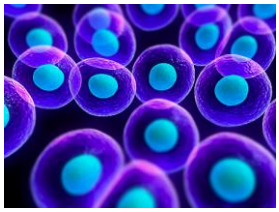
Accelerated Cure Project for MS

April 2018

Accelerating research towards a cure for multiple sclerosis

Stem Cells – The future of medicine?

There are more than 200 types of cells in the human body, for example blood cells, muscle cells and nerve cells, to name a few. Each cell type has a different makeup that is appropriate for its function. Stem cells are the foundation for every organ and tissue in the body. There are many different types of stem cells that come from different places in the body or are formed at different times in our lives. Some only exist prenatally (embryonic stem cells), while others are found during fetal development and remain in our bodies throughout life to repair tissue damage and replace lost cells (adult stem cells).



Stem cells are defined by two characteristics. They can self-renew (make copies of themselves) and differentiate (develop into more specialized cells). Beyond these two things, stem cells differ a great deal in their abilities and function. Embryonic stem cells are pluripotent, meaning when cultured they give rise to all of the body's cell types. Others (adult stem cells) are referred to as multipotent, meaning they can generate a few different cell types (generally in a specific tissue or organ).

Embryonic stem cells, as the name implies, are the cells of the developing embryo. They are obtained from the blastocyst, a ball of cells that forms three to five days after an egg cell is fertilized by a sperm. When scientists extract embryonic stem cells and grow them under special laboratory conditions, they retain the ability to give rise to all tissues and organs in the body. These cells are incredibly valuable as a renewable resource for studying normal development, disease processes, and treatments. However, the ethical considerations surrounding their use are considerable.

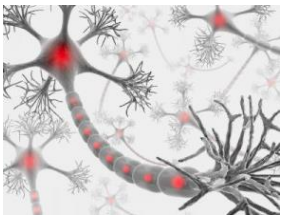
Adult stem cells are more specialized than embryonic stem cells. Typically, they produce the different cell types for the specific tissue or organ in which they are found. For example, hematopoietic stem cells, which are found in bone marrow and blood, are capable of producing all of the cells that make up the blood and the immune system (red blood cells, white blood cells and platelets). Neural stem cells from the central nervous system give rise to neurons, oligodendrocytes (myelin producing cells), and astrocytes (support cells). Mesenchymal stem cells (MSCs) are adult stem cells from stroma, the connective tissue that surrounds tissues and organs (sometimes called stromal cells). They are found in several places in the body, including the bone marrow, skin, and fat tissue. MSCs can differentiate into a variety of cell types. Some tissues and organs in the body contain small reserves of stem cells to replace cells from that tissue that are lost through normal day-to-day living or injury.

Induced pluripotent stem cells (iPSCs) are adult, tissue-specific stem cells that have been modified in the lab and converted into cells that behave like embryonic stem cells. While iPSCs share many of the same characteristics of embryonic stem cells, including the ability to give rise to all the cell types in the body, they aren't exactly the same. Researchers are studying these differences and various ways to create iPSCs to learn more about their function and potential use.

A stem cell therapy is a treatment that uses stem cells, or cells that come from stem cells, to replace or to repair a patient's cells or tissues that are damaged. The stem cells might be administered intravenously, via lumbar puncture, or transplanted into the damaged tissue directly. An autologous stem cell treatment is one in which stem cells are harvested from a person,

stored and given back to that same person. An allogenic treatment is one in which the donor and recipient of the stem cells are different people. The list of diseases for which there are approved stem cell therapies is extremely small. There are no approved stem cell treatments for MS at this time, however there is exciting progress being made as researchers study the potential of different types of stem cells to slow MS activity and to repair damage to the nervous system. It's important to note that much more research is needed before cell-based therapies become a viable MS treatment option.

Several stem cell-based approaches to treat MS are being tested in clinical trials. Autologous Hematopoietic Stem Cell Transplantation (HSCT) is an anti-inflammatory therapy. The goal of HSCT is to reset the immune system, which is responsible for damaging the brain and spinal cord in MS, and stop the inflammation that is responsible for disease activity. A person undergoing HSCT to treat MS is given some form of chemotherapy to stimulate the production of bone marrow stem cells and promote their release into the blood. Stem cells are then obtained from a blood sample and stored for later use. During the next step of treatment, the individual is usually hospitalized, and given a powerful mix of chemotherapies to kill or suppress immune cells throughout the body. The individual is usually also given antibiotics to help combat infection. The stored stem cells are then infused intravenously in hopes that the immune system will rebuild itself (a process that usually takes 3 to 6 months). After recovery, it is hoped that the newly formed immune system will function more normally. The studies to date suggest HSCT has potent, durable benefit in relapsing MS. However, there are substantial safety issues that need to be resolved and financial costs involved.



Clinical studies are currently underway to test the benefit of MSCs to repair the nervous system, specifically the myelin (a process called remyelination). This approach is similar to HSCT, except that the individual's immune cells are not destroyed or replaced. Instead, a person's own MSCs are isolated from their bone marrow or blood, multiplied in the lab, and then re-introduced in greater numbers into their body, either intravenously or via lumbar puncture. MSCs promote repair by stimulating oligodendrocyte progenitor stem cells (which develop into cells that make myelin) that are already present within the nervous system. They also have the ability to stimulate the formation of new blood vessels. There are some theories that one of the processes that may contribute to progressive MS is insufficient blood supply. Clinical trials with MSCs

have had promising results. However, a number of important questions have arisen concerning the type of cells that work best, delivery methods, technical aspects of cell production, safety issues and actual effectiveness. More research is needed before this approach can be used more generally.

One exciting avenue of research is the use of iPSCs for therapeutic purposes. In this approach, cells are obtained from an individual, for example from a skin biopsy. Using a series of genetic reprogramming techniques, they are turned into stem cells that can generate any type of human cell needed. A potential advantage of this approach is the reduced possibility the cells will be rejected by the person's immune system. This approach also bypasses possible ethical concerns surrounding the use of human embryonic stem cells. However, this research is still in its early stages.

Researchers are also exploring how neural stem cells might be used to replace the neurons and oligodendrocytes (myelin-forming cells) lost during the course of MS. This method shows promise, but there are a number of practical issues that need to be overcome. In addition, neural stem cells are typically harvested from embryonic or fetal brain, which raises the ethical issues surrounding the use of this tissue.

Exciting research is underway and significant progress has been made to better understand the potential of many types of stem cell treatments for slowing MS disease activity and for repairing damage to the nervous system. However, there is still a lot to learn about them. The media sometimes exaggerates the benefit of stem cell treatment and clinics often promote unapproved treatments to chronically ill or seriously injured patients. Patient testimonials and other marketing provided by clinics may be misleading. Beware of clinics that broadcast this language to market their treatments, instead of science-based evidence. It's important to watch for stem cell treatments offered without regulatory approval, or outside of a legitimate clinical trial. The National Institutes of Health maintain a database of clinical trials that patients and families can search for approved, actively recruiting studies. As stem cells come from different places in your body and have different functions, be wary of clinics offering treatments with stem cells originating from a part of your body unrelated to your disease or condition, or that offer the same cell treatment for a wide variety of conditions or diseases. Unless they are related, different diseases would be

expected to have very different treatments. Be wary of claims that stem cells will somehow just know where to go and what to do to treat a specific condition as they require careful instruction to become the specific cells needed to regenerate diseased or damaged tissue. If not properly directed, these stem cells may overgrow and form tumors. It's important to remember that autologous stem cell infusions or transplants are not automatically safe. Even though the risk of rejection is lower, the processes by which the cells are acquired, cultured, and then reintroduced into the body carry risks. Steer clear of clinics that gloss over or minimize these risks.

If you are considering stem cell therapy, it is important to discuss it and other options with your physician and other trusted members of your healthcare team before deciding on a course of treatment. Confirm that there is good scientific evidence that the treatment is safe and effective. Be sure that the providers have approval from an independent ethics committee, such as an Institutional Review Board (IRB), to make sure the risks are as low as possible and are worth any potential benefits, and that your rights are being protected. There should be a protocol that outlines the treatment in detail, and a consent form that clearly explains the details of the process, including the risks involved. You should have the opportunity to ask questions, should you have any, and only proceed with treatment when you are satisfied with information provided and have given permission to proceed.

Stem cell research holds tremendous promise for medical treatments, but scientists still have much to learn about how they work in the body and their capacity for healing. Numerous clinical trials are underway to determine what the optimal cells, delivery methods, safety, and actual effectiveness of these current experimental therapies might be for people with different forms of MS.