Storing adipose-derived stem cells

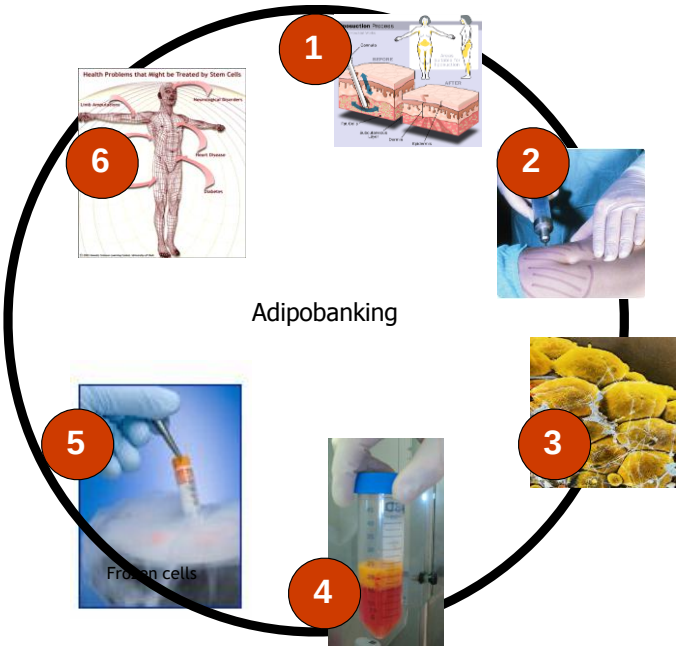
Cell therapies aimed at repairing and regenerating various tissues and organs offer alternative therapeutic solutions for an increasing number of pathologies. Even though embryonic stem cells are theoretically more plastic, their use is hampered by many limitations, imposed by regulations or related to ethical considerations and genetic manipulation. Adult stem cells, instead, can be obtained much more easily with no ethical problems, especially if their origin is autologous. Over the last few years, a number of research efforts focused on mesenchymal stem cells, isolated from the bone marrow, which *in vitro* have shown their adipogenic (adipose tissue), as well osteogenic (bone tissue), condrogenic (cartilage), miogenic (muscle tissue) and neurogenic (nervous tissue) potential, opening up a number of therapeutic opportunities in regenerative medicine. Yet, obtaining a sample of bone marrow is a rather painful and invasive manoeuvre for the patient, and the cell yield is not particularly significant. When compared with bone marrow-derived mesenchymal cells, adipose-derived mesenchymal stem cells are equally able to differentiate into cells and tissues of a mesodermic origin. Moreover, adipose tissue is easy to obtain, it is ubiquitous and present in most individuals, and can be obtained in large quantities under local anaesthesia, with minimum discomfort for the patient. Furthermore, the yield in stem cells for the same quantity of tissue is definitely higher for adipose tissue when compared with bone marrow.

In any case, to be employed for regenerative purposes and directly on the patient, stem cells must satisfy the following requirements:

1. they must be abundant (millions of cells)
2. they must be collected with a procedure that is as non-invasive as possible
3. they must be able to differentiate into many lineages in an adjustable and reproducible way
4. they must be appropriate for safe and effective transplantation into a recipient, whether autologous or allogeneic
5. they must be produced in compliance with Good Manufacturing Practices (GMPs)

Adipose tissue can certainly satisfy all of these requirements. With the increased incidence of obesity in our days, subcutaneous adipose tissue is abundant and easy to find. Adipose tissue can easily be collected through liposuction, certainly less invasive than bone marrow extraction. Plastic surgeons are generally familiar with this type of technique and can intervene with no discomfort for the patient. A small quantity of adipose tissue (100-200 ml) can be obtained with a simple local anaesthesia and yield a sufficient volume of stem cells; the yield of 1g of adipose tissue is 500 times higher than that of 1g of bone marrow.

For this reason, the Foundation has been working for some time on the process of extraction of stem cells from adipose tissue with a view to storing cells obtained from liposuction in liquid nitrogen, for later use to regenerate organs and tissues.



We can now affirm that the experimental part of the process has been successfully performed by the Foundation laboratories and that the clean room process validation has been carried out in compliance with guidelines issued by Swissmedic (the Swiss surveillance authority for medicines and medical devices). In the meantime Swissmedic has given its approval to start the project. This project entailed an R&D effort that lasted over 4 years, covering the whole process – from collection to freezing and thawing – so as to validate each single step. The phase turning this process into GMPs – Good Manufacturing Practices – necessary for the continuance of the project itself, was also concluded successfully. Swiss legislation, conforming with European rules, establishes that this process be GMP-compliant, so as to ensure the production of safe, effective cells, entailing no risk for patients and that can be used as a medicinal product. In order to reach this goal, all the phases of production must be monitored: quality assurance, personnel, reactants and instruments, documentation, manufacturing process and environment, quality control, analyses and release.

The purpose of quality assurance is to verify that the whole process is conducted according to pre-established procedures.

The personnel involved in each phase of the process must be adequately informed, know and employ the applicable operational procedures; this applies to operators performing cell collection, transporting samples to the lab, and to lab staff handling the sample in the clean room.

The reactants used in the process must be properly catalogued and controlled in terms of traceability and expiry.

The tools must be subject to daily maintenance and monitoring to ascertain their perfect operation.

The process of production of individual samples must be monitored and detailed in every phase, to ensure the traceability of every operation carried out.

The production environment must be constantly monitored to make sure that the “purity” of air always falls within set limits, especially in the production phase.

Quality control is essential to verify that the reactants and tools utilised in the manufacturing phase function correctly.

Analyses carried out on individual samples are fundamental for assessing sample quality before freezing and their future usability.

When a patient requests their use, adipose-derived MSCs can be used straight away and injected into the patient, or placed in culture, mainly to obtain a higher number of cells. Moreover, these cultivated cells can be differentiated *in vitro* into a specific type of tissue. In both cases, the process will be performed in compliance with GMPs, i.e., in a clean room.

To attain this goal – i.e., providing patients with cells cultivated and differentiated according to their own needs – other important aspects must be clarified and studied such as, in particular, identifying the most appropriate culture medium for cell cultivation, and demonstrate the genomic stability of cultured cells.

The project of banking adipose-derived stem cells is the first step towards making advanced cell therapies available to patients.