Fiscal Year:	FY 2016	**Task Last Updated:**	FY 06/09/2016
PI Name:	Smith, Scott M Ph.D.		
Project Title:	Astronaut Vision Issues and One Carbon Metabolism: Expanded Polymorphism Evaluation and Evaluation in a Potential Analog Population		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Biomedical countermeasures		
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:	scott.m.smith@nasa.gov	**Fax:**	FY 281-483-2888
PI Organization Type:	NASA CENTER	**Phone:**	281-483-7204
Organization Name:	NASA Johnson Space Center		
PI Address 1:	Biomedical Research and Environmental Sciences Division/SK3		
PI Address 2:	2101 NASA Pkwy		
PI Web Page:			
City:	Houston	**State:**	TX
Zip Code:	77058-3607	**Congressional District:**	36
Comments:			
Project Type:	FLIGHT,GROUND	**Solicitation / Funding Source:**	Directed Research
Start Date:	04/06/2016	**End Date:**	04/30/2019
No. of Post Docs:		**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 JSC
Contact Monitor:	Norsk, Peter	**Contact Phone:**	
Contact Email:	Peter.norsk@nasa.gov		
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Zwart, Sarah Ph.D. (Universities Space Research Association) Chang, Alice M.D. (Mayo Clinic, Rochester, MN) Gregory, Jesse Ph.D. (University of Florida) Chen, John M.D., Ph.D. (Mayo Clinic, Rochester, MN) Zeisel, Steven M.D., Ph.D. (University of North Carolina at Kannapolis) Gibson, C. Robert O.D. (Coastal Eye Associates) Mader, Thomas M.D. (U.S. Army (retired))		
Grant/Contract No.:	Directed Research		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	1. We have documented a genetic predisposition for some astronauts to develop ophthalmologic findings as described in 2011 by NASA's Space Medicine Division (1) known as VIIP (vision impairment/intracranial pressure). From a limited study of 5 single-nucleotide polymorphisms (SNPs), we found one SNP associated with a greater risk of ophthalmic findings (e.g., choroidal folds, cotton wool spots), and another SNP that was protective against optic disc edema. In light of these findings, we propose to evaluate a wider range of SNPs from the same metabolic pathway, to clarify and verify the relationship of genetics in some astronauts that may predispose to ophthalmic anomalies. Furthermore, we have identified a clinical population -- patients with polycystic ovary syndrome (PCOS) -- with several characteristics similar to those described in astronauts. The clinical findings shared by PCOS patients and astronauts with ophthalmic anomalies include higher homocysteine, increased retinal nerve fiber layer, increased incidence of white matter hyperintensities on MRI, increased androgen concentrations (or responses), and altered carbohydrate metabolism. PCOS patients have not been evaluated in detail regarding the occurrence of other anomalies observed in astronauts including choroidal folds, optic disc edema and cotton wool spots as well as changes in cycloplegic refraction, and optic nerve sheath diameter. While researchers have evaluated one-carbon metabolism pathway polymorphisms re: PCOS, and initial studies show an association with certain one-carbon polymorphisms, none have looked at the complete set of SNPs we propose here. Thus, this study has two major goals: 1. To extend the one-carbon pathway SNP assessment as related to astronaut ophthalmologic findings. 2. To evaluate patients with PCOS and/or Idiopathic intracranial hypertension (IIH) to assess one-carbon biochemistry and genetics and their possible correlation with ophthalmologic findings. While these studies alone will not identify the mechanism(s) of VIIP, we aim to clarify the genetic relationship to ophthalmic findings, and to document the utility of PCOS as a clinical population that could be used for studies that may ultimately allow for the definition of the mechanism of and means to prevent or treat these potentially vision-threatening processes in astronauts. Specific Aims 1. Test for multiple SNPs of the 85 major genes involved in one-carbon metabolism in ISS (International Space Station) crewmembers (a total of 523 SNPs), and relate these data to existing one-carbon biochemistry and metabolomic data, along with existing vision and related medical data. a. A secondary aim is to gather ethnicity data from the crewmembers, and characterize the extent to which ethnicity is predictive of ophthalmic issues after long-duration space flight. b. Another secondary aim is to evaluate the data collected in this (and the initial) one carbon metabolism genetics studies and cardiovascular data. To this end, we will request VO2 max (pre, in, post), Framingham Risk Score, resting heart rate and blood pressure (pre, in, post) diastolic and systolic, exercise heart rate and blood pressure (pre, in, post) diastolic and systolic, Vascular Compliance data share (heart rate, blood pressure, cardiac output and stroke volume), medications, diagnoses, BMI, and % body fat data from the Lifetime Surveillance of Astronaut Health project for evaluation relative to the one carbon genetic and biochemical data. 2. Compare the same one-carbon metabolism genetics and biochemistry and ophthalmologic data from patients in one of four treatment groups: i. women diagnosed with PCOS without IIH ii. women diagnosed with PCOS and IIH iii. women diagnosed with IIH without PCOS iv. controls (neither PCOS nor IIH) Subjects will be matched by age and body mass index (BMI). Statistical analyses will be used to evaluate the independent and shared contributions of age, body mass (BMI), and genetics on biochemical, and ophthalmologic outcomes, with False Discovery Rate adjustments to account for multiple comparisons. 3. A secondary aim is to combine the patient and control data from this study with ISS crewmember data in order to help inform us on whether or not these two cohorts (VIIP, PCOS) share similar associations among one-carbon metabolism genetics and biochemistry and ophthalmologic data identified in our earlier analyses.
Rationale for HRP Directed Research:	This research is directed because it contains highly constrained research. This study has two major goals: 1. To utilize existing samples where possible to extend the scope of the initial One Carbon study. This was initially submitted and reviewed in the NNJ14ZSA001N-OMNIBUS NRA. HRP Management has now asked we submit this as directed research. 2. To add testing to an ongoing clinical trial at the Mayo Clinic. Timing is critical given that study is ongoing. The primary study is a clinical trial of pharmaceutical treatment for PCOS. We propose to extend this study by collecting a blood sample for one carbon biochemical and genetic testing, along with ophthalmologic exams, with the aim of documenting the utility of this population as an analog group for future VIIP research.
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2016.
Bibliography Type:	Description: (Last Updated: 05/24/2023)