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SEARCH FOR PROTEINS OF BLOOD PROTEOME - REGULATORS OF BONE REMODELING IN COSMONAUTS

Abstract

Despite fundamental research of the influence of the space flight factors on bone tissue remodeling, the involvement of systemic and local factors is not fully understood. Presently, the methods of genomics and proteomics provide new opportunities for determination of potential markers of processes which are significant for gravitational physiology. The aim of this work was to study the signal proteins of the blood proteome - regulators of bone remodeling, and to construct the molecular associative links characterizing the processes of bone metabolism in cosmonauts after long space flights. Blood samples obtained from 18 Russian cosmonauts (44 6 years, males) in the framework of the experiment “Blood and urine proteomes” were analyzed. Venous blood was collected 30 days before the launch, a day after landing, and on 7th day after returning to the Earth. Quantitation was achieved by a well-established and highly-verified sample spectrometry analysis of isotope-labeled standards [I. Larina, A. Percy, C. Borchers, et al., 2017]. Data of multiple reactions monitoring was visualized and studied by means of Mass Hunter software for quantitative analysis (version B.07.00, Agilent). After identification, concentrations of 125 different proteins were determined, 19 of which conclusively differed for different experimental points (p-value ¡0.05). The use of the ANDSystem program allowed to reveal that three of the 19 proteins are directly related to the processes of bone tissue remodeling as regulatory proteins. Since one protein can participate in a variety of processes, the association of proteins with conclusively different concentrations (cystatin C, fetuin-A and fibronectin) and bone remodeling processes was analyzed using manual annotation. An associative gene-molecular network was constructed, revealing the connection between conclusively different proteins and biological processes in bone tissue. The rapid change in the combination of factors affecting the human body after landing causes an acute readaptation of bone remodeling, aimed at adapting to the

conditions of life on the Earth. Under these conditions, signaling proteins trigger a pathway that, over a period of 3-6 (or more) months, contribute to the recovering of bone mineral density and muscle contraction strength in accordance with the "genetic memory" about optimal compliance of bone metabolism parameters to the Earth's conditions. Microgravity-induced modification of the blood proteome makes it possible to identify molecular mechanisms involved in the adaptive response of the organism to changes in environmental conditions during space flight.