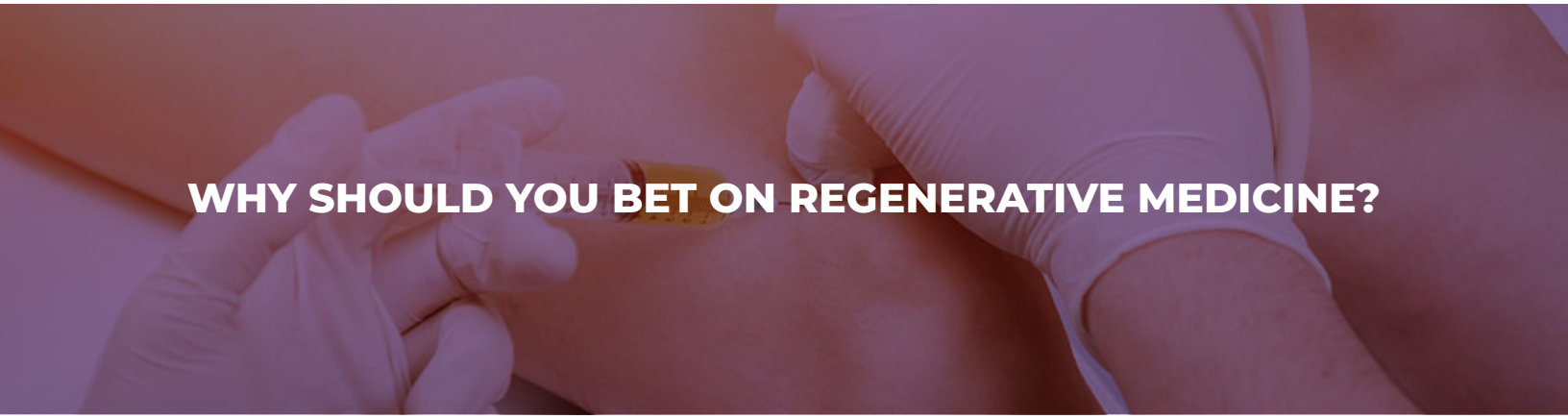
STEM CELL CENTER

BUILDING A CELL CRYOPRESERVATION BANK & DISTRIBUTION CENTER

The following document serves as a guide for building a cryopreservation bank for the storage of mesenchymal stem cells derived from umbilical cord tissue samples for clinical use. This document describes important points to consider including an overview of operations, quality control, personnel requirements, and Standard Operating Procedures, as well as the equipment and inputs required for the thawing and pre-processing of these cells, to meet all criteria for the operation of a cryopreservation stem cell bank.

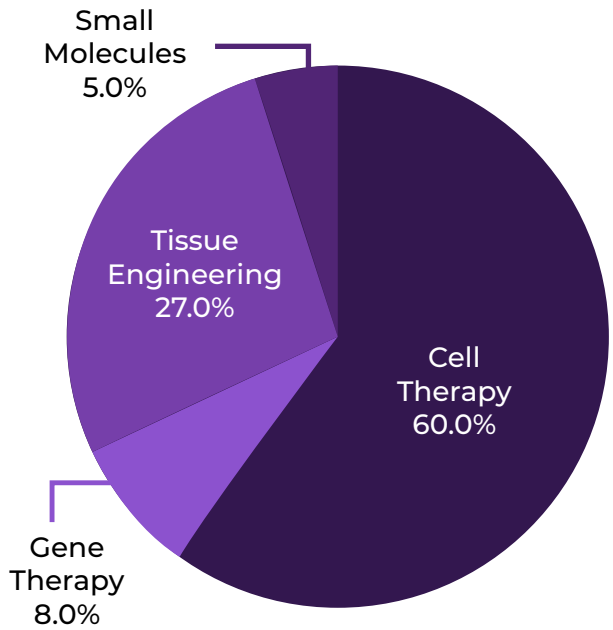


WHY SHOULD YOU BET ON REGENERATIVE MEDICINE?

Regenerative medicine is one of the most advanced fields of medical research today. Many consider it to be a scientific-medical specialty because it incorporates research and self-repair protocols where growth factors and adult regenerative cells derived from human tissue are applied to accelerate both tissue regeneration and homeostasis restoration processes.

In the last ten years, we have come to understand how cells identify and respond to signals, interact with their environment, and self-organize within tissues to accelerate and enhance the healing process. This understanding has allowed medical practitioners to manipulate these processes and apply them in the clinic to repair damaged tissues, stimulate new tissue formation, and continue to harness the organism's own regenerative capacities.

The Global Stem Cells Group is a leading regenerative medicine company. It endeavours to provide the necessary infrastructure, scientific training, and support to doctors so they can bring the latest applications of cellular therapies to their patients.



Cell therapy: Transplantation of engineered human cells for therapeutics applications.

Tissue engineering: Ex vivo growth of tissues/organs from progenitor cells using bio-scaffolds to reconstruct a part of the whole organ with natural functions.

Small molecules: Small cells or biologic agents that simulate dormant or endogenous cells to recover regenerative properties.

Gene therapy: A method to introduce genetic materials (DNA, siRNA, mRNA) in cells to compensate for aberrant genes or to induce protein expression.

WHAT'S THE PURPOSE OF HAVING A CRYOPRESERVATION BANK ?

The purpose of a mesenchymal cell bank is to stop the natural aging state of a mesenchymal stem cell, to retain the regenerative and anti-inflammatory properties that this kind of cell possesses at an early stage. The objective of cryopreservation from a clinical point of view is to store these biological products so that they can be used in the future as a regenerative medicine tool, to replace and/or repair cells and tissues damaged by natural aging, pathology, or trauma.

The construction of a cryostorage bank allows doctors to perform allogeneic cellular therapies and have a stock of young and naive mesenchymal stem cells available to be used with any patient. These cells are derived from umbilical cord tissue (UC-MSCs) and have been expanded in a laboratory and stored at specified concentrations to be available for use in cell therapies by doctors.

Our experience indicates that mesenchymal stem cells from the umbilical cord have advantages over other kinds of regenerative cells from other adult tissue given the intrinsic characteristics of being a young tissue, such as having a high capacity of Proliferation , and also having a high secretion of exosomes and growth factors that have a direct impact on tissue regeneration.

HOW CAN YOU BENEFIT YOUR MEDICAL PRACTICE WITH A CRYOPRESERVATION BANK?

Since regenerative medicine is a viable treatment option for complex diseases, where traditional medicine does not provide a satisfactory solution.It is becoming increasingly common among successful Regenerative Medicine Practices and Doctors with entrepreneurial tendencies not only to storage cells for immediate use in their own practice or patients, but also to build a platform to serve as a distribution center for other physicians and practices interested in upscaling their regenerative medicine capabilities.

By implementing a cryopreservation bank, you open your clinic up to:

- ✔ Immediate sample availability for use.
- ✔ Better patient outcomes, due to the higher quality and count of cells.
- ✔ Reduced shipping costs.
- ✔ Decreased probability of damage caused by transfer.
- ✔ Assured cell quality and viability.
- ✔ Increased profitability by serving as a distributor of cellular products to other clinics and centers.

Let Global Stem Cells Group provide you with the necessary infrastructure, scientific training, and support for building and managing a Cell Cryopreservation Bank for allogeneic cell products derived from neonatal tissue.

As part of your cell bank assembly, we will provide you with the following:

- ✔ Constant, hands-on training for staff on equipment and protocols.
- ✔ Advice on scientific matters, from laboratory practices to clinical application of stem cells.
- ✔ Delivery of Standard Operating Protocols.
- ✔ Timely delivery of biological certifications of delivered products.

BUILDING A CRYOPRESERVATION BANK

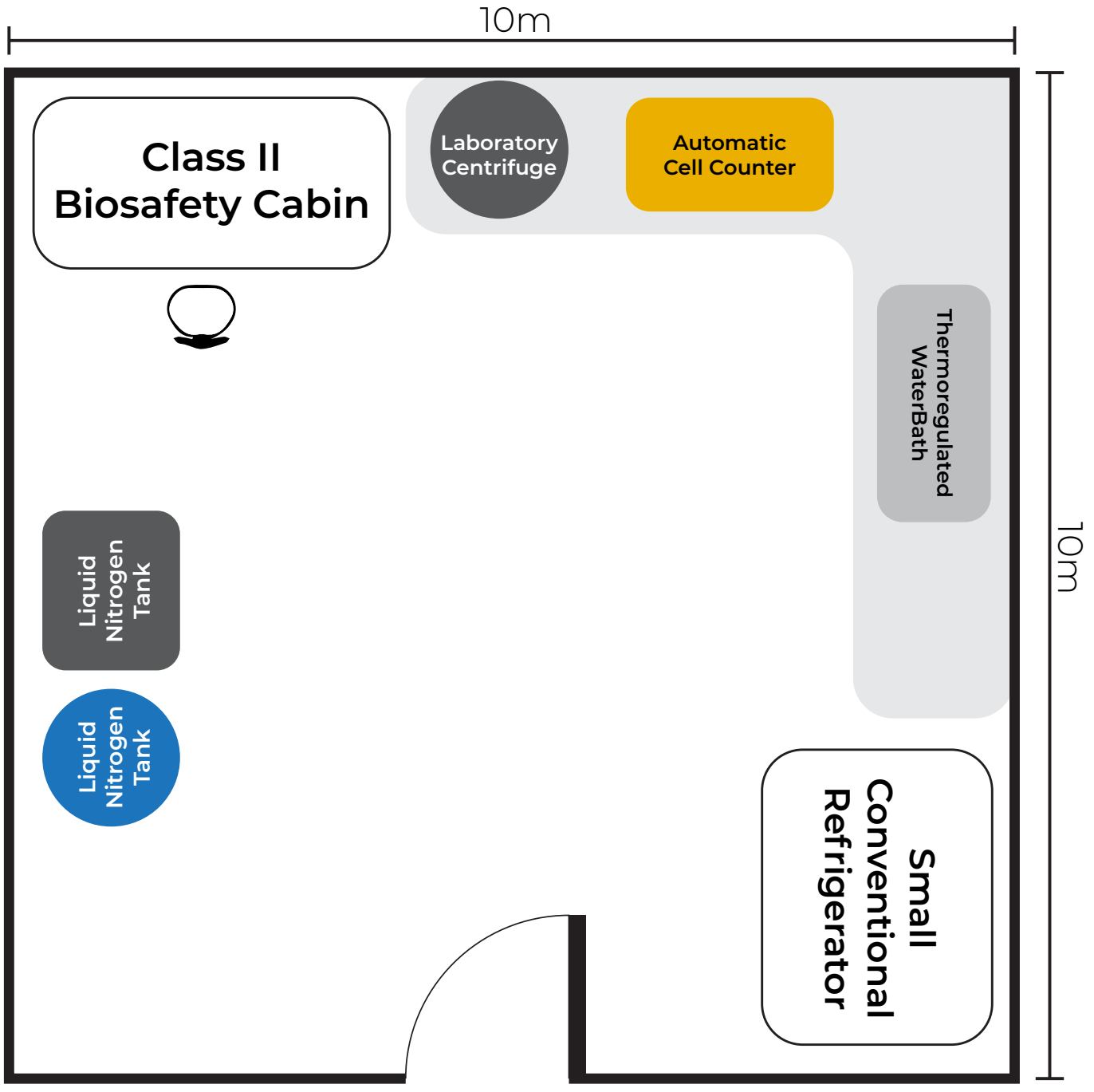
It is important to consider that a mesenchymal stem cell bank does not necessarily have to include an on-site lab for culture and expansion. In the early phases of the project, it is advisable to outsource the manufacturing process to a laboratory dedicated exclusively to the culturing and expansion of Mesenchymal stem cells, that can deliver consistent and high quality product. That being said, we believe that a good way to procure samples is the monthly or periodical shipment of samples, which can be shipped under cryopreservative conditions and which are stored by the cell bank in such conditions until processing, with the bank being responsible for the final laboratory processing for defreeze and portioning prior to application on the patient. This consists of taking the cellular precipitate pellet out of the container, centrifugation, and washing in controlled conditions of biosecurity before its later dosification and final application.

Our "Complete Solution" includes the following:

- ✓ Equipment, provisions, and the supply of cellular products and compounds
- ✓ A feasibility study of laboratory requirements
- ✓ Training and certification
- ✓ Installation and start-up
- ✓ Support & Consultation Service with our staff of Physicians

INFRASTRUCTURE

The cell bank must have a minimum floor area of 10m2. Its floors and walls must be made of a washable and non-porous materials such as plastic and metal, and all edges of surfaces must be rounded to avoid any puncture, which could possible compromise sterility.



EQUIPMENT

Class II Biosafety Cabin: Allows work to be done in a sterile environment to manipulate the tubes that contain UC-MSCs for their washing and evaluation process prior to infusion.

Automatic Cell Counter: Makes it possible to evaluate the number of cells and their viability before they are used on a patient.

Laboratory Centrifuge: Will facilitate the washing of cellular pellets in order to discard the supernatant that contains cryopreservation residues.

Small Conventional Refrigerator (Frigobar): Allows the bank to keep samples and reagents at controlled temperatures.

Liquid Nitrogen Tanks: Allows cryopreserved samples to be kept at -198°C, the very low temperature required for the preservation of the cellular properties of stored products. This also avoids water damage to the materials through the process of crystallization.

Thermoregulated WaterBath: Facilitates the thawing of samples to be processed for patient application by carefully raising them to the proper temperature.

CONSUMABLES AND PROVISIONS

There are many daily consumables that are common to clinical centers that are not outlined below because of their commonality. Below are those supplies that are more specific to the tasks to be performed.

- ✓ Sterile Centrifuge Tubes 15 mL.
- ✓ Centrifuge Tubes of 1-2 mL.
- ✓ Sterile Tips for Micropipettes.
- ✓ Sterile Gloves.
- ✓ Gloves for Nitrogen Tank Manipulation.
- ✓ Pack Sterile Clothing.
- ✓ Physiological Serum.
- ✓ Saline Phosphate Buffer.
- ✓ Trypan Blue Dye.
- ✓ Local Nitrogen Supplier for periodic loading of the tank.

CELLULAR PRODUCTS

The Center will have a range of cell lineages and products available, as well as patient treatment protocols and standard operating procedures (SOPs) used by our global clinical network, The main lineages and cellular products in the Global Stem Cells Group's Cryopreservation bank project are outlined below:

CELLGENIC
Flow Exosomes

Cellgenic Flow Exosomes (extracellular vesicles): The isolation of signaling vesicles filled with growth factors and proteins among other compounds emitted by stem cells are used for treatments rather than the stem cells themselves, which is a next-generation therapy. This process works by causing other cells to react to these signals and change their behavior accordingly. There is enormous therapeutic potential for extracellular vesicles, especially exosomes. Cellgenic Flow Exosomes contain approximately 300 billion exosomes per milliliter. Exosomes are nanoparticles that contain proteins and RNA. They can be transferred to other cells and can support tissue repair and homeostasis.

CELLGENIC
PURE

CellGenic Pure: derived from Umbilical Cord Blood contain nucleated living cells that exert an anti-inflammatory and immunomodulatory effect, which helps to optimize the cellular environment. The paracrine signals include a growth factor that secretes living nucleated cells that stimulate tissue to undergo mitosis and regenerate. Live nucleated cells can secrete growth factors over long periods, unlike amniotic products or placental derivatives that have very few nucleated living cells, if any. They only function during the half-life of the growth factor (from a few hours to a few days).

OPERATING A CRYOPRESERVATION BANK

HUMAN RESOURCES

A well-trained and well-organized laboratory staff is the key to any successful operation, and it needs to be aware of the repercussions that it's actions may have on the biological safety of the products that it manufactures. The person in charge of handling the biological products must be fully acquainted with the theoretical and practical foundations of working with biological materials under sterility. It is desirable that the staff have a knowledge of current regulations on health quality, hygiene, biosafety and the disposal of waste, as well as practical experience in microbiology.

Can be a professional with a degree in the following:

- ✔ Biochemistry
- ✔ Biotechnology
- ✔ Medicine
- ✔ Biology
- ✔ Medical Technologist specializing in Blood Banking
- ✔ Paramedical Technician

TRAINING AND CERTIFICATION

Global Stem Cells Group has played a leading and visionary role in training medical scientists to translate laboratory research into clinical practice. This certification program offers a cohesive curriculum designed to provide precise instruction in the basic concepts of cellular behavior, laboratory processes, and their practical application at the clinic or physician level.

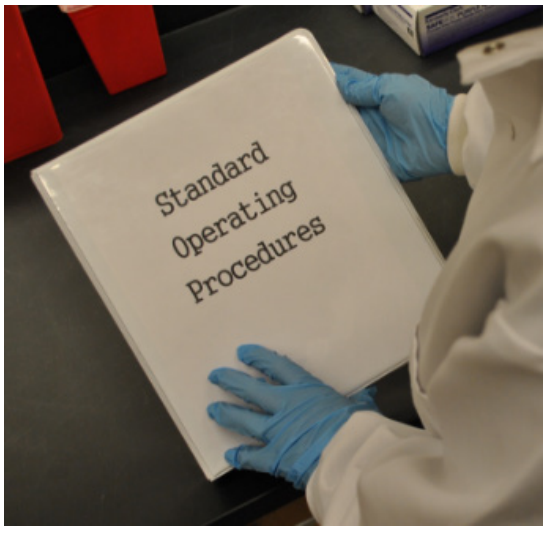
The program provides physicians with detailed instructions and hands-on practice for collecting all tissue samples, using laboratory equipment, processing, isolation protocols and dosification when utilizing cellular product, and how administering treatment to the patient. Having this information at hand is vital to succeed in managing effective cellular products, allowing one to know every step of the process and control its quality.

The Practical Experience includes the following topics:

- ✓ Operative Pre-Post Instructions
- ✓ Practical experience of fat tissue collection
- ✓ Practical experience in SVF insulation, washing, digestion, and centrifugation
- ✓ Photo-activation techniques and cellular counting
- ✓ Defrosting and freezing techniques for cellular products
- ✓ Dosing and handling liquid nitrogen freezers
- ✓ Puncture, extraction, and filtering techniques
- ✓ Equipment operation and practical experience under supervision

DOCUMENTATION, STANDARD PROCEDURES & QUALITY CONTROL

Having a firm control of the processes, inputs, infrastructure and intermediate products assures you that the final products or services made comply with the minimum quality requirements established both nationally and internationally, and allows you to avoid and detect in a timely and efficient manner any errors present in the products of the company. Quality control is a strategy used to ensure care and the continuous improvement in the quality offered by our products. The generation of a program of periodic general monitoring of the storage laboratory and processing of biological samples is necessary, as are records of cleanliness, maintenance, document reviews, and regular updating.



Standard Operating Procedures (SOPs)

Standard Operating Procedures (SOPs) are written documents containing step-by-step instructions on how to complete a work task, or handle a particular situation when it arises in the workplace. SOPs are used to ensure consistent and reproducible results with clear instructions, and are critical to maintaining consistent performance. The laboratory should write SOPs in a standard format for all laboratory activities, in order to ensure consistency, quality, and reliability, as well as the quality of the data generated. These SOPs must be readily available in work areas and accessible to personnel. We will deliver protocols for the cryopreservation unit that are consistent with the work that we do and must be carried out.

Documentation

In order to establish minimum criteria for the delivery and rejection of products, including the analysis of microbiological, serological, and cellular phenotypes, everything must be documented. Products should be found in a pure cellular state, which does not contain potentially pathogenic agents. If a product does not comply with the minimum quality requirements, regardless of whether its purpose of use is clinical or investigative, it must be disposed of. All of this needs to be ensured by the laboratory that produces UC-MSCs and goes with the cellular products that arrive at the installation of the cryogenic bank.

The traceability of the manipulation carried out on the sample is fundamental, and details of manipulations must be included. These details should include composition, machinery used, personnel in charge, date, lot, etc. In short, all the variables that do or may cause the final product to be altered. With this information, it is possible to deliver defined products to specific markets, with a guarantee of its origin and history. It also makes it easier to find problems as they occur, as it allows a retrospective look at the process undertaken to make the product. It is important that everything has a protocol, and that everything is documented, either written or digitally, including error reporting where necessary. Good documentation is a prerequisite for certifications, as it allows the cell bank to better support both itself and its customers

CONCLUSIONS

Today, mesenchymal stem cells have ushered in a new revolution for regenerative medicine, establishing a new paradigm in biomedical science and opening up new avenues of research that are being fervently pursued today. Prevalent, degenerative diseases of high social impact are being researched, and MSCs have been proven to be effective in the treatment of pathologies in different areas, including traumatology, aesthetic medicine, cardiology, general medicine, dentistry, urology, and gastroenterology.

Having a bank of cells allows the entity a position of prestige, for both being a pioneer in the field and for its ability to provide timely support to people looking for cell treatments.

In the last decade, the adult mesenchymal and hematopoietic stem cell industry has become more dynamic, with future prospects of constant growth. According to a study by www.rnrmarketresearch.com (A widely recognized US-based market research company), the market is expected to reach a worth of close to $7 billion by 2025, with an annual growth rate of 20% between 2019 and 2025.

Thanks to the wonders of scientific progress, cellular therapy has become a feasible alternative with great potential and a rapidly advancing field that provides excellent results.

Stem Cell Center

Enabling physicians to make the benefits of stem cell medicine a reality for patients around the world.

STEM CELL CENTER

Datran Center, 9100 S Dadeland Boulevard,
Suite 1500. Miami Fl. 33156. United States.

PHONE
305-560-5337

EMAIL
info@stemcellsgroup.com

WWW.STEMCELLCENTER.NET