

Spaceflight effects and molecular responses in the mouse eye: observations after NASA shuttle mission STS-133

Claudia Maria Prospero Ponce^a, Susana B. Zanello^b, Corey A. Theriot^c, Patricia Chevez-Barrios^{a,d}

^a Department of Pathology and Genomic Medicine, The Methodist Hospital, Houston, TX.

^b Division of Space Life Sciences, Universities Space Research Association, Houston, TX.

^c Wyle Integrated Science and Engineering, Houston, TX.

^d Pathology and Laboratory Medicine and Ophthalmology, Weill Medical College of Cornell University

Background: Human space exploration implies a combination of stressors including microgravity-induced cephalad fluid shift and radiation exposure. Ocular changes in astronauts leading to visual impairment are of occupational health relevance. The effect of this complex environment on ocular morphology and function is poorly understood. **Material and Methods:** Mice were assigned to a Flight (FLT) group flown on shuttle mission STS133, Animal Enclosure Module (AEM), or vivarium (VIV) ground controls. Eyes were collected at 1, 5 and 7 days after landing, and were fixed for histological sectioning. The contralateral eye was used for gene expression profiling by qRT-PCR. Routine histology and immunohistochemistry using 8-hydroxy-2'-deoxyguanosine (8-OHdG), caspase-3, glial fibrillary acidic protein (GFAP) and β -amyloid were used to study the eyes. **Results and Conclusions:** 8-OHdG and caspase-3 immunoreactivity was increased in the retina in FLT samples at return from flight (R+1) compared to ground controls, and decreased at day 7 (R+7), suggesting an increase in oxidative stress and cell apoptosis. FLT mice showed evidence of retinal pigment epithelium (RPE) apoptosis possibly secondary to oxidative damage. Although attenuation of RPE has been related to retinal choroidal folds in astronauts, it is yet to be determined whether or not increased RPE apoptosis may contribute to the formation of choroidal folds or may increase the risk for other retinal pathologies, such as AMD. β -amyloid was seen in the nerve fibers at the post-laminar region of the optic nerve in the flight samples (R+7). Deposition of β -amyloid has a strong correlation with mechanical trauma. The co-

expression of GFAP in astrocytes and oligodendrocytes in these same areas supports the possible mechanical origin probably secondary to intracranial pressure that is transmitted into the nerve, as a result of an increase in venous pressure associated to microgravity-induced cephalic fluid shift. However, there is the need to further investigate the nature of the changes through additional experimental work.

Gene expression of oxidative and cellular stress response genes was upregulated in the retina of FLT samples upon landing followed by lower levels by R+7. These results suggest that reversible molecular damage occurs in the retina of mice exposed to spaceflight and that protective cellular and molecular pathways are induced in the retina in response to these changes.