Fiscal Year:	FY 2016	**Task Last Updated:**	FY 11/30/2015
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Project Title:	Effects of Intracranial Pressure and 1-Carbon Metabolites on the Optic Nerve Sheath in VIIP Syndrome		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Sensorimotor Adaptation Team		
Joint Agency Name:		**TechPort:**	No
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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 / Funding Source:**	2014 NSBRI-RFA-14-02 First Award Fellowships
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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:	3	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
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Flight Program:			
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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 and to develop computational models to describe the remodeling that occurs in response in altered mechanical loading and homocysteine levels. A key component of identifying the cellular response to these perturbations was to mechanically characterize the (ON)/optic nerve sheath (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		

Task Description:	extracellular matrix of the tissue. 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. The next step in this process will be to determine the effects of physiological changes on these mechanical properties. 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). These findings were ultimately important in order to push forward with the rest of the project. The characterization of the ONS will help us evaluate the effects of culturing the tissue under various conditions, which will help identify key factors in the development of VIIP. In addition, we have verified our hypothesis that homocysteine induces remodeling in the ONS. In the coming year, we will perform more experiments with the addition of homocysteine to the cell culture medium to better understand homocysteine-induced remodeling mechanisms. We will simultaneously examine the effects of increased ICP. We expect that the synergistic effects of increased homocysteine levels and ICP will have a far greater impact on remodeling than either factor alone.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The results of this research could be used to help patients suffering from increased intracranial pressure. The purpose of this work is to identify the remodeling responses to increased intracranial pressure in the optic nerve, which can help in identifying possible interventions to mitigate the effects of the increased pressure. 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 pressure.
Task Progress:	The overall project aims were to characterize the synergistic effects of increases in ICP and homocysteine and to develop computational models to describe the remodeling that occurs in response in altered mechanical loading and homocysteine levels. Progress: We have developed and characterized a mechanical testing/culture system to deliver pressure and axial load to the pig ONS. We have determined the mechanical properties of control ONS that will be used as baseline values in our studies. In addition, we have shown that the optic nerve is under significant axial tension in vivo, indicating that axial stretch will be an important factor to consider in our cultures. Preliminary experiments indicate that homocysteine induces remodeling in the pig ONS in vitro. Next we will identify important parameters necessary for our models, so that predictive simulations can be run to reduce the number of costly and timely experiments that will need to be run.
Bibliography Type:	Description: (Last Updated: 07/26/2018)