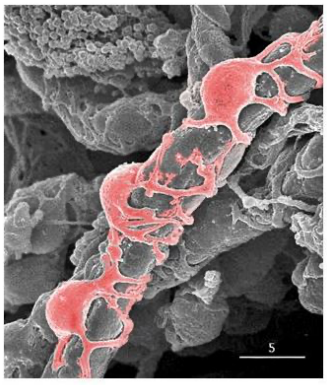
ZEHRCENTER
ORTHOPAEDICS
...because living with pain isn't really living!®

Regenerative Medicine Products

How do I choose the right biologic for me?

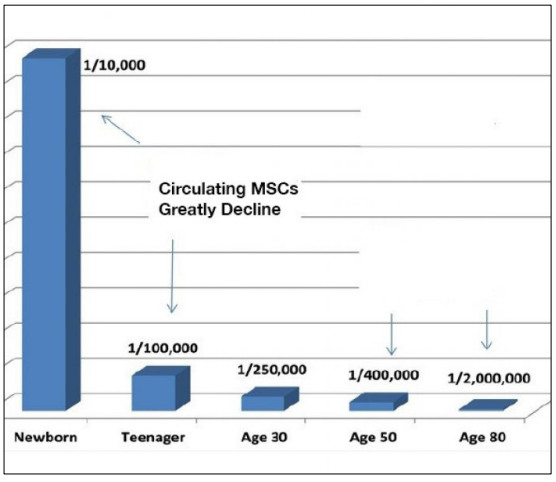
Stem Cells

In general, patients are typically unclear about the phrase "stem cell," so it is worthwhile to clear up some of the confusion at the beginning. Stem cells are scattered throughout our bodies but start out as cells called *pericytes* that lie inactive on small blood vessels, but which are mobilized quickly by many factors at a time of stress, injury, or needed repair work in our bodies. As infants, we start out with a relatively large number of endogenous stem cells throughout our bodies, but this number quickly declines to a point where, as senior adults, we have few viable stem cells throughout our bodies and subsequently have diminished healing capacity.



Pericytes on blood vessels. Courtesy Arnold Caplan and Bruno Peault

The average patient who develops arthritis and other degenerative disorders has relatively few functioning stem cells to affect a repair of the ongoing damage to their joints and muscles. Some physicians have chosen to collect a patient's own stem cells from either the pelvis bone or abdominal fat — which may seem like a great idea — but again, the number of cells that are available to collect is relatively small and — let's face it — they're old like you are!



Stem cells derived from the umbilical cord are a more vibrant source of cells and growth factors than are the cells harvested from a typical patient. They are "younger" and have been exposed to far less environmental mutagens than patient-derived cells and therefore are less likely to possess DNA mutations. In

addition, increased telomere length allows for greater potential to undergo more cell division cycles than cells from other sources.

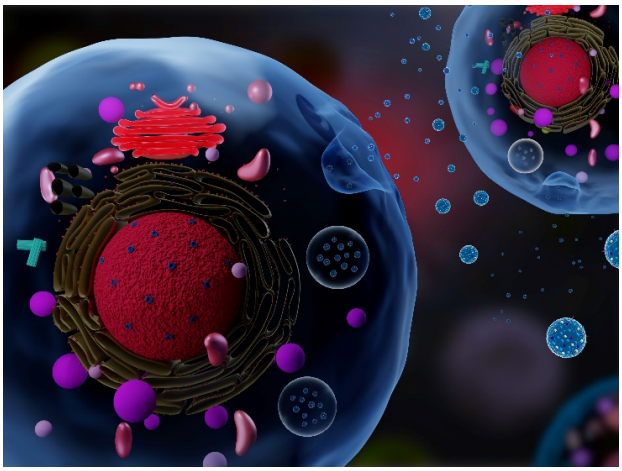
This is why at ZCO we have chosen to offer our patients stem cells that are processed from umbilical cord blood, one of the richest sources of bioactive proteins and growth factors currently available. These growth factors and cytokines may help in the formation of new blood vessels, suppression of the inflammatory response, and encourage the healing process.

The total nucleated cells of umbilical cord blood aid in the endogenous repair and release of proteins which communicate with and direct neighboring cells to positively impact the joint. This product gives patients a higher quality and volume of stem cells with far less risk associated with the harvesting of your own stem cells. The product is immunogenic and incapable of inducing an adaptive immune response, meaning there is minimal chance of being rejected by the recipient.

**Although this treatment is not covered by insurance, please let us explain how we can help you afford this state-of-the-art treatment.*

Extracellular Vesicles (EVs) | Exosomes

Although the blood cord stem cells are the complete package and considered the best source of trophic factors that affect healing change, an exciting alternative are the nanoparticle-sized extracellular vesicles (EVs) called exosomes. These small packets contain microRNA, growth factors, cytokines, and proteins which are released between cells, such as a stem cell, as a messaging or signaling function in order to communicate with or direct an action in neighboring cells by transferring its contents into these cells.



EVs can mediate cell-to-cell communication and are involved in many processes, including immune signaling, angiogenesis, stress response, senescence proliferation, and cell differentiation. In addition, EVs are involved in restoring tissue and repair of organ damage.

This form of cell-to-cell communication in which a cell produces a signal to induce changes in nearby cells, altering the behavior of those cells is called *paracrine* signaling. The molecules known as paracrine factors diffuse over a relatively short distance in contrast to endocrine factors (hormones) which travel considerably longer distances through our circulatory system.

In the past, it was thought that stem cells functioned principally in cell restoration or differentiation into various cell types. Current research has forced a paradigm shift in

thinking, suggesting that the beneficial effects of stem cells may be as a result of their paracrine actions wherein they secrete these potent trophic factors that modulate the molecular composition of the environment to evoke responses from local resident cells.

Isolating the therapeutic signal packets, exosomes, released by regenerative cells — and using them rather than the cells themselves — are the next generation in biologic therapy. The targeted cells will react to these messaging signals and will change their behavior accordingly. There is tremendous potential for this extraordinary biology associated with extracellular vesicles and nanoparticle technology.

One of the best sources for EVs | exosomes is the amniotic fluid collected at the time of a routine C-section delivery. The exosome product that we choose to use is procured from screened and qualified donors and the amniotic fluid processed according to standards and regulations established by the FDA. This high concentration of exosomes provides many times more growth factors, microRNA, and cytokines than a comparable volume of stem cells. They are a vital regenerative component with the ability to transfer information from one cell to another.

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