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PREFACE

Induced Pluripotent Stem Cells: Current Progress and Future Perspectives

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Conversion of cell fate is not only an essential biological question, but also has great clinical values. In early 1950s, cellular reprogramming was first achieved using the technique of somatic cell nuclear transfer (SCNT), which transferred the nuclear of somatic cells into an enucleated oocyte, thus converted the mature somatic cells into pluripotent state. Using this technique, *Xenopus laevis* and the famous sheep "Dolly" were cloned successfully in 1960s and 1990s, respectively. Following that, many other species have been cloned via the SCNT technique, and the mechanisms underlying cellular reprogramming have been extensively studied.

After SCNT, another breakthrough in cell fate conversion was achieved in 2006, with the Japanese scientist Yamanaka and his colleagues demonstrated that mouse fibroblasts could be reprogrammed into pluripotent state by exogenous expression of four transcriptional factors, Oct4, Sox2, Klf4 and c-Myc. Those induced pluripotent stem (iPS) cells have equivalent properties to embryonic stem (ES) cells, which can go indefinite self-renewal and can differentiate into various cell types of three germ layers both *in vitro* and *in vivo*. Subsequently, human iPS cells were also generated successfully, which were considered to have great clinical application potential for their promise to overcome the ethic and immune-rejection obstacles faced by ES cells. The recently established patient and disease-specific iPS cells have also opened new doors for exploring the pathogenesis of human disease and drug screening.

Since 2006, iPS cells have become one of the most attractive and competitive fields in life science research, many important progresses have been made during the past few years. Besides the early stage retrovirus transfection method for exogenous gene expression, various new approaches have been demonstrated to generate iPS cells successfully, including using non-integrative vectors, mRNAs or chemicals. These new methods have the potential to reduce the tumorigenesis risk of iPS cells by avoiding the genomic mutations caused by retroviruses, although the pluripotency of iPS cells produced by some of these methods still need to be further confirmed.

The immunogenicity of iPS cells is still a controversial issue. It was reported that iPS cells are immunogenic post transplantation, which may be caused by mutations during the reprogramming and long time *in vitro* culture process. However, there were also controversial reports about non-immunogenic iPS cells. It is critical to prevent or reduce the potential immunogenicity of human iPS cells post transplantation before applying them in clinical therapies.

Using approaches similar to the iPS technique, scientists have been able to convert one type of differentiated somatic cells into another type, without going through the pluripotent stage. This technique, named trans-differentiation, is considered to be less tumorigenic than the iPS approach, as the resulting cells are non-pluripotent. Nevertheless, how to precisely control the fate of reprogrammed cells to generate well differentiated and functional cells is a major task for all cell reprogramming techniques. And the therapeutic effects of either human iPS cells or their derivatives still need to be carefully investigated before some clinical trials could be launched.

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To introduce the recent progresses in cellular reprogramming, especially in the iPS cell research field, we have produced this special issue on iPS cell studies and related issues. We apologize for works or aspects not being covered here due to page limitations.

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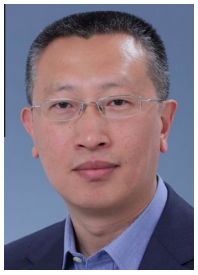

Qi Zhou, PhD, Professor and Director of State Key Laboratory of Reproductive Biology, Institute of Zoology, Chinese Academy of Sciences (CAS), China. Dr. Zhou is the Chief Scientist of the Stem Cell and Regenerative Medicine Project of CAS. The current research interests of his lab mainly focus on mechanisms of cellular programming and reprogramming, as well as developing new techniques to improve reprogramming efficiency and establishing cellular and animal models for basic and clinical researches. His group has created the first iPS animal "tiny" mouse, identified a molecular marker for assessing the pluripotency level of iPS cells, generated mouse haploid embryonic stem cell lines and obtained the first live transgenic mouse produced from haploid embryonic stem cells. He has published more than 60 papers in scientific journals including *Nature*, *Science*, *Nature Biotechnology*, *PNAS*, *etc*.