STEM CELLS: AN UPDATE OF ORIGINS & USAGE

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When expectant parents dream of their children's future, none considers serious illnesses or a rare genetic disorder as part of the picture. But when struck with disease, injury or any health problem, it is human nature to wish for some miraculous 'Spare Parts' to repair our body. Everybody, artists, scientists or just laymen, have fantasized at some time about such a superb healing process.

The concept of producing 'spare parts' of the body for replacement of damaged or lost organs lies at the core of the varied present biotechnological practices referred to generally as "Tissue Engineering".

The basic building blocks of this tissue engineering are "Stem Cells".
Recent basic and clinical research on stem cells has provided the possibility to develop these cells for therapeutic usefulness. This approach revolutionized cell-based therapy of illnesses and injuries. Examples include some degenerative diseases and age-related functional defects (heart failure, Parkinson's and Alzheimer's diseases, chronic liver injuries, arthritis …), some cancers and hematopoietic and immune system disorders, as well as some genetic diseases …

WHAT ARE STEM CELLS?

Stem Cells are the primitive cells that develop from fertilized ova of multicellular organisms. They start having a great potential to change into all the different cell types found in the adult. At first, they divide to provide more stem cells, and then these omnipotent Zygotic cells will transform and gradually differentiate into the other specialized cell types (placental and embryonic). As they go thru the varied stages of specialization, they lose some of their potential to differentiate; starting from multi-potent cells to end up with a single potency of what is known as Progenitor cells. Some of these little-differentiated progenitor cells remain active even in adulthood. They act as a repair system for the body. They continuously help restoring, replenishing and maintaining the normal self-renewing adult tissues and regenerative organs such as: blood, skin, or intestinal tissues.

There is a wide variety of stem cells originating from different tissue types:
1- Embryonic Stem (ESC's) are derived from the inner cell mass (ICM) of very early embryonic tissue. They are pluripotent, able to give rise to all three embryonic or primary germ layers: ectoderm, endoderm and mesoderm from which all tissues of the body are made.
2- Fetal Stem cells come from the organs of fetuses.
3- Adult Stem cells that are only somewhat differentiated cells. They can be extracted from different tissues and are named according to their tissue of origin:
- Hematopoietic Stem Cells (HSCs) are derived from blood,
- Mesenchymal Stem Cells (MSCs) come from bones, bone marrow, periosteum, synovium, and muscle. They have the capacity to differentiate into cells of the connective tissue lineages, including bone, fat, cartilage and muscle with great potential of clinical use in cardiovascular, neural and orthopedic applications.
- Adipose-derived stem cells from adipose tissue
- Dental pulp stem cells from deciduous teeth
- Umbilical Cord and Umbilical Cord Blood Stem Cells are a unique source of multipotent adult stem cells. The term "Cord Blood" is used for blood that is drawn from the umbilical cord and the placenta after a baby is born.

Up until recently, the afterbirth including the placenta and the cord with all the blood they contain was discarded as medical waste. However, the trend is changing as it was realized that they are rich sources of stem cells that may be frozen for later use in prospective therapies.
They can be made to grow Hematopoietic Stem Cells (HSC), Mesenchymal Stem Cells (MSC) as well as other types. Furthermore they contain high concentrations of cytokines, growth factors and hormones as well as B-cells and T-cells that are very important for some cell based therapies.

To pursue appropriate cell therapies, first the pertinent stem cells should be identified and harvested from the most related tissue to be then engineered according to the projected target. Use of postnatal stem cells is easier and safer. It has the potential to significantly alter the perspective of cell engineering and its resulting outcomes.
Use of embryonic stem cells is ethically controversial. Furthermore, they are unlikely to turn on their own into the cells needed to regenerate a specific tissue. They need to be coaxed to develop first into the specialized cell types before transplantation. They are harder to technically manipulate and may easily escape control to most likely grow into tumors.

ROLE OF STEM CELLS IN BASIC RESEARCH

Since the early 60's stem cells research has began and has spread into three major directions.

1- To study normal cellular development

Scientists observe how stem cells develop from a fertilized egg into a complex organism. They study the cellular division trying to understand the signals and mechanisms of when and what makes the cells differentiate and get specialized to form specific tissue types: skin, bone, brain or other; and conversely, what keeps them to simply replicate. Learning this control mechanism is of utmost assistance for further research.

2- To study diseases

Abnormal and aberrant cellular division will result on the other hand in cancer and other degenerative and birth disorders. Armed with the understanding of the genetic controls and triggers of normal developmental processes, researchers will gain information on how and what abnormalities can arise resulting in such diseases. This permits to the scientific community to anticipate and try new strategies for therapy.
That is why, for scientists to explore therapies of a specific cellular pathology in the laboratory, they need to grow cell lines with that pathology to work and experiment with. For this, they can conveniently use stem cells with this abnormality and grow them into the needed cell lines. Alternatively, they even can genetically engineer such stem cells to mimic that same pathology.

3- To provide a resource for testing new medical treatments

New medications and therapies could be tested for their safety on specialized human cells and tissues grown from stem cell lines. This yields more reliable results than from animal testing and this is actually what is being done with some cancer cell lines to test and screen potential anti-tumor drugs.

CLINICAL ROLE OF STEM CELLS RESEARCH

Currently medical research of stem cell transplantation is under way moving with big steps. Many medical advances are progressively implementing additional clinical applications to treat diseases and to replace damaged cells.
Already, blood-forming stem cell therapies proved very powerful. Bone marrow, mobilized peripheral blood, and umbilical cord blood all serve as primary sources of cells for Hematopoietic cell transplantation (HCT). It is a standard practice to treat a number of malignant and nonmalignant hematologic diseases with this form of therapy.
Healing of extensive burns is improving with stem cell based treatments.
Stem cells are also used in conjunction with other conventional approaches such as chemotherapy to improve the treatment of breast cancer.

Clinical trials are underway to infuse autologous cord blood stem cells to treat children with Type 1 diabetes. Preliminary data proved safety of this procedure and demonstrated a significant slowing in the loss of insulin production.

Pioneering research focused on evaluating the impact of autologous cord blood infusions in children diagnosed with cerebral palsy and other forms of brain injury. They would facilitate repair of damaged brain tissue by stimulating the creation of new blood vessels and neurons in the brain.

New therapies continue to emerge and many other potential treatments are currently tested in animal models. Some have recently been brought to clinical trials stage.
In a proof-of-concept study, rat pups exposed prenatally to alcohol and later injected with neural stem cells showed behavioral and cognitive improvements. Also neural stem cells are tried for the treatment of stroke.
As yet, there are no clinical trials in humans using MSCs derived from cord tissue. However, many studies used MSC derived from cord tissue to treat animal models of human diseases, including: Lung Cancer, Parkinson's Disease, Rheumatoid Arthritis, Sports injuries to cartilage, and Type 1 Diabetes
Embryonic stem cell are tested for the treatment of acute spinal cord injury. They hold the key to replace cells lost in many devastating diseases for which there are currently no sustainable cure. Hopefully they could also be made to differentiate into specific cell types opening the possibilities of renewable sources to replace degenerated cells and tissues. These will me the corner stone for the treatment of diseases like Parkinson's, heart diseases and diabetes.

The progress reached till now, encourages scientists and fund providers from all over the world to keep researching ways to harness stem cells. Great efforts are spent to learn more about their mysteries and to uncover additional diagnostic and treatment tools for various diseases and conditions. Experimenting new ways to shape and control different types of stem cells brings us closer every day to the creation of new treatments.

There is tremendous optimism that stem cell therapies will someday be available to provide the needed "Spare Parts" to treat a wide range of human diseases and conditions.

Drawbacks and obstacles to be yet overcome

There are still several aspects that are not yet completely resolved.
We are still learning about how to direct stem cells to become the right cell type, the best ways to transplant them, and to grow only as much as we need them to. Discovering how to do all this is taking time.

First issue is the host immune response to the implanted cells in case they are not from the same person (autologous). Tissues cannot safely be transplanted haphazardly from one person to the other. Compatibility of the two individuals is to be strictly matched. A successful transplant is when there is no host-versus-graft reaction or vice versa. Depending on the nature of the tissue that is transplanted, this match can be more or less stringent.
For the bone marrow, successful transplants require a complete match between the six key HLA tissue types of the donor and patient; which is known as a '6/6 matches'.
Cord blood transplants achieve the same level of success with less strict matching of only a '4/6 match'. (It is interesting to know that while the odds that two siblings have a complete 6/6 match is about 25%, the odds they will have a 4/6 match is about 40 %.)
Ideally, to eliminate this host-versus-graft reaction the best results will come from autologous transplants. Accessible sources of autologous adult stem cells in humans include:

1. Bone marrow, which requires extraction from bones (typically the femur or iliac crest)
2. Adipose tissue (lipid cells), which requires liposuction from fatty areas
3. Blood, that is taken through pheresis; wherein blood is drawn from the donor, passed through a machine extracting the stem cells and then the other portions of the blood are returned to the donor.
4. Umbilical cord and blood that is stored in special tissue banks since birth.

Unfortunately, autologous transplants are not always the best solution for many conditions like. Genetic diseases and other diseases with a genetic predisposition cannot be treated by an autologous transplant since the stem cells will be carrying the same affected genes and would predispose to recurrence of the same condition. This is the case of some cancers, leukemia, immunological and all known genetic disorders.

A second obstacle is the need to master'Homing' mechanisms that guides the delivered cells to the site of injury or to where they are intended to be within the body. Many techniques are being experimented with, some more successful than others. Sometimes, though in pre-clinical animal studies, researchers luckily note positive observations such as how cord blood stem cells selectively migrate to injured cardiac tissue to improve overall heart function,

And last, a major lacuna is the need to completely master how local signals and factors that influences the implanted stem cells to trigger the proper differentiation in vivo. Once transplanted inside the body the cells need to integrate and function in concert with the body's other cells. For example, to treat many neurological conditions the cells we implant will need to grow into specific types of neurons. To work properly, they will also have to know which other neurons to make connections with and how to make these connections.