Commentary

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Cell Therapy and Gene Therapy

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Cell Therapy

A technology that relies on replacing diseased or dysfunctional cells with healthy, functioning ones. Whole blood transfusions, packed red cell transfusions, platelet transfusions, bone marrow transplants, and organ transplants are all forms of cell therapy. Cell therapy may be applicable to some types of cancer, neurological diseases such as Parkinson disease and amyotrophic lateral sclerosis (Lou Gehrig disease), spinal cord injuries, and diabetes. A great range of cells can serve in cell therapy including blood and bone marrow cells, mature and immature solid tissue cells, adult stem cells and, most controversially, embryonic stem cells.

Different type of cell therapy

The most common type of cell therapy is blood transfusion, and the transfusion of red blood cells, white blood cells, and platelets from a donor. Another common cell therapy is the transplantation of hematopoietic stem cells to create bone marrow which has been performed for over 40 years. As with gene therapy, cell therapy subtypes can be classified in different ways. This is currently no formal classification system for cell therapies. Here the different types of cells used for cell therapy have been classified by cell potency. Four types of pluripotent stem cells and four types of multipotent stem cells obtained from adult tissue are described.

Embryonic stem cells (ESCs): These are pluripotent stem cells derived from embryos. Generally, the embryos used to isolate stem cells are unused embryos generated from in vitro fertilization (IVF) for assisted reproduction. As ESCs are pluripotent they retain the ability to self-renew and to form any cell in the body. ESCs have the advantage of versatility due to their pluripotency, but the use of embryos in the development of therapeutic strategies raises some ethical concerns. In addition, stem cell lines generated from embryos are not genetically matched to the patient which can increase the chance that the transplanted cell is rejected by the patient's immune system.

Induced pluripotent stem cells (iPSCs): A differentiated adult (somatic) cell, such as a skin cell is reprogrammed to return to a pluripotent state. These cells offer the advantage of pluripotency but without the ethical concerns of embryonic stem cells. iPSCs may also be derived from the patient and thus avoid the problem of immune rejection. iPSCs are produced by transforming the adult cell with a cocktail of genes usually delivered via a viral vector. While the efficiency of the process has been greatly improved since inception, the relatively low rate of reprogramming remains a concern. Another concern is that iPSCs are derived from adult cells and are therefore "older" than embryonic stem cells as evidenced by a higher rate of programmed cell death, lower rates of DNA damage repair and increased incidence of point mutations.

Nuclear transfer embryonic stem cells (ntESCs): These pluripotent cells are produced by transferring the nucleus from an adult cell obtained from the patient to an oocyte (egg cell) obtained from a donor. The process of transferring the nucleus reprograms the egg cell to pluripotency. As with iPSCs, the derived cells match the nuclear genome of the patient and are unlikely to be rejected by the body. However, the major advantage of this technique is that the resulting ntESCs carry the nuclear DNA of the patient alongside mitochondria from the donor, making this technique particularly appropriate for diseases where the mitochondria are damaged or dysfunctional. A drawback of ntESCs is that the process of generation is cumbersome and requires a donor oocyte. At the time of writing stem cell production using this technique has only been shown in lower mammals.

Parthenogeneticembryonic stem cells (pES): The final option for obtaining pluripotent cells is from unfertilized oocytes. Here the oocyte is treated with chemicals that induce embryo generation without the addition of sperm (parthenogenesis) and ESCs are harvested from the developing embryo. This technique generates ESCs that are genetically identical to the female patient. However, this method is in the early stages of development and it is not known if cells and tissues derived from parthenogenesis develop normally.

Hematopoietic stem cells (HSCs): HSCsare multi-potent blood stem cells that give rise to all types of blood cells. HSCs can be

found in adult bone marrow, peripheral blood, and umbilical cord blood.

Mesenchymal stem cells (MSCs): MSCsare multi-potent cells present in multiple tissues including umbilical cord, bone marrow, and fat tissue. MSCs give rise to bone, cartilage, muscle, and adipocytes (fat cells) which promotes marrow adipose tissue.

Neural stem cells (Nscs): Adult neural stem cells are present in small number in defined regions of the mammalian brain. These multi-potent cells replenish neurons and supporting cells of the brain. However, adult neural stem cells cannot be obtained from patients due to their location in the brain. Therefore, neural stem cells used for cell therapies are obtained from iPSCs or ESCs.

Epithelial stem cells: Epithelial cells are those that form the surfaces and linings of the body including the epidermis and the lining of the gastro-intestinal tract. Multi-potent epithelial stem cells are found in these areas along with unipolar stem cells that only differentiate into one type of cell. Epithelial stem cells have been successfully used to regenerate the corneal epithelium of the eye.

Immune cell therapy: Cells that rapidly reproduce in the body such as immune cells, blood cells or skin cells can usually do so ex vivo given the right conditions. This allows differentiated, adult immune cells to be used for cell therapy. The cells can be removed from the body, isolated from a mixed cell population, modified and then expanded before return to the body. A recently developed cell therapy involves the transfer of adult self-renewing T lymphocytes which are genetically modified to increase their immune potency to kill disease-causing cells.

Gene Therapy

Human gene therapy seeks to modify or manipulate the expression of a gene or to alter the biological properties of living cells for therapeutic use.Gene therapy is a technique that modifies a person's genes to treat or cure disease. Gene therapies can work by several mechanisms:

• Replacing a disease-causing gene with a healthy copy of the gene

• Inactivating a disease-causing gene that is not functioning properly

• Introducing a new or modified gene into the body to help treat a disease