

Editorial Remark: Proliferation and Differentiation of Stem Cell Research

Stem cells possess two remarkable properties: self-renewal to keep the stem cell pool replenished, and differentiation to turn into various cell types in the body. These unique features not only enable their application in basic biomedical research but also in drug discovery/development and especially in regenerative medicine for the treatment of many incurable diseases. No wonder, stem cell research has captured the imagination of both the scientific community and general public alike. The last several years have witnessed a proliferation of stem cell research activities and an extension (or differentiation in stem cell terms) to multiple disciplines. To highlight this proliferation and differentiation of this research field, we invited experts to review several major topics.

In the first article, Dr. Junying Yu described her recent breakthrough work on human induced pluripotent stem (iPS) cells. Together with Dr. James Thomson, the first scientist who isolated human embryonic stem cells (ESCs), Dr. Yu derived ESC-like cells directly from human skin cells via transfer of four genes. Their work, along with the work by Shinya Yamanaka, is the most significant advance in stem cell research since the establishment of human ESCs. It presents a conceptual framework for generating immune-complement cell sources for therapy without destroying human embryos or cloning, therefore, circumventing ethical and legal concerns that have hampered this field.

Drs. Ngan F. Huang and Song Li gave an overview of various types of stem cells and their utilities in regenerative medicine. They pointed out that the optimal stem cell type

will likely overcome the hurdles of consistency of isolation and expansion, immune rejection, survival, and teratoma formation.

To use stem cells in regenerative medicine, they first need to be expanded and differentiate to desired cell types in sufficient quantity and quality. As explained by Prof. Gen-Sheng Feng, achieving these goals requires a thorough understanding of the intracellular signaling pathways involved in decisions on self-renewal and differentiation of ES cells. This is perhaps the most important subject in stem cell biology today.

A potential dark side of stem cells associates them to cancer formation. Recently, there has been a surge of interest in the cancer stem cell theory. Some believe that this theory could explain the genesis of many cancers and have immense implication in cancer therapy. Dr. Xiao-dong Zhu reviewed the status of cancer stem cell research and highlights the therapeutic potential and the unanswered questions of this hypothesis.

Stem cell research has spawn all over the world, including our home country China. In his overview of stem cell research in China, Prof. Guo-Tong Xu provided a thorough survey of the leading stem cell researchers in China and their works. This information not only reveals the stature of a field exceptionally supported by the Chinese government, but also leads some readers to potential collaborators.

We hope that this timely collection conveys the excitement of stem cell research, and that the readers are left with same impression – for stem cell research, the future is happening.

Glossary in Stem Cell Research

Adult stem cells (成体干细胞)

Stem cells found in tissues of a developed, adult organism. These stem cells can give rise to specialized cell types of the same tissue, i.e., a heart stem cell can give rise to a functional heart muscle cell. It is still unclear whether adult stem cells can turn to all other cell types of the body.

Allogenic stem cell transplantation (异基因干细胞移植)

Stem cells from one member of a species transplanted to a genetically different member of the same species.

Autologous stem cell transplantation (同基因干细胞移植)

Stem cells transplanted from one individual back to the same individual. Such transplants do not induce an immune rejection.

Blastocyst (囊胚)

The spherical cell mass of a very early embryo consisting of ~150 cells. It contains a fluid-filled cavity, a cluster of cells called the inner cell mass (ICM) from which embryonic stem cells are derived

Bone marrow stromal cell (骨髓基质细胞) or bone marrow mesenchymal stem cells (骨髓间叶干细胞)

A mixed population of cells derived from the non-blood forming fraction of bone marrow. They are capable of growth and differentiation into a number of different cell types including bone, cartilage and fat.

Cancer stem cell (肿瘤干细胞) or Tumor-initiating cell (肿瘤起始细胞)

A cell or a population of cells with stem cell properties that hypothetically initiates and gives rise to the entire tumor.

Cloning (克隆)

A process in which an organism produces one or more genetically alike copies of itself by asexual means. The term can also be

Historic Milestones in Stem Cell Research

- 1950s Scientists worked on cloning frogs
- 1960s Chinese scientist Tong, Dizhou performed cloning in fish
- 1969 First bone marrow transplant performed for leukemia patients
- 1978 First IVF baby born from fertilization of human eggs in vitro
- 1981 Mouse ES cells isolated from explanted inner cell mass of blastocyst
- 1987 Development of gene targeting technology using mouse ES cells
- 1988 First umbilical cord blood transplant
- 1980s Hematopoietic stem cells isolated by fluorescence-activated cell sorter
- 1997 Leukemia stem cells found – beginning of the cancer stem cell hypothesis
- 1996 Dolly, the sheep – the first cloned mammal born through somatic cell nuclear transfer technique
- 1998 First human ES cell line derived from human blastocysts by James Thomson at the University of Wisconsin
- 1999-2001 Demonstration of significant differentiation abilities of adult stem cells isolated from several tissues
- 2001 The Bush administration announced policy to fund research on existing embryonic stem cell lines
- 2003 Putative cancer stem cells found in solid tumors
- 2004 Huang of South Korea claimed generation of stem cell lines from cloned human embryos, which was later found fraudulent
- 2004 California passed Proposition 71 to create a funding agency for stem cell research – California Institute of Regenerative Medicine (CIRM)
- 2006 Japanese scientist Yamanaka discovered iPS – reprogramming of mouse skin cells to ES-like cells
- 2007 Yamanaka and Yu/Thomson independently published iPS for human cells, a major breakthrough toward stem cell therapy

applied to a group of cells undergoing replication by repetitive mitoses (cell divisions).

Differentiation (分化)

A process of development with an increasing level of organization or complexity of a cell or tissue and more specialized functions.

Embryonic germline cells (胚芽干细胞)

Pluripotent stem cells derived from the primitive germline cells with properties similar to embryonic stem cells.

Embryonic stem cell (胚胎干细胞)

Cells derived from the inner cell mass of a developing blastocyst. An ES cell is of self-renewing (replicating itself), pluripotent (forming all cell types found in the body) and theoretically immortal.

Hematopoietic stem cells (造血干细胞)

The precursors of blood cells residing in the bone marrow system

Hematopoietic stem cell transplantation (造血干细胞移植)

Transplantation of hematopoietic stem cells with blood-forming potential. They provide rapid and sustained reconstitution of blood formation.

Induced pluripotent stem cells (iPS cells) (诱导多功能干细胞)

Pluripotent stem cells artificially induced from non-pluripotent cells, typically adult somatic cells, by inserting certain genes. iPS cells are believed to be identical to natural pluripotent stem cells, such as embryonic stem cells in many respects, but the full extent of their relation to natural pluripotent stem cells is still being assessed. They offer hope to therapy without immune rejection, and eliminate the ethical controversy of using embryos.

Parthenogenesis (单性生殖)

Virgin birth, a form of reproduction where an oocyte develops without a sperm. Parthenogenesis occurs commonly among insects and other arthropods. Artificially

inducing parthenogenesis with human eggs may be a means to isolate stem cells from an egg, without fertilization.

Pluripotent stem cells (多功能干细胞)

The stem cells that can become all the cell types found in an implanted embryo, fetus, or developed organism.

Progenitor cell (前体细胞)

An early descendant of a stem cell that can only differentiate, but cannot renew itself. A progenitor cell is often more limited in the kinds of cells it can become than a stem cell.

Regenerative medicine (再生医学)

Medical interventions that repair damaged organs, most commonly by using stem cells to replace cells and tissues damaged by aging or by diseases.

Reproductive cloning (生殖性克隆)

Somatic cell nuclear transfer used for the production of a fetus and delivery of a live offspring that is genetically identical the donor of the somatic cell DNA. Human reproductive cloning is banned in most countries.

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Somatic cells (体细胞)

All the cells within the developing or developed organism with the exception of germline (oocyte and sperm) cells.

Somatic cell nuclear transfer (SCNT) (体细胞核移植)

A technique in which the nucleus of a somatic cell is transferred into an egg which had its nucleus removed. Cells and tissues derived from such process have the same genetic material as the donor somatic cells, and therefore, prevent immune rejection if transplanted into the same donor (**therapeutic cloning**). If the SCNT egg is implanted into the womb of an animal, an individual will be born as a clone with identical genes as the somatic cell (**reproductive cloning**).

Stem cells (干细胞)

Cells that are capable to self-renew (replicating themselves by cell division), as well as to differentiate into mature, specialized cells (pluripotency).

Umbilical cord stem cells (脐带血干细胞)

Stem cells present in the umbilical cord. Umbilical cord stem cells are similar to stem cells that reside in bone marrow, and can be used for the treatment of leukemia, and other diseases of the blood. Efforts are now being undertaken to collect these cells and store them in freezers for later use (cord blood banks)