Fiscal Year:	FY 2017	**Task Last Updated:**	FY 03/10/2017
PI Name:	Raykin, Julia Ph.D.		
Project Title:	Effects of Intracranial Pressure and 1-Carbon Metabolites on the Optic Nerve Sheath in VIIP Syndrome (Postdoctoral Fellowship)		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Sensorimotor Adaptation Team		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	30318	**Congressional District:**	5
Comments:			
Project Type:	GROUND	**Solicitation:**	2014 NSBRI-RFA-14-02 First Award Fellowships
Start Date:	11/01/2014	**End Date:**	10/31/2016
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:	0	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Ethier, Christopher (MENTOR/ Georgia Institute of Technology)		
Grant/Contract No.:	NCC 9-58-PF04102		
Performance Goal No.:			
Performance Goal Text:			
	POSTDOCTORAL FELLOWSHIP This grant studies the impact of variations in intracranial pressures (ICP) and 1-carbon metabolites on the development of Visual Impairment/Intracranial Pressure (VIIP) syndrome. Our specific objective is to identify the effects of ICP and 1-carbon metabolites on cellular remodeling in the optic nerve. Cellular remodeling has been implicated in many pathologies. Elucidation of the cellular mechanisms involved in VIIP will help identify possible interventions to treat/prevent the occurrence of VIIP. The overall project aims were to characterize the synergistic effects of increases in ICP and homocysteine on optic nerve sheath (ONS) remodeling. A key component of identifying the cellular response to these perturbations was to mechanically characterize the ONS as this tissue has not yet been mechanically described. One major impact of the cellular response to mechanical loading is the alteration of the extracellular matrix of the tissue.		

Task Description:	In order to identify the changes in these properties it was necessary to establish baseline values. We have determined that the optic nerve is under significant axial stretch in vivo, suggesting that current computational models might need to be altered to account for these stretches. In addition, we have been able to determine the axial and circumferential moduli of the optic nerve dura. Another important finding from this work was that the addition of homocysteine to the culture medium of ONS led to an increase in the MMP expression in a dose dependent manner (MMP is an important indicator that remodeling is occurring). In addition, we have shown that mechanical stretch and homocysteine synergistically contribute to the remodeling response of ONS cells.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The results of this research could be used to help patients suffering from increased intracranial pressures. The purpose of this work is to identify the remodeling responses to increased intracranial pressures in the optic nerve, which can help in identifying possible interventions to mitigate the effects of the increased pressures. In addition, 1-carbon metabolites may play an important role in the remodeling response of the optic nerve. Health care providers could monitor levels of 1-carbon metabolites to predict individual responses to raised intracranial pressures.
Task Progress:	The overall project aims were to characterize the ONS mechanics and the synergistic effects of increases in ICP and homocysteine on the ONS. Progress: We have developed and characterized a mechanical testing/culture system to deliver pressure and axial load to the pig ONS. In addition, we have shown that the optic nerve is under significant axial tension in vivo. Our experiments indicate that mechanical loading and homocysteine synergistically stimulate remodeling of ONS cells and that homocysteine induces remodeling in the pig ONS in vitro.
Bibliography Type:	Description: (Last Updated: 07/26/2018)
Articles in Peer-reviewed Journals	Raykin J, Snider E, Bheri S, Mulvihill J, Ethier CR. "A modified gelatin zymography technique incorporating total protein normalization." Anal Biochem. 2017 Mar 15;521:8-10. http://dx.doi.org/ ; PubMed PMID: 28069453 , Mar-2017
Articles in Peer-reviewed Journals	Raykin J, Forte TE, Wang R, Feola A, Samuels BC, Myers JG, Mulugeta L, Nelson ES, Gleason RL, Ethier CR. "Characterization of the mechanical behavior of the optic nerve sheath and its role in spaceflight-induced ophthalmic changes." Biomech Model Mechanobiol. 2017 Feb;16(1):33-43. Epub 2016 May 28. http://dx.doi.org/ ; PubMed PMID: 27236645 , Feb-2017
Articles in Peer-reviewed Journals	Mulvihill JJE, Raykin J, Snider EJ, Schildmeyer LA, Zaman I, Platt MO, Kelly DJ, Ethier CR. "Development of a platform for studying 3D astrocyte mechanobiology: Compression of astrocytes in collagen gels." Ann Biomed Eng. 2018 Feb;46(2):365-374. Epub 2017 Nov 27. https:// ; PubMed PMID: 29181720 , Feb-2018