UMBILICAL CORD MESENCHYMAL STEM CELLS (MSC)

Stem cells are the foundation for every organ and tissue in the body. They are found in the nearly every organ and tissue in the body and have the ability to regenerate into additional stem cells or differentiate into specialized cells. In many tissues, stem cells serve as a sort of internal repair system, dividing, differentiating, and stimulating cells to replenish. When an organ or tissue is injured, inflamed, or needs renewal such as the natural aging process, the organ or tissue releases compounds that promote the release of stem cells from the bone marrow. The organ or tissue also releases compounds that attracts stem cells to migrate to the organ where they proliferate and differentiate into cells of this organ, supporting the natural process of renewal. For example, before some immunosuppressive therapy for cancer, stem cells from the bone marrow are removed and stored. Once the treatment is completed, the stem cells are re-inserted for replacement and repair of the immune system. For more information, go to: https://stemcells.nih.gov/info/basics.htm.

All stem cells—regardless of their source—have three general properties:

1. Stem cells are capable of dividing and renewing themselves, sometimes after long periods of inactivity.
2. Stem cells are unspecialized; they can make another stem cell or a different cell type (asymmetric division).
3. Under certain physiologic or experimental conditions, stem cells can be induced to become tissue or organ-specific cells with special functions. In some organs, such as the gut and bone marrow, stem cells regularly divide to repair and replace worn out or damaged tissues and cells. In other organs, such as the pancreas and the heart, stem cells appear to only divide under special conditions.

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. For example, embryonic stem cells exist only at the earliest stages of development. Other types of tissue-specific (or adult) stem cells appear later during fetal development and remain and replicate throughout life. Thus, there are two basic sources for therapeutic stem cells –your own (autologous) or from another donor (allogeneic).

Autologous Stem Cells are cells harvested from your own body via liposuction from your fat or through bone marrow aspiration. Although not approved in the USA, some facilities take stem cells and grow them in a culture medium for 7-10 days to induce replication. When the numbers have been expanded, the stem cells are then reintroduced into the body. Because stem cells are derived from the patient, there is no chance of rejection by the body. However, it is believed that the **regenerative potential of stem cells decline rapidly with age.**

Because both liposuction and bone marrow aspiration **create inflammation**, and because stem cells seem to be attracted to areas of inflammation, after injection a certain number of the stem cells may return to their original location from which there were obtained. However, the number of stem cells in the bone marrow decrease with age. Data suggest that we age, in part, because our self-renewing stem cells grow old as a result of DNA damage, toxicity, nutritional imbalances, and infections. Mechanisms that suppress the development of cancer, such as senescence and apoptosis, may also induce a decline in the replicative function of certain stem-cell types with advancing age (*Nature Reviews Molecular Cell Biology* Sep 2007;8:703-13). In other words, aging is associated with a decreased regenerative capacity of stem cells. Thus, the use of your own (autologous) stem cells has disadvantages.

Neonatal Stem Cells can be obtained from the umbilical cord and placenta. Throughout pregnancy, the umbilical cord functions as the lifeline between the mother and baby, carrying nutrient-rich, oxygenated blood from the placenta to the developing baby via the umbilical vein. The baby, in turn, pumps nutrient-depleted, deoxygenated blood back to the placenta through the umbilical arteries. The cord tissue surrounding the umbilical vein and arteries acts is a unique connective tissue called the stroma (or Wharton's Jelly), and acts as a cushion, preventing twisting and compression to ensure the cord blood flow remains steady and constant. Umbilical stromal cells embedded in the collagen-rich matrix of Wharton's Jelly are unique compared to other tissue cells – they have mesenchymal stem cell characteristics and induce the differentiation of umbilical cord stromal cells into several types of cell lineages such as heart muscle (cardiomyogenic), cartilage (chondrogenic), bone (osteogenic), and fat cell (adipogenic) types.

What about the risk of rejection using umbilical cord mesenchymal stem cells from another person? A pregnant mother is not adversely affected by the cells that lie within the placenta or umbilical cord that bridges the mother and child, who has its own unique immune make-up and cellular markers. Because the cells of the umbilical cord do not belong to either the mother or the baby, they do not acquire the genetic markers of either. This is a key difference between mesenchymal cord stem cells and other sources. As a result, umbilical cord tissue cells can be considered a "universal donor." Another key characteristic of umbilical cord mesenchymal cells is that they have yet to begin to differentiate. This is like having "blank" cells that can be developed into whatever type of tissue is needed for repair or rejuvenation. This is exactly why mesenchymal stem/stromal cells (MSC), are so desirable; they are ready to regenerate and differentiate to variety of tissues without risk of stimulating immune rejection. Unlike embryonic stem cells, Umbilical Cord MSC do not promote tumors.

It is important to distinguish stem cells obtained from umbilical cord BLOOD versus umbilical cord TISSUE

Umbilical cord BLOOD *contains hematopoietic stem cells that form blood-related cells in the body such as red and white blood cells. Umbilical cord blood stem cells share characteristics similar to those found in adult bone marrow, which are also capable of becoming other cells. Cord blood contains a mixture of maternal and fetal cells. Because the maternal cells have markers unique to the mother, it is possible for the recipient to have a reaction to the stem cell transplant, just as might occur with a kidney or heart transplant. Cord blood stem cells are currently used to treat a range of blood disorders and immune system conditions such as leukemia, anemia and autoimmune diseases.*

Umbilical cord TISSUE *also contains self-renewing cells, mesenchymal stem/stromal cells (MSC), which develop into structural and connective tissues. Unlike stem cells found in the cord blood and bone marrow, MSC can give rise to a variety of tissues including bone (osteoblasts), cartilage (chondroblasts), stromal cells, connective tissue and other types of tissues. MSC are also in many adult tissues and their characteristics depend on where in the body they come from. In other words, umbilical cord stem cells have characteristics that set them apart from cord blood and adult bone marrow stem cells:*

1. *Flexibility (or plasticity): cord MSC has the potential to change into other cell types like nerve cells, bones cells, muscle cells, etc. This special property enables MSC to adapt more easily to the needs of the patient after they have been "transplanted."*
2. *Homing: cord MSC seem to preferentially travel to sites of tissue damage or injury.*
3. *Engraftment: cord MSC appear to unite with other tissues without being rejected as being foreign.*

Umbilical Mesenchymal Stem Cells are obtained from umbilical cords and placentas delivered via Cesarean section. The donation mother consents to the use of her tissue, and she is screened for a variety of infections (eg- Hepatitis B and C, HIV, syphilis) in addition to a maternal health questionnaire. They are retrieved by a cord blood bank in Salt Lake City and the cells are extracted and frozen using a very specialized technique to preserve their viability. The umbilical cord is also sampled for contamination after processing. Every cell is tracked from the maternal donor source to the recipient. Each 2 mL vial contains an estimated 3 million or 60 million Umbilical cord MSC. Neither the cells or the procedure is billable to insurance. Umbilical cord MSC are gently infused intravenously over a few minutes or can be injected into muscles or directly into joints.

Not all stem cells being used by medical doctors are the same. High numbers of cells does not mean they are alive or active. Stem cells do have a limited number of replications, and so stem cells obtained and amplified or stimulated may not produce the same effects as those obtained directly from the umbilical cord tissue. The handling of the stem cells once they have been preserved is critical to maximizing not only the number of viable stem cells but also the ability of the stem cells to replicate. Stem cells are regulated by their mitochondria, the energy producing organelle found inside cells. Good mitochondrial function, good stem cells. The only problem is that stem cells, in order to stay stem cells, have to stay undifferentiated, meaning that their mitochondria have to stay quiescent - not dividing, meaning that there must be minimal oxidative stress, since oxidative stress is what pushes the stem cells into differentiation. For this reason, the handling of stem cells before implantation is critical. Although proper prolonged storage in a deep-frozen state does not significantly affecting their viability, once the stem cells have been received in the office, it is optimal to transplant them within a few weeks.

In addition, preparing the recipient through individualized nutrition and detoxication is especially important. For this reason, stem cells may be administered in an enriched solution of specific amino acids, vitamins, and minerals. The following have been shown to promote stem cell release from your own bone marrow and this may enhance your response to MSC even further:

- ❑ Stem XCell™ Pro 1 twice a day
- ❑ Optimized Fucoidan 926 1 twice a day without food
- ❑ Aloe/200X™ 1 twice a day
- ❑ Organ-specific Peptide BioRegulators 200mg 1 twice a day (through https://www.antiaging-systems.com/250-peptide-bioregulators)
- ❑ Exercise
- ❑ Localized Pulsed Electromagnetic Fields (PEMFs)
- ❑ Localized Q1000 LLL using the 808E probe

It is suggested that reactive oxygen species (ROS, which we measure in the office using the FRAS) may regulate stem cells release/replication *(Antioxid Redox Signal*. 2014;20(12):1902–16). Low levels of ROS keep stem cells quiescent, while higher levels result in secretion of growth factors that activate stem cells, and excessively high levels of ROS cause stem cells to commit apoptosis (cellular suicide) (*Nature Chemical Biology* 2010;6:411–7). For example, excessive exercise forms reactive oxygen species and thus stimulates the release of stem cells into the circulation.

It is important to remember that although MSC transplants can provide dramatic improvements in many aspects of health, the effects depend on your health and as such there are no guarantees. In addition, while a single infusion of MSC can be powerful, it is not realistic to expect a single infusion to be a cure all. A series of MSC infusions/injections every 3-4 months is considered by many to be the best way to get the most out of MSC. There is no specific contraindication to repeatedly receiving MSC, and 4 infusions done over the course of a year as a start with the enriched nutrient infusions in between is often presented as a packaged program.

If you receive MSC into a joint or muscle, medical ozone and an enriched solution of specific amino acids, vitamins, and minerals may be included in the procedure. There are separate informational handouts and consents for the use of ozone and the clot enrichment (OCM) procedure.

Body parts (including MSC from any source) that are "minimally manipulated" do not fall under the regulation of the FDA. The question then comes down to the definition of "minimal manipulation," and how much manipulation causes a body part to qualify as a drug? There is a tremendous amount of information available on the internet but investigate with a particular distinction about the type of cell being discussed. If you have further questions, please ask Dr. Kaslow. Your signature below indicates that you have had the opportunity to ask questions about Umbilical Cord Mesenchymal Stem Cells.

Signature:_____

These statements have not been evaluated by the Food and Drug Administration. This product, process, procedure is not intended to diagnose, treat, cure, or prevent any disease.