Fiscal Year:	FY 2017	**Task Last Updated:**	FY 02/09/2017
PI Name:	Delp, Michael Ph.D.		
Project Title:	Effects of Spaceflight on Ocular Oxidative Stress and the Blood-Retinal Barrier		
Division Name:	Space Biology		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	SPACE BIOLOGY--Cellular and molecular biology		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	(1) Cell & Molecular Biology (2) Animal Biology: Vertebrate		
Space Biology Cross-Element Discipline:	(1) Developmental Biology (2) Neurobiology		
Space Biology Special Category:	(1) Translational (Countermeasure) Potential		
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Comments:	Previous affiliations were University of Florida (mid-2007-June 2014), West Virginia University (mid-2005 to mid-2007), and Texas A&M University (1995 to mid-2005).		
Project Type:	FLIGHT	**Solicitation / Funding Source:**	2014 Space Biology Flight NNH14ZTT001N
Start Date:	02/01/2015	**End Date:**	01/31/2019
No. of Post Docs:	1	**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA ARC
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Flight Program:	ISS		
Flight Assignment:	Tissue Sharing NOTE: Extended to 1/31/2019 per NSSC information (Ed., 3/12/18) NOTE: Extended to 1/31/2018 per F. Hernandez/ARC (Ed., 2/12/17)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Pecaut, Michael Ph.D. (Loma Linda University) Mao, Xiao Wen M.D. (Loma Linda University)		
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Performance Goal Text:			

Task Description:	Approximately 29% of astronauts on short-term (~2 wk) space shuttle flights and 60% on long-duration (~6 mo) missions to the International Space Station (ISS) are reported to have experienced some impairment in distant or near visual acuity. These visual disturbances have been hypothesized to be related to increases in intracranial pressure (ICP) and intraocular pressure. Modeling studies have shown that a compromise in the integrity of the vascular blood-brain barrier (BBB) would serve to elevate ICP. While much attention has been directed toward the role of the cerebral vasculature in elevating ICP, little work has been done to examine conditions of the vasculature in the eye and the potential role of microgravity in altering the blood-retinal barrier (BRB), which maintains a similar function in the eye for regulating intraocular pressure as the BBB in the cranium. One condition known to compromise the BRB is oxidative stress. For example, in diabetic retinopathy, the leading cause of blindness in Western society, elevations in oxidative stress compromise the BRB and increase vascular permeability in the eye. The proposed studies through the ISS Rodent Tissue Sharing Opportunity will provide new and important information regarding the effects of spaceflight on oxidative stress in the eye and its potential deleterious effects on the BRB.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Through the collection of 300 post-flight questionnaires, it has recently been reported that that approximately 29% of astronauts flying short-duration missions and 60% of astronauts on long-duration missions experience an impairment of distance and near visual acuity. Furthermore, some of these changes remain degraded for years after flight. It is hard to imagine a more severe, prevalent, and potentially intractable condition threatening human space exploration than the loss of visual acuity. In 2010, NASA Space Life Sciences at Johnson Space Center in Houston held a Visual Impairment Intracranial Pressure (VIIP) Summit of leading clinicians and scientists with expertise in ophthalmology and cerebral fluid dynamics, and it was hypothesized that the visual impairment experienced by astronauts was the result of a microgravity-induced cephalad fluid shifts and corresponding increases in ICP and intraocular pressure. The proposed studies will provide new and important information regarding the effects of spaceflight on oxidative stress in the eye, its potential deleterious effects on the blood-retinal barrier and, consequently, factors that may function to increase intraocular pressure. In addition, understanding the relation between oxidative stress in the eye and disruption of the blood-retinal barrier may provide new insight into other conditions that affect visual acuity, including diabetic retinopathy, the leading cause of blindness in Western society, where elevations in oxidative stress compromise the blood-retinal barrier and increase vascular permeability in the eye.
Task Progress:	Mouse eye tissue was obtained from two separate missions to the International Space Station (ISS) and are described as Study 1 and 2 below. Study 1. The first study was a NASA mission testing the Rodent Research Hardware System, called the Rodent Research-1 (RR-1), where mice (female, C57Bl6/J, 16wk old at time of launch) and hardware payload was transported to the ISS on a SpaceX-4 CRS-4 Dragon cargo spacecraft. During this mission, which was launched September 20, 2014 and returned October 25, 2014, astronauts transferred ten flight mice (Group 1) to a habitat to validate NASA hardware and operations. A transporter and identical habitat were tested at Kennedy Space Center in Florida as ground control units based on a 4-day delay. Ground control groups consisted of environmental ground control mice (Group 2) housed in RR-1 flight hardware within an environmental simulator under the same conditions as the ISS, vivarium control mice (Group 3) housed in standard vivarium cages, and basal control mice (Group 4) from the same cohorts as the flight mice. At the end of the mission, the flight and ground control mice were sacrificed and some tissue (not eyes) was dissected from some of the mice (flight mice dissected on-orbit 37 days after launch). On-orbit dissections were conducted by astronauts using the Microgravity Science Glovebox. After dissection, the remaining carcass or whole carcass of the animals were frozen. Subsequently, at NASA Ames Research Center in California, the frozen carcasses were thawed and the eyes and other tissues were removed. The eyes were re-frozen once they were removed from the carcass and shipped to Florida State University on September 22, 2016. Study 2. The second study was a collaborative arrangement between the Japan Aerospace Exploration Agency (JAXA) and NASA. This study was part of the larger “Mouse Epigenetics” program under the direction of JAXA Principal Investigator Dr. Satoru Takahashi, a Professor at Tsukuba University in Japan. This investigation included two flight groups that were transported to the ISS on the SpaceX-9 mission. These animals spent approximately 30 days on the ISS. The first group of flight mice (n=6, male) were exposed to μG, while the second group of flight mice (n=6, male) were exposed to continuous artificial-G (1G) while they were in the Habitation Cage Units through the use of a short-arm centrifuge. After 30 days on-orbit the animals were returned to Earth alive on August 26, 2016 and dissected two days later in San Diego, California. Ground control mouse studies were completed in Japan after the return of the flight mice. Control mice (Transportation/Habitation cage controls, n=6; Vivarium controls, n=6) were acquired on August 31, 2016 at the JAXA animal facility in Tsukuba, Japan. Transportation/Habitation cage control mice were acclimated to the water lixit system and flight food from August 31 through September 22. They were then habituated to the Transportation Cage Unit (to simulate launch and flight to ISS housing) from September 22 – 26, and then they were placed in the Habitation Cage Units from September 26 – October 31 to simulate time on the ISS. They were then placed in the Transportation Cage Unit October 31 – November 3 to simulate the return to Earth flight. The mouse dissections took place on November 3. Control mouse eye tissue was shipped to the US and delivered on November 9, 2016. During the dissection, the right eye from each animal (flight and control) was fixed and kept by Principal Investigator (PI) Delp. The left eye from each animal was sectioned into two separate halves; the front half of the eye (including the cornea, ciliary body, and muscle) and the back half of the eye (including retina, macula, choroid, optic nerve, and associated vasculature). Both halves were frozen, and the front half of the eye was maintained by JAXA investigators, while the back half of the eye and the lens were maintained by PI Delp. Results: From the RR-1 mice, the retinas were isolated from the frozen eyes under rapid thaw process. RNA/DNA were extracted from the retina. QC data showed that the samples are suitable for RNA sequencing. These studies are currently in progress. Proteins lysates have been prepared for multiplex proteomics from the frozen eyes of the JAXA flight and ground control mice. Assay and data analyses are underway. Fixed ocular sections are being stained for markers of oxidative stress and apoptosis.

Bibliography Type:	Description: (Last Updated: 06/21/2023)