REVIEW ARTICLE

Skin Stem Cells

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Abstract

The future development of medicine will greatly depend on research, knowledge and clinical application of stem cells. In recent years, stem cells especially; skin stem cells have been very interesting and amazing targets for study and scientific application in the following fields : 1- Cell-based therapy; 2- Regenerative medicine and tissue engineering; 3- Gene therapy; 4- Therapeutic cloning; 5- More efficient new drugs with fewer side effects.

Keywords: skin stem cells, pluripotent stem cells, cell - based therapy

Introduction[1-8]

Skin is the largest and heaviest organ of the human body. Skin is readily accessible and there are so many stem cells in the skin. As one of the unique properties of skin stem cells, they can be used for research, investigation, and clinical application in regenerative medicine.

In November 2007, scientists reported that they reprogrammed regular skin cells in human to behave just like embryonic stem cells. Direct reprogramming of somatic cells to pluripotent state, thus" reverses the developmental arrow of time", and is considered by some to be the "holy grail" of stem cell research[1,6,7]. This stem cell breakthrough has been named as the first of the top 10 scientific discoveries of the year 2007.

Once the result in human cells is confirmed, these advances will enable the creation of patient - stem cell lines to study different disease mechanisms in the laboratory[1,2,6,7].

What are stem cells? [2,6,7,9]

Stem cells are unspecialized cells that have two important characteristics that distinguish them from other cells in the body.

First, they can replenish their numbers for long periods of time through cell division.

Second, after receiving certain chemical signals, they can differentiate or transform into specialized cells with specific functions, such as a heart cell, nerve cell or skin cell.

Stem cells can be classified by the extent to which they can differentiate into different cell types:

- Totipotent stem cells can differentiate into any cell type in the body plus placenta, which nourishes the embryo. A fertilized egg is a type of totipotent stem cell.
- Pluripotent stem cells are descendants of the totipotent stem cells of the embryo which develop about four days after fertilization and can differentiate into any cell type, except for totipotent stem cells and cells of the placenta.
- Multipotent stem cells are descendants of pluripotent stem cells and antecedents of specialized cells in particular tissues. For example hematopoietic stem cells in the bone marrow, neural stem cells in nervous tissue and skin stem cells.
- Progenitor cells (or unipotent stem cells) can produce only one cell type. For example erythroid progenitor cells only differentiate into red blood cells.

At the end of the long chain of cell divisions are "terminally differentiated " cells, such as liver cell or keratinocytes, which are permanently committed to specific functions. These cells stay committed to their functions for the life of the organism or until tumor develops which in this case the cells dedifferentiate; or return to a less mature state.

There are three sources of stem cells:

- Embryonic stem cells (ESCs) are derived from 4- to 5-day-old embryo, known as blastocyst which consists of 100 - 200 cells. As ESCs are pluripotent and relatively easy to grow in cell culture, they are attractive candidates for use in stem cell therapies.
- Adult or somatic stem cells are undifferentiated cells that are found in small numbers in most adult tissues. However, they are also found in children and can be extracted from umbilical cord blood.

• Embryonic (or fetal) germ cells are pluripotent stem cells derived from so-called primordial germ cells; which are the cells that give rise to the gametes (sperm and eggs) in adults obtained from the area in 5- to 9-week-old embryo/fetus.

The primary role of adult stem cells in the body is to maintain and repair the tissues in which they are found. They are usually thought of as a multipotent cell giving rise to a closely related family of cells within the tissue.

Research is now being conducted on both adult and embryonic stem cells to determine the characteristics and the potential of both in curing diseases.

Skin stem cells and their history[10-27]

The first embryonic stem cells were isolated in mice in 1981, but it was not until 1998 that researchers managed to derive stem cells from human embryo.

From spring 2004 to 2005, researchers from Universities of Pennsylvania and California, identified stem cells of hair follicle of mice whisker and cultured them. In different culture media, these stem cells yielded neurons, smooth muscle, melanocytes, and keratinocytes.

In January 2006, Vogel and colleagues From National Cancer Institute successfully isolated and characterized genes expressed by human hair follicle stem cells. They reported that isolation, cultivation and propagation of these stem cells are important for tissue engineering approach to treating disorders of the hair and skin.

Martin and Evans discovered how to make mouse embryonic stem cells, enabling any genetic alteration to be transferred to the germ-line and hence to the next generation.

In summer 2006, Takahashi and Yamanaka stunned the scientific community with their study showing molecular reprogramming of mouse somatic cells into induced pluripotent stem (iPS) cells using just four factors: OCT4, SOX2, KLF4 and C-MYC.

In November 2007, two teams of scientists independently discovered a way to turn ordinary human skin cells into stem cells with the same characteristics as those derived from human embryo. The crux of the breakthrough report, published online by the journals “Cell” and “Science”, is a direct reprogramming technique that adds a cocktail of four genetic factors to run -of – the- mill human skin cells.

By over-expressing the transcription factor quartet of OCT4, SOX2, KLF4 and C- MYC in adult human fibroblasts, Takahashi and Yamanaka and their colleagues successfully isolated human pluripotent stem cells that resemble human embryonic stem cells by all measured criteria. This is a significant turning point in nuclear reprogramming research with broad implication for generating patient-specific pluripotent stem cells for research and therapeutic applications. The work of these teams is still at the level of basic research.

Advantages and applications of skin stem cells[28-35]

Skin stem cells are located in the epidermis, the dermis and hair follicle bulge area.

Skin and hair follicle stem cells are abundant, easily accessible, ultimate sources of actively growing pluripotent adult stem cells.

Skin also represents a large reservoir for other adult stem cells; including mesenchymal, hematopoietic and neural stem cells.

Skin stem cells can be used for research and managing disorders such as:

- Skin cancer
- Wounds and ulcers, burns and injury
- Genetic disorders and congenital defects
- Auto-immune diseases
- Hair loss and alopecia
- Cosmetic surgery and hair transplantation
- Anti-aging procedures and cosmeceuticals applications

The whole idea of stem cell based therapies is that the stem cells could be used to replace or repair cells damaged or destroyed by diseases or injuries.

In addition, skin stem cells have these advantages:

1- Less rejection process in autologous and allogenic application (immune privileged).

2- The capability of transforming to other cell types including mesenchymal, hematopoietic and neural cells.

3- Skin stem cells can be used without legal, moral and ethical restrictions, in contrast to embryonic stem cells derived from embryo.

Conclusion[36-42]

The most immediate use of the skin cell-derived stem cells will be basic investigation of mechanisms behind diseases. It could take many years before the technique could be made safe for use in human being. Once the results in human cells are confirmed by direct reprogramming of somatic cells to a pluripotent state (iPS), these advances will enable the creation of patient-specific stem cell lines to study different disease mechanisms in the laboratory.

Such cellular models also have the potential to dramatically increase the efficiency of new drug discovery and to provide valuable tools for toxicology testing.

Furthermore, this reprogramming system could make the idea of customized patient-specific screening and therapy both possible and economically feasible.

Finally, the work will have a powerful impact on the intense debate regarding the moral, religious and political aspects of embryonic cell research.

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