Fiscal Year:	FY 2021	**Task Last Updated:**	FY 03/26/2021
PI Name:	Zanello, Susana Ph.D.		
Project Title:	Evaluation of Hindlimb Suspension as a Model to Study Ophthalmic Complications in Microgravity: Ocular Structure and Function and Association with Intracranial Pressure		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **SANS**:Risk of Spaceflight Associated Neuro-ocular Syndrome (SANS)		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	susana.b.zanello@nasa.gov	**Fax:**	FY
PI Organization Type:	NASA CENTER	**Phone:**	832-576-6059
Organization Name:	KBR/NASA Johnson Space Center		
PI Address 1:	Human Research Program Chief Scientist Office		
PI Address 2:			
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City:	Houston	**State:**	TX
Zip Code:	77058	**Congressional District:**	36
Comments:	NOTE (January 2021): PI now at KBR/NASA JSC as of December 2020. Previously at imec USA from June 2019-November 2020; NASA JSC (KBRwyle) from August 2017 until spring 2019. Prior to August 2017, PI was with Universities Space Research Association.		
Project Type:	Ground	**Solicitation / Funding Source:**	2011 Crew Health NNJ11ZSA002NA
Start Date:	02/01/2013	**End Date:**	01/01/2021
No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	1	**Monitoring Center:**	NASA JSC
Contact Monitor:	Brocato, Becky	**Contact Phone:**	
Contact Email:	becky.brocato@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: End date changed to 1/1/2021; note also with PI move to imec USA-Florida, PI's 3 projects were combined into one grant, 80NSSC19K1666 ; however, reporting will be required individually, per HRP (Ed., 11/4/19) NOTE: End date changed to 9/30/2019 per JSC HRP; PI at Universities Space Research Association for a period; now back at NASA JSC (KBRwyle) (Ed., 11/19/18) NOTE: This project had some delays and is still underway with an end date now of 9/30/2018. It moved from an Internal Project to Grant NNX15AW48G starting 10/1/2015, per A. Allcorn/HRP (Ed., 8/31/16)		
Key Personnel Changes/Previous PI:	November 2019: Corey Theriot, PhD, is now CoInvestigator per HRP; Patricia Chevez-Barrios is also CoInvestigator at this time. January 2014 report: Addition of Patricia Chevez-Barrios (collaborator, The Methodist Hospital, Houston) for ocular pathology		
COI Name (Institution):	Parsons-Wingerter, Patricia Ph.D. (NASA Ames Research Center) Vizzeri, Gianmarco M.D. (University of Texas Medical Branch) Chevez-Barrios, Patricia M.D. (The Methodist Hospital Research Institute) Theriot, Corey Ph.D. (University of Texas Medical Branch-Wyle)		

Grant/Contract No.:	80NSSC19K1666 ; Internal Project ; NNX15AW48G
Performance Goal No.:	
Performance Goal Text:	
Task Description:	An animal ground-analog is being tested as a model to induce cephalad fluid shifts and evaluate whether ocular structural changes similar to those produced in humans after exposure to a microgravity environment occur in rodents subjected to tail suspension. In vivo ocular measures and tissue analysis were performed in hindlimb suspension (HS) and normal posture control rats. Intraocular pressure (IOP), intracranial pressure (ICP), and optical coherence tomography (OCT) scans of the retina were evaluated before, during, and after HS. Retinal microvascular changes will be evaluated by computerized analysis of retinal flat mounts specifically stained to image the microvasculature. In order to study cellular responses that are possibly associated with the stress of variations in translaminar pressure in the retina due to cephalad fluid shift, whole transcriptome gene expression analysis was performed and immunohistochemistry of specific markers was done on histologic sections. This study will lead to better characterization and problem definition of the Spaceflight Associated Neuro-Ocular Syndrome (SANS), and in turn, it will evaluate the need for countermeasures to mitigate the risk. NOTE (Ed., July 2019): PI now with imec USA; PI still resides in Houston and works remotely with FL office. NOTE (Ed., December 2018): PI at Universities Space Research Association for a period; now back at NASA JSC (KBRwyle) as internal project. NOTE (Ed., 8/31/16): This project had some delays and is still underway with an end date now of 9/30/2018. It moved from an Internal Project to Grant NNX15AW48G starting 10/1/2015, per A. Allcorn/Johnson Space Center Human Research Program.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Mechanical and oxidative stress anticipated to occur due to the fluid shift caused by hindlimb suspension are thought to be common occurrences in ophthalmic conditions on Earth, namely glaucoma, diabetic retinopathy, macular degeneration. Molecular pathways implicated in the histopathology of SANS may shed light on common mechanisms shared with the above mentioned Earth-bound diseases, and thus, in future therapies to prevent and/or ameliorate these disease conditions.
Task Progress:	The Spaceflight Associated Neuro-ocular Syndrome (SANS) observed in astronauts is hypothesized to be associated with microgravity-induced fluid shifts. Presently, there is a need for an animal model of SANS in order to investigate its pathophysiology. We used the rat hindlimb suspension (HS) model to examine the relationship between the assumed cephalad fluid shifts, intraocular (IOP) pressure, and the molecular responses to the prolonged change in body posture elicited in the retina in order to assess its value as a model of SANS. Young male, young female, and old male Long Evans rats were subjected to HS up to 90 days. Animals completing 90-day suspension were further studied for recovery periods up to 90 additional days at normal posture. IOP measures showed elevated pressure in HS animals for all cohorts with differences in the course of the response between the cohorts. Transcriptomics evidence supported a response to HS in the rat retina that was affected by age and sex. Several molecular networks were identified that suggest stress imposed by HS affected the retinal vasculature, oxidative and inflammation status, pigmented epithelium function, and glial activation. The CSNK1A1-TP53 pathway was implicated in the response in all cohorts. The most significant gender-specific genes were involved in cytoprotection, eye development and function, and may explain gender-dependent vulnerabilities to certain eye diseases. The results presented constitute the conclusion of this study and support the hypothesis that underlying changes in the biology of the retina subjected to simulated microgravity involve both the neural and vascular retina.
Bibliography Type:	Description: (Last Updated: 09/04/2023)
Articles in Peer-reviewed Journals	Theriot CA, Chevez-Barrios P, Loughlin T, Beheshti A, Mercaldo ND, Zanello SB. "The impact of hindlimb suspension on the rat eye: A molecular and histological analysis of the retina." Gravit Space Res. 2021 Sep 17;9(1):86-103. https://doi.org/10.2478/gsr-2021-0007 , Sep-2021
Articles in Peer-reviewed Journals	Lagatuz M, Vyas RJ, Predovic M, Lim S, Jacobs N, Martinho M, Valizadegan H, Kao D, Oza N, Theriot CA, Zanello SB, Taibbi G, Vizzeri G, Dupont M, Grant MB, Lindner DJ, Reinecker HC, Pinhas A, Chui TY, Rosen RB, Moldovan N, Vickerman MB, Radhakrishnan K, Parsons-Wingerter P. "Vascular patterning as integrative readout of complex molecular and physiological signaling by VESsel GENeration Analysis." J Vasc Res. 2021 Jul;58(4):207-30. Review. https://doi.org/10.1159/000514211 ; PMID: 33839725 , Jul-2021
Articles in Peer-reviewed Journals	da Silveira WA, Fazelinia H, Rosenthal SB, Laiakis EC, Kim MS, Meydan C, Kidane Y, Rathi KS, Smith SM, Stear B, Ying Y, Zhang Y, Foox J, Zanello S, Crucian B, Wang D, Nugent A, Costa HA, Zwart SR, Schrepfer S, Elworth RAL, Sapoval N, Treangen T, MacKay M, Gokhale NS, Horner SM, Singh LN, Wallace DC, Willey JS, Schisler JC, Meller R, McDonald JT, Fisch KM, Hardiman G, Taylor D, Mason CE, Costes SV, Beheshti A. "Comprehensive multi-omics analysis reveals mitochondrial stress as a central biological hub for spaceflight impact." Cell. 2020 Nov 25;183(5):1185-201.e20. https://doi.org/10.1016/j.cell.2020.11.002 ; PMID: 33242417; PMCID: PMC7870178 , Nov-2020
Articles in Peer-reviewed Journals	Vyas RJ, Young M, Murray MC, Predovic M, Lim S, Jacobs NM, Mason SS, Zanello SB, Taibbi G, Vizzeri G, Parsons-Wingerter P. "Decreased vascular patterning in the retinas of astronaut crew members as new measure of ocular damage in spaceflight-associated neuro-ocular syndrome." Invest Ophthalmol Vis Sci. 2020 Dec 1;61(14):34. https://doi.org/10.1167/iovs.61.14.34 ; PMID: 33372980; PMCID: PMC7774106 , Dec-2020