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Innovations in regenerative medicine that improve the results of stem cell treatment: 3D cultivation, in vivo modeling of stem cell niche, and prenatal stem cells exosomes

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Statement of the Problem: Hair loss is currently being addressed by hair follicle transplantation. However, for large areas of alopecia, the patient does not have enough hair for autotransplantation. Proliferation and differentiation of stem cells (SCs) require a specific microenvironment – "stem cells niche". For in vivo modulation of organ-specific niches during SCs transplantation could be useful fetal tissue extracts (FTEs). Exosomes are small vesicles that are secreted by various cell types, including SCs. Exosomes can be carried to distant sites via biological fluids and may, therefore, induce the phenotypic modifications in recipient cells. Methodology & Theoretical Orientation: Multiplying SCs of hair follicles in 2D culture and introduce them into the scalp skin to form de novo hair follicles were unsuccessful. We developed a technology for creating new hair follicles from SCs in 3D cultures. Also, we investigated the content of growth factors in FTEs; and studied the efficacy of FTEs in patients who did not respond to SCs treatment. Finally, we created the rejuvenation program, which includes SCs transplantation and exosomes of SCs administration.

Findings: The SCs were transferred to a 3D culture where the formation of primary hair follicles suitable for transplantation occurred under the influence of a specific combination of growth factors. We showed the high efficacy of using FTEs for modeling the SCs niche in the treatment of liver cirrhosis and non-healing wound in patients who did not have the positive response to previous SCs treatment. Transplantation of prenatal hepatoblasts, hematopoietic SCs, and fetal liver extracts administration showed efficacy in 75% of liver cirrhosis cases that was characterized by the significant decrease of liver fibroscan density, decrease of portal hypertension and ascites, decrease or normalization of biochemical markers of liver damage. In patients with chronic non-healing wounds administration of FTEs activated the wound epithelialization with complete healing. Patients GAIS results after rejuvenation program: optimal cosmetic results – 78.9%; significant improvement but not complete correction – 9.7%; improvement, but required additional correction – 11.3%. The program significantly reduces the biological age and Frailty Index that evidences about the decrease in risk of aging disease appearance.

Conclusion & Significance: 3D cultivation, in vivo modeling of SCs niche and prenatal SCs exosomes can significantly improve results of the use of SCs in regenerative medicine.

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