Medical & healthcare, Tissue engineering, Regenerative medecine

Injectable prevascularized mature adipose tissues (iPAT) to achieve long-term survival in soft tissue regeneration

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Abstract

The study introduces a method for enhancing soft tissue regeneration using injectable prevascularized mature adipose tissues (iPAT). It involves culturing mature adipocytes, adipose-derived stem cells, and endothelial cells from patients, embedded in fibrin gel with collagen microfibers. The iPATs are injected into mice for up to 12 weeks, showing promising results in thriving and integrating effectively. The prevascularization helps nutrient and oxygen supply, enhancing their integration with surrounding tissue. This research holds promise for medical applications like breast reconstruction, wound healing, and tissue repair.

Background & Results

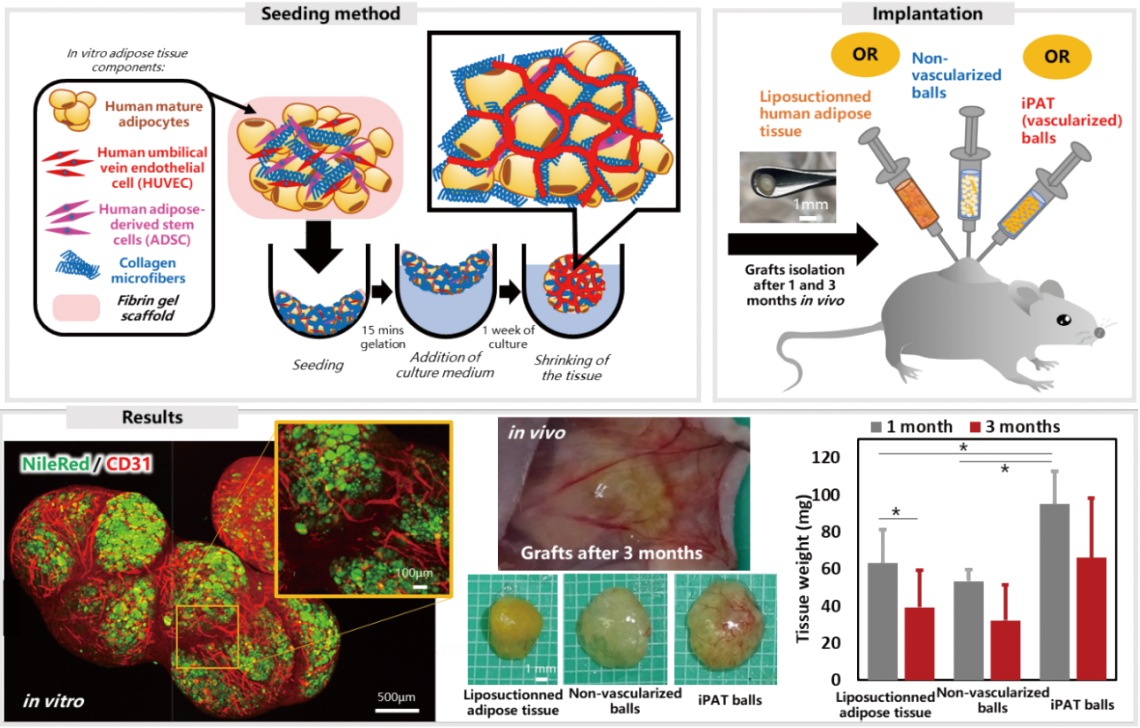
Adipose tissue regeneration is crucial for various medical applications, including cosmetic surgery, post-tumor resection, and trauma treatment. Current methods, like fat reinjection from liposuction, face challenges such as graft resorption and volume loss due to inadequate vascular support. To address these issues, we developed collagen microfiber tissues that can guide blood vasculature development while protecting mature adipocytes. The created injectable prevascularized mature adipose tissues (iPAT) mix mature adipocytes, adipose-derived stem cells (ADSCs), and endothelial cells (HUVEC) from patients, embedded in a fibrin gel with the collagen microfibers.

The iPAT balls were cultured with high viability, maintaining the mature adipocytes unilocular lipid vesicle phenotype. Co-culture with ADSCs and HUVEC allowed for a dense vasculature similar to in vivo conditions, allowing fluid diffusion for nutrient transport. After injection, iPAT balls can merge into a bigger size tissue in subcutaneous. Compared to non-vascularized adipose balls and liposuctioned adipose tissues, iPAT showed higher graft retention, fewer fibrotic areas, and superior cell survival after 1 and 3 months of implantation in mice. RNA-sequencing analysis also revealed upregulated angiogenesis-related genes. Additionally, lymphatic and neural networks were observed in iPAT, indicating a potential mechanism for tissue survival. Finally, rheological analysis showed that iPAT grafts exhibited elastic behavior similar to in vivo adipose tissue, and cryopreservation possibility was confirmed, allowing for future reinjections.

Significance of the research and Future perspective

These findings suggest that iPAT may offer a promising solution for adipose tissue transplantation with improved graft retention, angiogenesis, and cryopreservation capabilities, making it a valuable option for various clinical applications with customized implant volumes.

Future research will now focus on longer-term studies, in bigger size animals, and scaling up the process.



Patent	JP2023101792A, WO2022091822A1, JP2021145677A
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