Stem cell research: From molecular physiology to therapeutic applications

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Stem cell research promises remedies to many devastating diseases that are currently incurable, ranging from diabetes and Parkinson's disease to paralysis. Totipotent embryonic stem cells have great potential for generating a wide range of different human cells that can be used to restore malfunctioning or damaged cells and tissues in patients.

Recent studies have shown that pluripotent stem cells derived from adult bone marrow, the umbilical cord and the placenta could also be induced to differentiate into a variety of different tissues. In this issue, we have invited several scientists in China to summarize their pioneering works in the stem cell research field.

Since 2001, Dr. Alex Yu Zhang has been a professor at Capital Medical University in Beijing and is Director of Cell Therapy Center at Xuanwu Hospital. His current research interest focuses on the understanding of basic biological properties of stem cells and developing nonhuman primate models for stem cell-based therapy of degenerative diseases. He has developed a stem cell mediated expression system for treating Parkinson's disease and his research using pancreatic progenitor cells for treating diabetes has demonstrated efficacy in monkey models.

Professor Zhang has written an overview of cell replacement therapy of Parkinson's disease, which has been studied in both animal models and human patients for more than 20 years. Recent progress in stem cell biology has indicated that it is possible to avoid immunorejection of either nuclear transfer embryonic stem cells or induced pluripotent stem

cells. On the other hand, recent post mortem analysis of patients who received fetal brain cell transplantation revealed that implanted cells are prone to degeneration just like endogenous neurons. Thus it appears that future cell replacement studies will have to focus on ameliorating disease symptoms as well as on slowing the progression of the disease[1].

Professor Robert Chunhua Zhao from the Chinese Academy of Medical Sciences is Executive Director of the National Center for Stem Cell Research. His group has taken stem cell therapy into phase II clinical trials in China, and is the leading runner in stem cell therapeutics. They have identified a mesenchymal stem cell (MSC) population from human fetal bone marrow and found that these cells could differentiate not only into osteogenic, adipogenic and endothelial lineages, but also hepatocyte-like cells, and neural and erythroid cells. They remained in some tissues and organs during gestation and could give rise to different kinds of pluripotent stem cells and thus could potentially contribute to self-repair and self-renewal of tissues and organs. They generated cells not only for the damaged tissues in which they reside, but also for damaged tissues at other locations in the body via migration triggered by proinflammatory cytokines and growth factors. The potential use of MSCs in tissue regeneration has been shown in several models, including skin, muscle, lung, heart and the small intestine. MSCs have emerged as a promising therapeutic modality for tissue regeneration and autoimmune disease, although the mechanisms underlying the immune-modulatory effects of MSCs have not yet been clearly defined. In this review, Professor Robert Zhao summarizes the current literature on the complex mechanism of MSCs' immune modulation and clinical studies, and discusses future directions for utilizing MSCs for clinical treatments[2].

Professor Hongkui Deng from Peking University is working on the differentiation of human embryonic stem cells into pancreatic beta cells to treat diabetes. He is one of the two winners in China of the Bill and Melinda Gates Foundation's "Grand Challenges in Global Health". He

obtained $1.9 million for his proposal to use stem cells to create mouse models for testing HIV and hepatitis C vaccines. Professor Deng has written a summary of recent progress in human embryonic and inducible pluripotent stem cell differentiation into functional pancreatic islet cells and discusses the challenges for future work[3].

Professor Qi Zhou is assistant Director of the Institute of Zoology at the Chinese Academy of Sciences. He has been studying the mechanism of differentiation and de-differentiation, cellular plasticity and totipotency of pluripotent cells, as well as that of somatic cells. He intends to build various cellular and animal models for human diseases, to uncover mechanisms underlying these different cellular processes and to discover new ways to improve cloning efficiency, which will provide a powerful tool for the study of mammalian reprogramming and ultimately offer important opportunities for regenerative medicine. Professor Zhou has helped to build the National Stem Cell Bank in Beijing, where clinical grade stem cell lines and patient specific cell lines have been created for future drug target candidate screening and therapeutic applications. Professor Qi Zhou has written a summary on human parthenogenetic embryonic stem cells as one potential resource for stem cell therapy[4].

Professor Lin Liu from Nankai University has been working on creating versatile patient-specific pluripotent stem cell lines that can be reliably used to fulfill the promise of stem cell therapy in regenerative medicine. Dr. Lin Liu's group found that pES cells generated from immature oocytes in mice exhibit pluripotency resembling fES cells, as evidenced by similarly high chimera production and germline transmission. Thus, immature eggs may provide an efficient source of autologous stem cells for regenerative medicine. This group also tested whether pESCs can be generated from older females. Drs. Lingyi Chen works on mechanisms of early embryonic differentiation. In their review of current special topics on stem cells, Drs. Lingyi Chen and Lin Liu analyze the current state of iPS research, particularly on limitations and advancements in

this field, and propose possible future directions to meet the challenges of iPS cells for clinical applications[5].

Stem cell research has made significant progress in the past decade. Some therapeutic applications are coming closer to being on the market, but it is still hard to predict if and when stem cell therapy will replace largely traditional therapeutics. Given the early indications for success, we hope to see promising remedies for the many current uncurable diseases being made available in the clinic over the coming years.

More information:

1 Ren Z, Zhang Y. Cell therapy for Parkinson's disease - So close and so far away. Sci China C-Life Sci, 2009, 52: 610—614

2 Wang L, Zhao R C. Mesenchymal stem cells targeting the GVHD. Sci China C-Life Sci, 2009, 52: 603—609

3 Zhang D, Jiang W, Shi Y, et al. Generation of Pancreatic islet cell from human embryonic stem cell. Sci China C-Life Sci, 2009, 52: 615—621

4 Hao J, Zhu W, Sheng C, et al. Human parthenogenetic embryonic stem cells: One potential resource for cell therapy. Sci China C-Life Sci, 2009, 52: 622—636

5 Chen L, Liu L. Current progress and prospect of induced pluripotent stem cell. Sci China C-Life Sci, 2009, 52: 622—636

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