Summarizing these data we hypothesized that Hippo signaling can be involved in regulation of the oocyte selection during the first wave of oocyte death. We compared the mRNA expression levels of the main participants of the Hippo cascade in mammals (mst1/2, lats1/2, yap) between the developmental stages (E14,5 - 18,5) of *Mus musculus* embryos by qRT-PCR. It turned out that the expression level of the main kinases (mst1/2 and lats1/2) increased at the E16,5 stage, but decreased at 17,5. The ovarian cyst break-down takes place during these late stages of development, so the rise of the kinases' expression can be connected with this process. The immunocytochemical staining of the embryonic ovaries for LATS1/2 and YAP showed that these proteins were mainly localized in the somatic cells of the ovary. The cyst break-down occurs with the direct involvement of somatic (future follicular) cells, that are necessary for the primordial follicles' formation. So the condition of the somatic cells around the oocytes can be the factor of oocyte selection. Understanding of this process can help to find out the ways of ovarian reserve restoration and maintainance in the females of reproductive age. The work was funded by the Fund of President RF research project MK-378.2020.4. *The authors marked with an asterisk equally contributed to the work.

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Proteomics investigation of microgravity conditioned human primary stem cells, in presence of SrHA nanoparticles

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Microgravity-induced osteoporosis is one of the main problems affecting astronauts during and after space traveling. Furthermore, osteoporosis and non-union fractures still represent worldwide problems. Nanotechnological applications are gaining field as remarkable solutions to improve bone healing, especially where conventional drug approaches fail. Our group developed and characterized calcium and strontium hydroxyapatite nanoparticles (nCa-HA and nSr-HA, respectively) 1 as a countermeasure for osteoporosis (NATO project). Nanoparticles efficacy was studied on human bone marrow-derived mesenchymal stem cells (hMSCs), both under Earth's gravity (G) and simulated microgravity (μG), using a Random Positioning Machine (RPM). The investigation was conducted in terms of gene expression, extracellular matrix protein composition and proteome characterization 2. Particularly, hMSCs proteome has been studied using a bottom-up and label-free approach. Samples have been in-gel digested and analyzed with EvosepOne online coupled to the mass spectrometer. Data Independent Acquisition (DIA) was conducted to obtain a high proteome coverage. Results were statistically process and significative difference in the analyzed proteomes were correlated to the gravity and the nanoparticles treatment variables. The enrichment of the differentially expressed proteins between G and μG highlighted the involvement of actin filament organization, ossification and angiogenesis pathways. Furthermore, pathways involving actin filament organization were found enriched also in the presence of nSr-HA, both in G and μG. Gene expression analysis showed up-regulation of the osteogenic markers in the presence of strontium. Although further analysis and validation of these data will be carried on, preliminary conclusions suggest nSr-HA are counteracting the effects of μG, promoting ossification in hMSCs.

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Skeletal muscle as a source of mesenchymal stem cells for autologous cell therapies

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Advanced cell therapies employing autologous mesenchymal stem cells (MSCs) for joint regeneration have shown promising results in alleviating symptoms despite the lack of detailed understanding of the underlying mechanism of action. To date, the most well-recognized tissue sources of mesenchymal stem cells in regenerative medicine are autologous bone marrow and adipose tissue. The biological properties of MSCs from other sources such as skeletal muscle, however, are poorly understood. The aim of our study was to compare the skeletal muscle MSCs with well-recognized bone and bone marrow-derived MSCs in osteoarthritis patients. Paired samples of skeletal muscle and trabecular bone tissue were obtained from 21 patients with osteoarthritis. MSCs were isolated using collagenase digestion and isolated cells compared using ex vivo immunophenotyping and detailed in vitro analyses. These included the colony forming unit fibroblast assay, growth kinetics, senescence, multilineage potential, immunophenotyping (CD90, CD73 and CD105), and gene expression profiling. Freshly isolated MSCs from skeletal muscle showed improved viability over bone-derived MSCs, with similar mesenchymal fraction. Muscle-derived MSCs also showed superior clonogenicity, higher growth rates, lower doubling times, as well as superior osteogenic and myogenic properties compared to bone-derived MSCs. We also showed a positive correlation between CD271 expression in skeletal muscle MSCs and adipogenesis. Due to their superior properties skeletal muscle-derived MSCs represent a suitable candidate for autologous stem-cell therapies. Previously published in: Čamernik K et al. (2019) Stem Cell Res 38