Mesenchymal stem cells and regenerative medicine: how lipogems technology make them easy, safe and more effective to use

Abstract

Lipogems® was designed to harvest, process and inject aspirated fat tissue which is washed, emulsified and rinsed, while adipose cluster dimensions are gradually reduced in a completely closed device by only mechanical forces. Lipogems® tissue product represents a natural implantable bioreactor that incorporates the main elements for a perfect natural regenerative response: the Scaffold (the adipose tissue structure), the Cells (Pericytes/MSCs), and the Grow factors (secreted cytokines and chemokines).

The local injection of such a tissue is a living graft, which can work for long time enhancing the natural local healing potential. It has been used safely and effectively in thousands of patients, in human and veterinary medicine in many different clinical applications. The device has obtained general FDA clearance in 2014 and in 2016 for specific arthroscopic use. The purpose of this short review is to present the concepts of Lipogems® technology and an update in bibliography so that whoever is interested can easily search for more information. Figures and videos are easily available on google search so have not been added to this review.

Adipose tissue as the Ideal MsCs source

MSCs are found as pericytes in all capillaries of all tissues of our body and the concept that fat tissue is an optimal source is now well established. MSC of fat (ASCs) are very numerous compared to other tissues. Fat tissue is available in most patients and can be easily harvested with a minimally invasive surgical approach, using a blunt cannula and syringe vacuum, offering a highly viable ASC population with optimal differentiation potential that is maintained with aging. These cells can differentiate in vitro into several cell lineages, such as adipocytes, chondrocytes, osteoblasts, and myoblasts. In addition, they naturally secrete many bioactive molecules working as a sort of “mini-drugstore” that modulates the local immune response and creates an ideal regenerative environment. The use of ASCs, expanded or simply obtained by enzymatic treatment as SVF (Stromal Vascu-lar Fraction), created a huge interest and both in vitro and in vivo studies clearly demonstrated their anti-inflammatory and regenerative potentials. Nevertheless, the prolonged ex vivo expansion may lead to cell senescence, thus leading to clinical results below expectations. In addition, the majority of the proposed techniques have complex regulatory issues. In the last few years, we have been facing a significant number of studies aimed at improving the therapeutic effects provided by this adipose transfer and structural fat grafting techniques. In an effort to optimize this regenerative potential, MSC enrichment techniques, essentially based on enzymatic or mechanical devices, have been proposed. In our experience, a minimally manipulated fat tissue is preferable, not only from a regulatory prospective, but mainly because of the biological rationale. Indeed, mechanically derived MSC versus enzymatically isolated MSC have shown to have better differentiation potential, wider secretome and a large population with optimal differentiation potential that is maintained with aging. Lipogems® technology guarantees all of the requirements in an easy, quick, disposable device and represents a very promising “natural” approach in different fields.

The Lipogems® system

The Lipogems® system incorporates a new technology to harvest, process and transfer adipose tissue. The technical part of the procedure is well described both in journal articles and in the web (https://www.youtube.com/results?search_query=Lipogems+system). The resulting product is composed of small intact adipose tissue clusters and contains pericytes retained within an intact stromal vascular niche. It is now well established that cells defined as MSCs exhibit perivascular location and pericyte identity in vivo. Pericytes are structural cells embracing the external wall of the microvessels and capillaries of the stromal vascular fraction of fat tissue and, after an injury such as inflammation or a damage of the vascular wall, they detach from the capillaries and gradually convert into activated regenerative MSCs. Such pericyte-to-MSC activation entails the release (through exosomes) of regenerative factors and bioactive molecules which would make the transplanted Lipogems® product acting as a “personalized drugstore”. The exquisite balance between angiogenic, anti-inflammatory, immunomodulatory, anti-apoptotic, anti-microbial, mitotic, anti-scarring properties of MSCs allows a completely natural tissue repair and regeneration. The second main characteristic of Lipogems® is related to the time-advantage. Indeed, the gentle mechanical method allows obtaining a ready-to-use product in less than 20 minutes compared to the several hours, days or weeks required for the enzymatic digestion of the liposapirate and eventual in vitro cell expansion with substantial delay in the clinical application. In addition, Lipogems® is minimally manipulated according to the regulations set forth by the FDA. It received the FDA clearance as a class II medical device for processing autologous adipose tissue (510(k) first approval in US in December 2014 and new clearance in November 2016 for arthroscopic applications. The reduction of adipose cluster dimensions from 2-4, 5mm before processing to 0.3-0.7mm of the final product, maintaining a perfect structural integrity, improves its ease of handling and post-transplant engraftment, due
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Clinical applications of lipogems

Lipogems has been shown to be safe and seems to work clinically much better than enzymatically iso-lated MSCs (both SVF or cultivated) as the preserved niche within a natural adipose scaffold works as the ideal “functional unit”. In general surgery, Lipogems® has been used as a valid approach for the treatment of fecal incontinence and anal fistulas, showing impressive long term real morphological regeneration of muscle and neurological function. In oncology, Lipogems® has been proved useful when injected in atrophied tissue after radiotherapy. The regenerative potential in musculoskeletal diseases is impressive and more extended clinical trials are currently performed worldwide to confirm the first outstanding results. In orthopedic surgery, most patients with joint degenerative and inflammatory diseases may benefit of Lipogems® intra and peri-articular injection. After injection of a variable quantity of Lipogems® (2-12 ml depending from the joint), patients generally reported a brilliant immediate improvement of symptoms with long-term pain resolution. In many cases, patients previously candidate for surgery, no longer needed it because of the complete or substantial resolution of their symptoms. Preoperative and post-operative X-ray and MRI comparison showed a possible regeneration of the articular cartilage and a widening of the joint space 6 to 18 months after treatment. Moreover, the orthopedic use Lipogems® has also proved to be rewarding to foster repair in injured ligaments or tendons, in meniscal lesions, around surgical wounds, inside and around osteoto my gaps. These finding have been confirmed in Vet-erinary Medicine where Lipogems is becoming the product that rescue damaged tissues with a regenerative environment and allow multicenter comparative studies. Clinical trials have been and are now ongoing to strengthen its critical analysis and further develop and accelerate innovative therapeutic strategies and clinical protocols.

Conclusion

Adipose tissue is the ideal source for extracting but above all for using MSCs since (i) it can be easily accessed and harvested via a minimally invasive surgical procedure, (ii) it can be found in sufficient quantities in most people and (iii) it guarantees an adequate amount of progenitor cells with a good vi-ability and minimally age-related differentiating potential. The Lipogems® technology naturally optimizes fat tissue healing properties. Without using enzymes, additives or centrifugations, but relying upon the use of mild mechanical forces, the Lipogems® system yields a micro-fragmented product that rescue damaged tissues with a regenerative environment for a long time. A number of randomized and controlled studies are now ongoing to strengthen its critical analysis and further develop and accelerate innovative therapeutic strategies and clinical protocols.

Acknowledgements

None.

Conflict of interest

Carlo Tremolada is the president and founder of Lipogems company.

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