Human placenta-derived stromal cells mitigate select immune responses to simulated weightlessness

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Space flight presents unique risks to human health. Microgravity and social isolation are important space flight stressors which have vast impact on multiple systems such as the musculoskeletal, immune and central nervous system (CNS). To explore candidate countermeasures against tissue decrements caused by spaceflight, we performed a pilot study with PLacental-eXpanded stromal (PLX) cells. PLX cells secrete factors that modulate the immune system, but do not trigger host immune responses, enabling treatment in subjects that have intact immune systems. These cells had previous success in treating critical limb ischemia and acute radiation syndrome in murine models. In this study, 4-month-old female mice underwent 30 days of hindlimb unloading (HU) in single housing conditions to simulate long-term weightlessness and isolation. HU and normally ambulating controls were administered with PLX cells or sham-injected with Plasmalyte. We hypothesized that administration of PLX cells will mitigate some of the effects caused by prolonged HU. We found that treatment with PLX cells was well tolerated as indicated by body weights, circulating corticosterone levels and immune organ response to injection of the cells. HU led to the expected decreases in soleus muscle weights and bone loss. We did not observe any protective properties of the PLX cells in the musculoskeletal system but found that the cell treatment partially protected from a subset of HU-induced immune and CNS changes. In the hippocampus, protein levels of 9 of 44 cytokines were downregulated by HU. PLX administration mitigated changes in expression of 8 of these cytokines, including IL-2, IL-6 and MCP-1. To our knowledge, this is the first report on the protective effects of PLX-PAD against HU-induced changes in the cytokine milieu of the CNS. Our findings warrant further studies, which includes testing in actual spaceflight.