New Life
Regenerative Medicine®

About Us

New Life Regenerative Medicine is an FDA regulated and multi-state licensed tissue bank specializing in birth tissue. Our processing is performed at our sister cGMP laboratory, Invitrx Therapeutics, located in Irvine, California. With offices located on both the east and west coast, New Life is happy to provide regenerative medicine products to practitioners nationwide.

At New Life, we are committed to helping improve the quality of lives for those individuals suffering from pain, injuries, aging and, sometimes, just from effects of day to day living. With New Life products, we strive to help people feel better and look better.

Quality Assurance

Birth Tissue is donated by healthy mothers at the time of scheduled cesarean section. All donations fall under the Anatomical Gift Act meaning that any compensation to the donor is not allowed.

Through an informed consent process, the expectant mother must submit her past medical and social history which is prescreened through an extensive and complete medical review and pre-natal evaluation This process is performed prior to delivery utilizing the protocols established by various regulatory agencies. Prior to the recovery of birth tissue, stringent guidelines must be met. Eligibility for tissue donation is based on the following:

- Medical, sexual and social history
- Physical exam
- Tissue retrieval possible within acceptable time limit
- Patient with no known high risk for HIV or hepatitis
- Patient free from transmissible disease
- Patient free from active malignancy
- Patient free from sepsis/systemic infection
- Serology results

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Additionally, prior to delivery, the mother is tested for communicable diseases following the requirements of the Food and Drug Administration (FDA), Center for Disease Control (CDC), and the American Association of Tissue Banks:

TESTING	PURPOSE
HIV I/II Ab	Antibody to HIV Virus Type 1
HBsAG	Hepatitis B Surface Antigen
HBc Ab	Hepatitis B Core Antibody
HCV Ab	Hepatitis C Antibody
HIV I/II NAT	HIV and HCV Nucleic Assay Testing
RPR	Syphilis Detection Test
WNV	West Nile Virus

The recovery is performed by specifically trained technicians at the time of the delivery and no harm is brought to the mother or her newborn. Parents will still have the option of storing the cord blood, if desired.

All processing is performed in CLIA certified laboratories following the guidelines of both the FDA and the American Association of Tissue Banks. In addition to serologies, culturing is performed in every step of the process. All products are retested, through a third party, post processing to demonstrate the absence of bacterial and fungal pathogens.

Birth tissue has been used for over 100 years for a broad range of therapeutic applications. However, it is only recently that birth tissue was discovered to have great clinical benefit when cryopreserved to protect its residual cells. Since the discovery of birth tissue as a viable cellular matrix, there have been no reports of disease transmission. Additionally, birth tissue is considered immune privileged and as such does not express Class II antigens. Finally, birth tissue products are easy to use as it can be applied directly into the injured site. To date, tens of thousands of patients have been treated with these types of products.

Cellular DNA

DNA is a very large, highly negatively charged molecule (even fragments of DNA are large and highly charged). DNA will not go into another cell unless you overcome a cell's natural defenses. For instance, in the lab, we can jolt the cells with high voltage electricity or use chemicals that mask DNA's positive and negative charges or, in the lab, create a viral vector to enable transfection.

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The DNA fragments would have to go through the cell's outer plasma membrane and then the nuclear membrane, a process that does not occur naturally.

Our bodies fight hard against naked DNA to stay healthy. It's one of the ways our bodies fight viral DNA. Our blood has nucleases, which chew up DNA and its smallest building blocks. Some cells (like macrophage) can take up DNA, but their job is to chew it up and recycle the building blocks.

DMSO Containing Cryo-Preservative

We regularly have patients and doctors contact us to see if a cellular product that is Dimethyl Sulfoxide (DMSO) - free is available. We routinely evaluate new cryo-preservatives as they come onto the market and have not found a better alternative. Many cryo-preservatives do not work as well as DMSO (in terms of cell viability) or are not suitable for clinical applications. For example, while propylene glycol is a good, non-toxic cryo-protectant, our consulting pharmacologist advised against use due to the possibility of an uncomfortable burning sensation to the patient.

Another factor is that the FDA is very comfortable with DMSO. It has a long record of safety and success. (Yes, a few patients may be sensitive or allergic to it, but it is a very small percent.). Sometimes patients who are allergic to sulfa antibiotics are also sensitive to DMSO (dimethyl sulfoxide).

Other companies may have posted that DMSO is not safe. This may be due to that fact that decades ago, the industrial-grade DMSO caused problems because it contained impurities. These issues disappeared when a higher purity became available. We use GMP grade DMSO, the highest quality available. The toxicity of DMSO is quite low: In animal testing, the acute oral toxicity (LD50) is 7,920 mg/kg in mice. This is higher than what is used today on the magnitude of thousands of mg/kg.

Coloration in RESToR™

Occasionally we are asked about the pink coloration that may be present in our RESToR product. This discoloration occurs when there is free heme (derived from Greek "αἷμα haima") in the sample prior to processing. Heme is most commonly recognized component of hemoglobin, which is the oxygen carrying component of blood that creates the red pigment.

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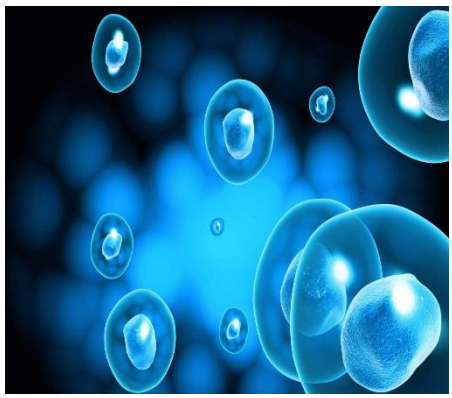
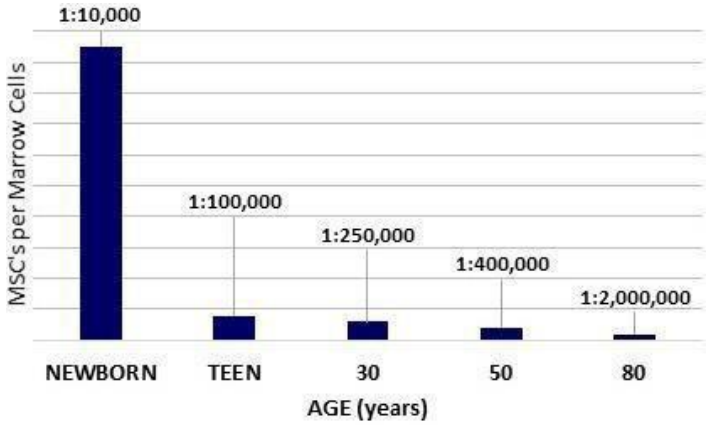
Heme itself is naturally released due to the intrinsic instability of hemoglobin. In the body, heme is naturally metabolized by macrophages (a type of white blood cell that surrounds and kills microorganisms, removes dead cells, and stimulates the action of other immune system cells) and cleared from the blood. There should be no issues since the contribution of heme to the patient is negligible. Heme is not a red blood cell and does not possess any MHC or DR antigens and, therefore, is not immunogenic.

Stem Cells….Is More Better?

Stem cell therapy is taking the regenerative medicine world by storm… but should stem cells get all the credit? It's a common misconception that stem cells are the only component needed in regenerative medicine to kickstart the healing and regenerative process and the higher the cell count, the better. However, it is the patient's own stem cells that do the work, not the stem cells contained in products; these cells serve as a vehicle to deliver signaling molecules. While we agree that cells are an important part of regenerative medicine, and in some cases, particularly when treating autoimmune diseases, equally important, if not more important, are the "dream team" of components. Comprised of growth factors and cytokines, these chemical messengers enhance the body's natural ability to heal and regenerate. In addition, collagens, proteins, hyaluronic acids, and peptides assist in harnessing the body's power of true healing.



Many companies are utilizing procedures that extract the patient's own stem cells via adipose (belly fat) or bone marrow aspirate (a small plug of bone usually taken from the ilium (hip bone). These procedures are considered invasive, have a higher risk of infection and may cause additional pain to the patient. When using your own stem cells, it is important to mention that they are as old as you are. As we age, the number of stem cells and their quality drastically diminish. With a decrease in stem cell quality, a person of advanced age will not heal and regenerate like a young child would. New Life Regenerative Medicine products are



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derived from birth tissues, which means the components in these products are at day one strength.

Signaling Vesicles

With the increase in advertisements, and social media, people are relating regenerative medicine therapies to "stem cell" treatments. Typically, when discussing regenerative medicine, the first question we are asked is "what is the stem cell count". Regenerative medicine is much more than just stem cells whose outcome is very dependent on the age of the patient from whom they are being harvested. (Figure 1). In many cases, taking your own stem cells is not effective as older cells are less robust in the production of growth factors, micro RNA and messenger RNA and are frequently limited in total number.

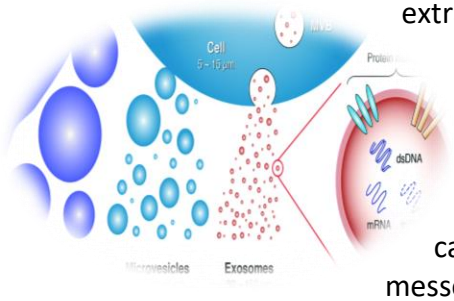
One of the most valuable aspects of a science-driven approach to regenerative medicine is that our understanding evolves with the science. We once bought into the same "stem cell-based therapy" model that everyone else touts, but as scientists scrutinized the data, they came to embrace a view shared by hundreds of other leading regenerative medicine researchers – including the father of the mesenchymal stem cell, Dr. Arnold Caplan.

In June 2017 Dr. Caplan published an article: *Mesenchymal Stem Cells: Time to Change the Name*. In this article Dr. Caplan refers to these cells as "medicinal signaling cells", capable of releasing paracrine effectors which thereby influence the body via immunomodulatory and trophic mechanisms. These bioactive factors recruit the patient's stem cells, which reside throughout all the tissues of our bodies and affect the phenotypic and physiological expression of our immune system. So, if these bioactive factors are so effective, why is so much attention paid to stem cells. The answer lies in the fact that the old textbooks remain on the shelves and those who have read them continue to preach their teachings. In addition, alternative therapeutic options have only recently become available on the marketplace. One of these options is extracellular vesicles (EVs).

EVs, measuring 40 to 100 nm are nano-sized vesicles containing biological signaling molecules that mediate **cell–cell** signaling. Formed by inward budding of membranous vesicles in a multi-vesicular body, they fuse with the plasma membrane to release these ultra-tiny vesicles. EVs contain transmembrane proteins from their parent cells, which are important in regulating uptake by other cells. By conserving these transmembrane proteins, it has been shown that uptake is facilitated by other cells to a much greater degree than if the cargo was simply released into the extracellular environment.

EVs are important in autocrine signaling (local between same cells), paracrine signaling (local between different cells) and endocrine signaling (between distant cells). Science and

studies show that EVs from placental tissues, whose MSCs secrete a cargo rich in growth and immunomodulatory substances, are a much better source than those harvested from an older individual. Of course, any resident stem cell traveling to the areas of concern, will then secrete EVs specific to themselves and will be modified by their own local extracellular microenvironment. This information includes messenger RNAs, micro RNAs, and various proteins. The intrinsic durability of the EVs makes them uniquely durable and naturally biocompatible. Additionally, the wide spectrum of proteins and messenger RNA contained within EVs allows for a vastly greater capacity of information compared with single molecule messengers like hormones, growth factors and cytokines. Finally, the transmembrane protein receptors allow EVs to traffic or home to areas of injury and inflammation while facilitating uptake by numerous cells.



Unlike MSCs, EVs demonstrate several advantages distinct from their parent cells. They can travel systemically without the risk of clumping (as is seen with large peripheral intravascular doses of MSCs). As much smaller particles, EVs do not demonstrate a first pass effect into the lungs when administered intravascularly. EVs can cross the blood-brain barrier easily without utilizing diuretics such as Mannitol. While allogeneic MSCs may be perceived as foreign by the innate and adaptive immune system and quickly whisked away, EVs are able to evade the immune response. EVs from healthy stromal cells do not contain DNA, so that there is no risk of malignant transformation. Alternatively, autologous MSCs are of the same age as the donor patient and are therefore limited by the inherent age of the individual. Older cells are less robust in the production of growth factors, micro RNA and messenger RNA and are frequently limited in total number.

EVs derived from MSCs provide many therapeutic benefits including regenerative and immunomodulatory capabilities which dictate their indications. The trophic effects of EVs require an understanding of the patient's own stem cells in which they act upon.

Stem cells lie dormant within niches throughout our bodies. This population of cells are partially undifferentiated and once activated can proliferate and migrate to sites of injury where they acquire a mature phenotype in order to facilitate repair and remodeling.

Many of the anti-fibrotic benefits of MSC EVs are attributable to several factors. They produce large amounts of TGFß3 which regulates cell adhesion and extracellular matrix formation. In scar repair they increased the ratio of Collagen Type III to Type I. Additionally, MSC EVs displayed inhibition of granulation tissue leading to fine reticular collagen with fewer fibroblasts. Finally, MSC EVs prevent apoptosis (cell death) through numerous techniques.

Highlights of FDA's New Stem Cell Guidance Announcement

Contains Nonbinding Recommendations

(each page of the FDA Guidelines is prefaced with the above statement)

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

A little more clarity:

- The FDA stated that it will exercise "enforcement discretion" for 3 years for those products that don't pose a significant safety concern! This enforcement moratorium should be music to the ears of stem cell manufacturers that wish to comply but need the time and money to do so.
- It appears that FDA will give plenty of time to interested parties to meet with FDA and develop plans to come into compliance.

Excerpts from FDA Guidelines

Section 1271.10(a)(2) (21 CFR 1271.10(a)(2)) provides that one of the criteria for an HCT/P to be regulated solely under section 361 of the PHS Act is that the "HCT/P is intended for homologous use only, as reflected by the labeling, advertising, or other indications of the manufacturer's objective intent." As defined in 21 CFR 1271.3(c), homologous use means the repair, reconstruction, replacement, or supplementation of a recipient's cells or tissues with an HCT/P that performs the same basic function or functions in the recipient as in the donor. It is not necessary for the HCT/P in the recipient to perform all the basic functions it performed in the donor, in order to meet the definition of homologous use. However, to meet the definition of homologous use, any of the basic functions that the HCT/P is expected to perform in the recipient must be a basic function that the HCT/P performed in the donor.

This criterion reflects the Agency's conclusion that there would be increased safety and effectiveness concerns for HCT/Ps that are intended for a non-homologous use, because there is less basis on which to predict the product's behavior, whereas HCT/Ps for homologous use can reasonably be expected to function appropriately (assuming all of the other criteria are also met). In applying the homologous use criterion, FDA will determine what the intended use of the HCT/P is, as reflected by the labeling, advertising, and other indications of a manufacturer's objective intent, and will then apply the homologous use definition.

Homologous use means the repair, reconstruction, replacement, or supplementation of a recipient's cells or tissues with an HCT/P that performs the same basic function or functions in the recipient as in the donor (21 CFR 1271.3(c)), including when such cells or tissues are for

autologous use. We generally consider an HCT/P to be for homologous use when it is used to repair, reconstruct, replace, or supplement:

- Recipient cells or tissues that are identical (e.g., skin for skin) to the donor cells or tissues, and perform one or more of the same basic functions in the recipient as the cells or tissues performed in the donor; or,
- Recipient cells that may not be identical to the donor's cells, or recipient tissues that may not be identical to the donor's tissues, but that perform one or more of the same basic functions in the recipient as the cells or tissues performed in the donor.

New Life Response

For our part, we will continue to build on a firm commitment to produce safe and effective regenerative medicine products under the most rigorous cGMP conditions. We recently expanded our manufacturing operations in Irvine, California into a new 10,000 sq. ft facility. The building is outfitted with Class 7 cleanrooms, Class 5 biosafety hoods and is fully cGMP validated and operational.

Our development strategy now includes the submission of an IND (Investigational New Drug) for umbilical cord blood, cellular Wharton's Jelly and extracellular vesicles. We will be joining a small elite group of manufacturers that have applied for FDA "pre-market approval." We will continue to take full advantage of these regulatory opportunities to bring patients innovative, and scientifically proven regenerative cell therapies especially for life-threatening diseases.