, 2:4
doi: http://dx.doi.org/10.4172/2157-7013.S1.16

OMICS Group Conferences
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International Conference & Exhibition on
Cell Science & Stem Cell Research

29 Nov - 1 Dec 2011 Philadelphia Airport Marriott, USA

Exploring novel pathways of cell reprogramming and transdifferentiation for targeted stem cell therapies

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Embryonic stem (ES) cells have become a major focus of scientific interest as a potential source for both, transplantable cells in regenerative medicine, and disease modeling. Human induced pluripotent stem (iPS) cells would represent an appealing option for the use of ES-like patient-specific cells as no embryos or oocytes are required for their derivation. However, crucial safety issues have to be addressed in order to create human iPS cells that are clinically useful as the classical iPS technique involves permanent genetic manipulation that may result in tumor formation. Our research focuses on the derivation of safe iPS cells, targeted differentiation into transplantable neural precursors and its application for disease modeling. In contrast to conventional gene transfer strategies the direct introduction of proteins and synthetic mRNA into cells bypasses the risk of insertional mutagenesis and thus offers an alternative to genetic intervention. We show that protein transduction is a powerful approach to deliver biologically active proteins directly into cells. This paper presents the use of biologically active cell-permeant reprogramming factors to i) induce pluripotency in somatic cells and ii) study the molecular mechanism of reprogramming. Thus far, viral transduction of transcription factors still represents the preferred, most robust reprogramming system. We performed efficient reprogramming transgene removal by cell-permeant recombinases to genetically clean such virally transduced human iPS cells. Finally, novel strategies will be presented for the targeted differentiation into neural lineages employing small molecules and instructive factors.

Biography

Frank Edenhofer, Ph.D., is the Head of the Stem Cell Engineering Group at the Institute of Reconstructive Neurobiology at the University of Bonn, Germany. He gained his PhD in Biochemistry from the Ludwig-Maximilians University of Munich in 1997. During his PhD studies he worked on molecular mechanisms underlying Prion-mediated neurodegeneration under supervision of Ernst-Ludwig Winnacker. In 1998 he joined the laboratory of Klaus Rajewsky (Institute for Genetics, University of Cologne) for a post-doctoral fellowship to train (stem) cell culture and mouse embryo manipulation. After receiving a junior researcher award in 2002 he established a research group at the University of Bonn. He has published more than 35 papers in reputed journals.