

The effects of placental-expanded (PLX-PAD) stromal cell treatment, hindlimb unloading, and isolation on the behavior of female mice

Amalia K. Luthens^{1,2}, Amber M. Paul^{2,3}, Charles Houseman^{2,4}, Metadel Abegaz^{2,4}, Steffy Tabares Ruiz^{2,4}, Nathan O'Neil^{2,4}, Racheli Ofir⁵, Jacob Cohen², April E. Ronca^{2,6}, Ruth K. Globus², Candice GT Tahimic^{2,7,8}, Linda Rubinstein^{2,3}

¹University of Colorado Boulder, Boulder 80302, USA, ²Space Biosciences Division, NASA Ames Research Center, Moffett Field, California 94035, USA, ³Universities Space Research Association / NASA Academic Mission Services, ⁴Blue Marble Space Institute of Science, Seattle, Washington 98154, USA, ⁵Pluristem Inc., Tel Aviv, Israel, ⁶Wake Forest Medical School, Winston-Salem, North Carolina 27101, USA, ⁷KBR, Houston, Texas 77002, USA, ⁸Department of Biology, University of North Florida, Jacksonville, Florida, 32224 USA

Abstract (Word Limit: 300)

Spaceflight can lead to altered immune responses and inflammation (Crucian et al. 2014) and elevated levels of inflammation are connected to anxiety and depression. A recent study on the International Space Station showed that mice exhibited a novel circling behavior during spaceflight (Ronca et al. 2019). However, there is still a gap in knowledge on how microgravity impacts behavior. In this current study, we performed 30 days of hindlimb unloading (HU) on four-month old female mice and analyzed select behavior from video image capture. We also determined the effects of PLacental-eXpanded stromal cells derived from the maternal placenta (PLX-PAD), alone and in combination with HU and isolation, on behavior. We have previously shown that PLX-PAD mitigates select inflammatory responses and changes in cytokine expression caused by HU. In-cage behaviors were analyzed in HU or control female mice treated with 2 injections of PlasmaLyte (Sham) or PLX-PAD (n=7/group). We found that PLX-PAD decreased exploratory behaviors compared to Sham-treated mice at night. Normally loaded (NL) PLX mice slept less than NL Sham mice during the day, and HU animals had significantly higher involuntary movement during sleep compared to NL animals, suggesting sleep disruption. Overall, we show that both HU and PLX affect important behavioral factors. This experiment is the first to study the effects of PLX-PAD on behavior. Additional studies are needed to define the behavioral changes in spaceflight and test possible countermeasures.