SCENARIO 1: Type I Diabetes

Researchers are working to develop a stem cell therapy that will regenerate insulin-producing pancreatic cells in type 1 diabetes patients. Pancreatic cells are lost in these patients when their immune system attacks them. A recent clinical trial involving 23 type 1 diabetes patients showed that 20 became insulin independent for at least four years after a hematopoietic stem cell transplant [ref 1]. Hematopoietic stem cells give rise to blood and immune cells. The goal of this type of therapy is to reset the immune system and improve tolerance of self cells in the pancreas [ref 2].

Other researchers are pursuing a different strategy. Pluripotent stem cells (both ES and iPS cells) can be directed to differentiate into functional pancreatic beta cells in a dish [ref 3]. Researchers at the Nevada Cancer Institute transplanted iPS cell-derived beta cells into diabetic mice to restore insulin production and normal glucose levels [ref 4]. This experiment has not yet been carried out in humans. However, islet cell transplants from cadavers serve as a proof-of-concept that a cell therapy can successfully restore control of blood glucose levels in diabetes patients [ref 5].

A third approach to curing diabetes is to activate adult stem cells already present in the pancreas and direct them to become beta cells [ref 6]. Researchers have successfully used this approach to restore pancreatic function in mouse models [ref 7]. Similarly, researchers have been able to change certain types of differentiated pancreas cells (that would normally produce digestive enzymes) into insulin-producing beta cells [ref 8].

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SCENARIO 2: Parkinson's Disease

Parkinson's disease is a prime candidate for stem cell therapy. This progressive neurological disease is caused by the loss of midbrain neurons that produce the neurotransmitter dopamine [ref 1-2]. Dopamine coordinates movement, learning, and the reward pathway.

Stem cell therapies have been attempted in clinical trials for Parkinson's disease since the 1980s. Most of these experiments used dopamine-producing cells obtained from fetuses [ref 3-4]. Although the transplanted cells survived and some patients benefited from the treatment, others suffered from severe dyskinesia (lack of controlled muscle movement).

As an alternative to fetal tissue, researchers are turning to pluripotent stem cells (both ES and iPS cells) as a treatment for Parkinson's disease. Researchers have already worked out the steps necessary to differentiate pluripotent stem cells (both ES and iPS cells) into dopamine-producing brain cells. Recent work has focused on improving the safety of cell-based therapies. iPS cells are attractive because they eliminate the risk of immune rejection. And a cell sorting technique separates undifferentiated stem cells—which tend to form tumors—from neurons before they are transplanted into patients.

Transplanting dopaminergic neurons (derived from either ES or iPS cells) improves motor control in rat models of Parkinson's disease [ref 5-6]. A similar iPS cell therapy has not yet been tested in humans.

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SCENARIO 3: Heart Disease

Since the first heart transplant took place in 1967, researchers have continued to develop new and improved treatments for heart disease. Stem cells have now emerged as a viable option for repairing damaged heart tissue. Bone marrow stem cells, for example, have been used in clinical trials to treat more than 1000 patients after a heart attack [ref 1].

Researchers recently isolated adult stem cells from a human heart via a biopsy [ref 2]. They showed these cardiac stem cells can be expanded then reintroduced into mouse hearts to regenerate tissue. Similarly, cardiac stem cells can also be used to grow thin patches of heart tissue in a dish. Preliminary studies in the rat suggest these tissue patches can be grafted into the heart to repair damage [ref 3].

The long-term goal is to engineer an entire heart for transplantation, from a patient's own stem cells. This would eliminate the risk of immunological rejection. Human iPS cells can be led to differentiate into functional heart muscle cells and are therefore a good cell source for heart repair [ref 4]. Researchers at the University of Minnesota Center for Cardiovascular Repair have engineered a scaffold that will help them grow a human heart [ref 5].

Starting with a cadaver's donor heart, they were able to remove all the living cells and leave behind only the extracellular matrix. The scaffold holds the shape of the heart and its blood vessels, allowing the flow of oxygen and nutrients as the heart grows. They plan to try both embryonic and adult stem cells to seed the heart scaffold. The hope is that the stem cells will migrate and differentiate to assemble a vascularized and fully functional heart.

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SCENARIO 4: Nature of Stem Cells

Differentiated cells can be "reprogrammed" to look and act like stem cells from an embryo [ref 1]. In early reprogramming experiments, scientists removed the nucleus from either an egg cell or a human embryonic stem (ES) cell and replaced it with the nucleus from a differentiated skin cell [ref 2]. The resulting cells were pluripotent, meaning they could differentiate into many different cell types. Scientists deduced that egg cells and ES cells contain certain factors that can reprogram a differentiated cell's DNA, bringing it back to an embryonic state.

Researchers at Kyoto University wanted to figure out which of the factors present in eggs and embryos were responsible for reprogramming. They identified 24 genes that they thought might be important, and used retroviruses [ref 3] to deliver them into skin cells taken from a mouse tail. Adding these genes made the cells pluripotent. Gradually they eliminated genes from the mixture until they identified the minimum number of factors (or gene products) required to reprogram a nucleus. They were surprised to find that adding just four genes (Oct3/4, Sox2, c-Myc, and Klf4) was sufficient to reprogram the nucleus and make the mouse skin cell pluripotent [ref 4].

The same researchers later reprogrammed human skin cells by adding the same four genes [ref 5]. Stem cells that are generated by reprogramming the nucleus of a somatic cell are now called induced pluripotent stem cells (or iPS cells).

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SCENARIO 5: Lupus

Systemic lupus erythematosus (SLE) is an autoimmune disease that primarily effects young adult women. Most patients are able to manage the disease with aggressive immunosuppressive medications. However, some patients do not respond to medication and the disease becomes life threatening. A stem cell transplant therapy for this subset of patients is now in clinical trials [ref 1]. The purpose of the therapy is to reset the patient's immune system and thereby restore organ function.

First, a patient's own blood is removed and treated to enrich for bone marrow stem cells that will give rise to healthy immune cells. After chemotherapy destroys the remaining blood and immune cells, the enriched stem cells are returned to the patient by intravenous injection. The hope is that the injected stem cells will be able to repopulate a patient's bone marrow and heal the immune system.

Forty-eight patients received this treatment. About half were disease-free after five years, and no patients died. It is too early to tell whether the therapy cures the disease or simply slows its progression. But scientists hope that it may be a safe, effective alternative for patients whose lupus resists traditional therapies. Interestingly, this same type of stem cell transplant has been used for decades to treat a number of other diseases, including certain forms of cancer [ref 2].

An additional stem cell transplantation therapy for lupus is currently being investigated in mouse models [ref 3].

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