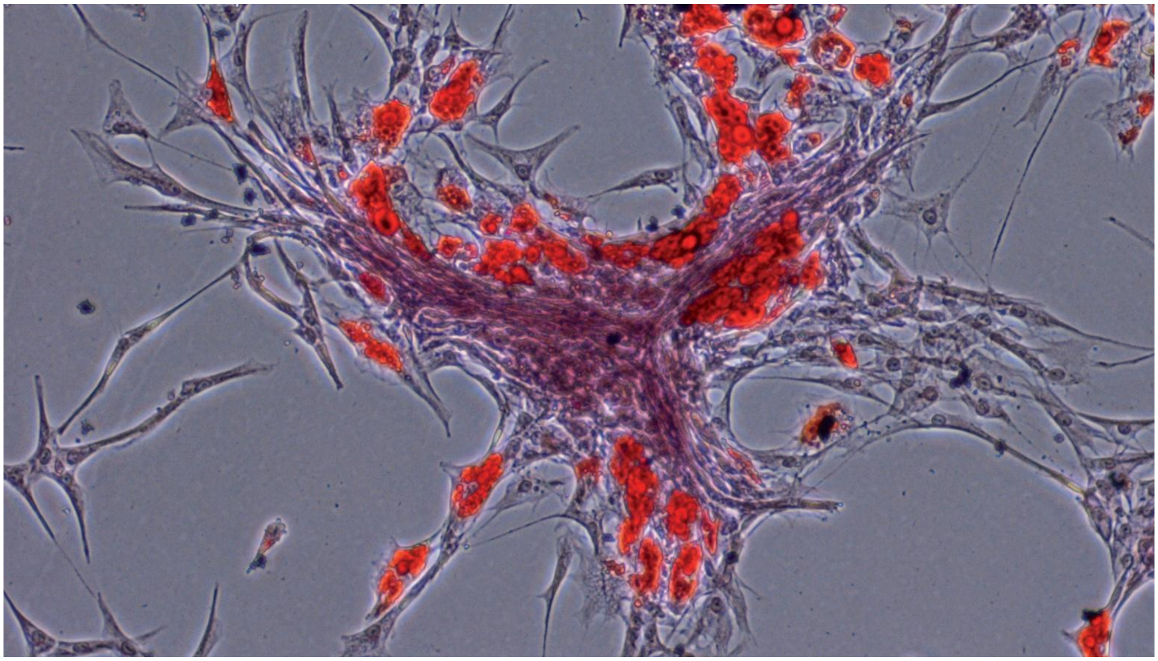
A device for stem cell separation

A stem cell is an undifferentiated cell characterised, on the one hand, by its ability to differentiate into specialised cells and, on the other, the ability to multiply almost endlessly while maintaining its characteristics unchanged.

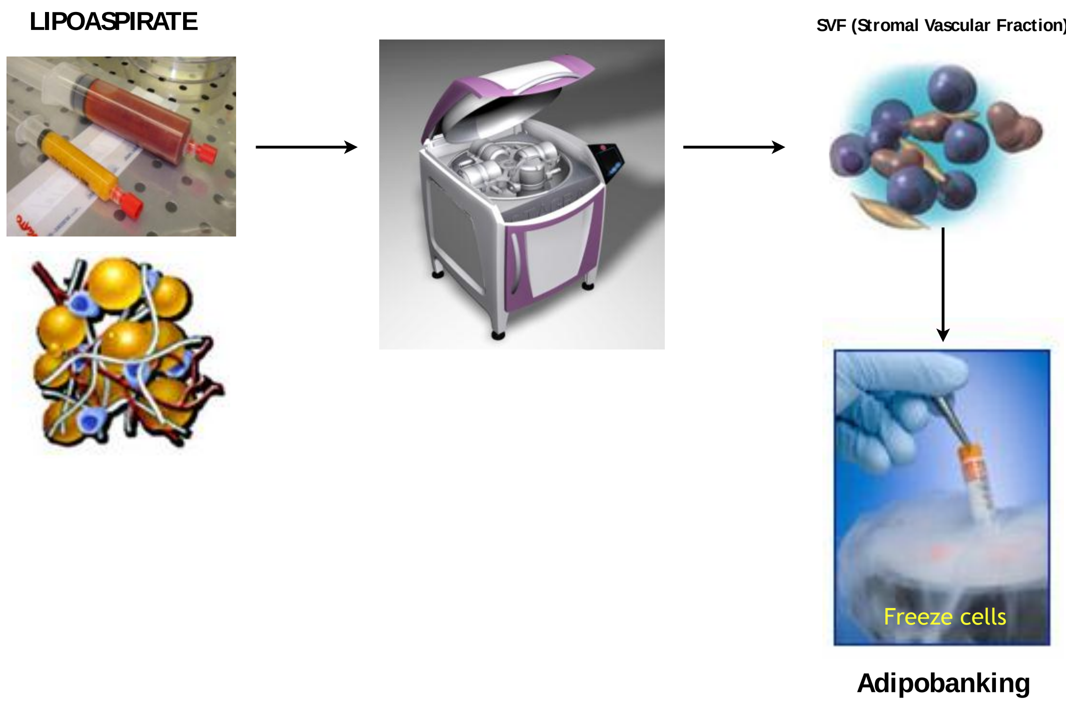


In particular, the definition of stem cells applies mostly to animals – yet, plant meristems also have stem cells. In general, all multicellular organisms can be said to possess stem cells. Animal stem cells – and, in particular, human stem cells – are currently the focus of extensive research especially in the medical field, with a view to using them in the future to regenerate tissues or create new tissues and organs.

Stem cells from adipose tissue
Thanks to adipose-derived mesenchymal cells, anyone can recover one's cell pool and store it for future use through cryopreservation. Adult stem cells constitute an unlimited source of cells of pharmacological and medical interest.
The presence of multipotent stem cells is confirmed in bone marrow, muscles and blood vessels – yet, stem cells are rare in these tissues. They are equally difficult to isolate and amplify *ex vivo*. Adipose tissue could thus be a particularly interesting cell source for cell therapies. It features a number of favourable traits in this respect: it constitutes approximately 10% of body weight in a healthy adult, and up to 50% in obese people; its use entails no ethical problems; it is extracted without major difficulty or problems through liposuction, routinely performed on patients under local anaesthetic. Moreover, it should not go unnoticed that adipose tissue can contain from 15% to 30 % of mesenchymal stem cells, very important in regenerative medicine.

Purpose of the project
The protocol used to extract adipose-derived mesenchymal stem cells needs a processing time of approximately 2.5 hours per sample and the process currently employed, being totally manual, is not fully compliant with GMPs (Good Manufactures Practices) and closed system requirements, thus failing to ensure top-level sterility and cleanliness levels. This project aims at creating a device (device + disposable sterile kits) to reduce treatment times and, at the same time, enable the simultaneous processing of multiple adipose tissue samples.

This solution will ensure fully-closed adipose tissue processing, thus significantly reducing processing times and costs for adipose tissue stem cell banking. A device of this kind would make it possible, for a biological tissue banking structure, to process some 6,000 samples every year.



Expected results
The following main results are expected from this project:

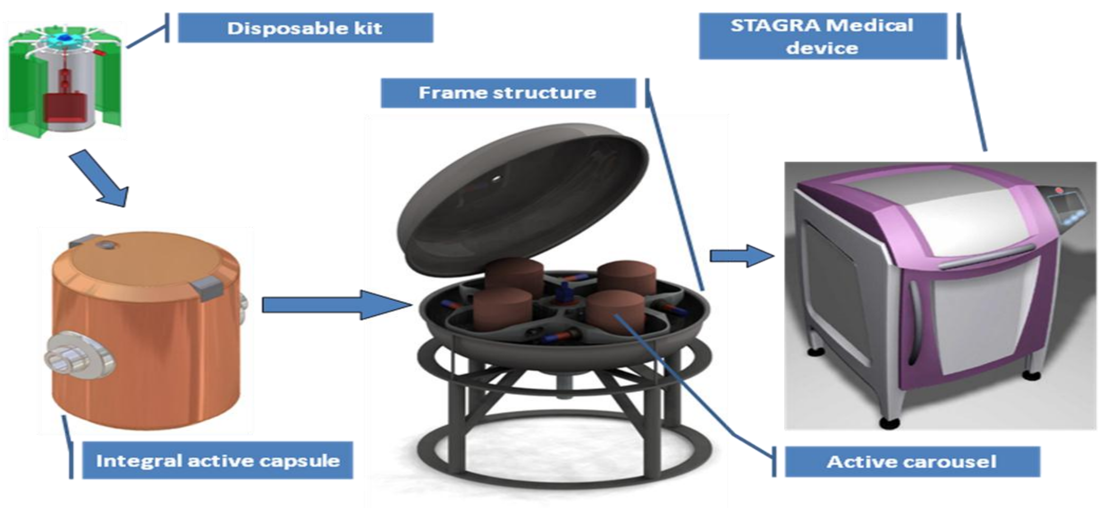
1. Construction of a functional prototype featuring the expected performance (extraction of a high number of mesenchymal stem cells per volume unit)
2. Development of a demo system using technology suited to engineering the end product
3. Selection of contractors manufacturing the different components of the complete system.

Project progress
The overall architecture of the device was conceived considering the following key functions and characteristics:

- Volume of the biological sample to be treated
- Complete process in a sterile closed circuit
- Autoclavability of some device sections
- Handling of bio-chemical products within the sterile circuit
- Thermal conditioning for the digestion phase of the extraction process
- Automatic recognition of transition between the usable part and waste
  Forced addensation of stem cells extracted through 400g centrifugation
- Re-suspension of the cell thickened for the following storage phase
- Treatment of up to 4 samples simultaneously
- Automatic recording of the individual steps of the process and drafting of a final extraction report for the data bank

The functions, characteristics and manual extraction protocol have resulted in the designing of a device basically consisting of the following units:

1. **Disposable kit**: The disposable kit is a closed-circuit biochemical sterile lab into which samples to be processed and reactants needed for stem cell extraction are introduced. The presence of a piston and of a multi-way rotary valve guarantees, through external actuators, fluid handling and processing.
2. **Capsule**: As seen in the previous point, the disposable kit needs actuators to act on the valve and piston to ensure correct fluid movement. Actuators are housed in a capsule – in particular, on the lid and bottom. Moreover, the capsule features a safety handle and can be separated from the device for sample loading and/or transfer operations, as well as an autoclavable hermetic safety cell.
3. **Centrifuge**: The extraction protocol phases include centrifugation and tilting of the capsules. Centrifugation at 400g is necessary to compact stem cells – isolated from the original fat sample – into a pellet for washing and purification. The tilting of the capsule, on the other hand, is intended to produce the opposite effect, i.e., the re-suspension of cells in a given fluid volume. The electromechanical structure used for this purpose consists of the transmission/rotor sub-set, which is also the system that transfers energy from the static and rotary sections of the device.
4. **Control**: From an electric viewpoint, the device features a distributed control consisting of a user console connected to a main PC-based operating section, connected at the same time with the four capsule satellite sub-units.
5. **Body:** All the sections described are housed in a bearing structure that protects both the most delicate inner parts of the device and the operators using it.



STAGRA general structure

Positive impact on the medical, social and health sectors

The extraction of mesenchymal stem cells from adipose tissue is, beyond any doubt, an extremely interesting procedure, of huge potential when associated with reconstructive surgery.
Currently, stem cells derived from adipose tissue have already been used in breast reconstruction after partial mastectomy, using adipose tissue extracted by liposuction from the patient herself, enriched with own mesenchymal stem cells and re-implanted in the breast to be re-modelled.
An equally huge potential concerns cell therapies currently representing a key challenge for the future treatment of a large number of diseases, such as: Alzheimer’s disease, Parkinson’s

disease, bone marrow diseases, cardiac and cerebral crises, burns, diabetes, rheumatoid arthritis and so on.