

<b>Fiscal Year:</b>	FY 2021	<b>Task Last Updated:</b>	FY 01/22/2021
<b>PI Name:</b>	Smith, Scott M Ph.D.		
<b>Project Title:</b>	Astronaut Vision Issues and One Carbon Metabolism: Expanded Polymorphism Evaluation and Evaluation in a Potential Analog Population		
<b>Division Name:</b>	Human Research		
<b>Program/Discipline:</b>			
<b>Program/Discipline--Element/Subdiscipline:</b>	HUMAN RESEARCH--Biomedical countermeasures		
<b>Joint Agency Name:</b>	<b>TechPort:</b>	No	
<b>Human Research Program Elements:</b>	(1) <b>HHC:</b> Human Health Countermeasures		
<b>Human Research Program Risks:</b>	(1) <b>SANS:</b> Risk of Spaceflight Associated Neuro-ocular Syndrome (IRP Rev I)		
<b>Space Biology Element:</b>	None		
<b>Space Biology Cross-Element Discipline:</b>	None		
<b>Space Biology Special Category:</b>	None		
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<b>Zip Code:</b>	77058-3607	<b>Congressional District:</b>	36
<b>Comments:</b>			
<b>Project Type:</b>	FLIGHT,GROUND	<b>Solicitation / Funding Source:</b>	Directed Research
<b>Start Date:</b>	04/06/2016	<b>End Date:</b>	09/30/2022
<b>No. of Post Docs:</b>		<b>No. of PhD Degrees:</b>	
<b>No. of PhD Candidates:</b>		<b>No. of Master' Degrees:</b>	
<b>No. of Master's Candidates:</b>		<b>No. of Bachelor's Degrees:</b>	
<b>No. of Bachelor's Candidates:</b>		<b>Monitoring Center:</b>	NASA JSC
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<b>Flight Program:</b>			
<b>Flight Assignment:</b>	NOTE: End date changed to 9/30/22 per C. Ribeiro/HHC HRP (Ed., 6/30/21) NOTE: End date changed to 10/01/2021 per PI (Ed., 1/7/21) NOTE: End date changed to 12/31/2020 per PI (Ed., 1/9/2020) NOTE: Extended to 4/30/2020 per PI (Ed., 1/28/19)		
<b>Key Personnel Changes/Previous PI:</b>			
<b>COI Name (Institution):</b>	Zwart, Sara Ph.D. ( University of Texas Medical Branch ) 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 Chapel Hill ) Gibson, C. Robert O.D. ( Coastal Eye Associates ) Mader, Thomas M.D. ( U.S. Army (retired) )		
<b>Grant/Contract No.:</b>	Directed Research		
<b>Performance Goal No.:</b>			

<b>Performance Goal Text:</b>	
	<p><b>Background</b> We have documented a genetic predisposition for some astronauts to develop ophthalmologic issues. 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 proposed two studies which were combined in this project. Thus, this project has two major goals:</p> <ol style="list-style-type: none"> <li>1. To extend the one-carbon pathway SNP assessment as related to astronaut ophthalmologic findings. (One Carbon Expansion study)</li> <li>2. To evaluate patients with polycystic ovary syndrome (PCOS) and/or Idiopathic intracranial hypertension (IIH) to assess one-carbon biochemistry and genetics and their possible correlation with ophthalmologic findings. (PCOS study)</li> </ol> <p>While these studies alone will not identify the mechanism(s) of astronaut ophthalmologic issues, 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.</p>
<b>Task Description:</b>	<p><b>Specific Aims</b></p> <p>The study has the following specific aims:</p> <ol style="list-style-type: none"> <li>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.</li> <li>2. Compare the same one-carbon metabolism genetics and biochemistry and ophthalmologic data from patients in one of four treatment groups: <ol style="list-style-type: none"> <li>i. women diagnosed with PCOS without IIH</li> <li>ii. women diagnosed with PCOS and IIH</li> <li>iii. women diagnosed with IIH without PCOS</li> <li>iv. controls (neither PCOS nor IIH)</li> </ol> </li> </ol>
<b>Rationale for HRP Directed Research:</b>	<p>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.</p>
<b>Research Impact/Earth Benefits:</b>	<p>While much research is in progress to understand vision issues in astronauts, a key question remains as to why only some individuals are affected. Our preliminary data suggest that some individuals may have a genetic predisposition for vision issues, related to one-carbon metabolism. Our initial study was intentionally constrained given our concerns about it being the first study involving individual genetic testing at NASA. In light of the crewmember response to that study (&gt;97% participation) and the initial findings from that effort, we now propose to evaluate a wider range of one-carbon metabolism SNPs, to help clarify and verify that one-carbon metabolism is indeed the source of this effect, and to identify possible associations with ethnicity. The results of this study could be profound, and may have significant implications for the direction of NASA vision countermeasure research, for operational decisions regarding treatment of affected astronauts, and for informing the general medical and scientific communities, where research is ongoing to understand the role of one-carbon metabolism genetics in other cerebrovascular issues.</p>
<b>Task Progress:</b>	<p>One Carbon Expansion data analysis is underway. PCOS (polycystic ovary syndrome) Study-- recruitment was halted due to the pandemic, and sample and data analysis are underway.</p>
<b>Bibliography Type:</b>	Description: (Last Updated: 03/19/2022)
<b>Articles in Peer-reviewed Journals</b>	Patel ZS, Brunstetter TJ, Tarver WJ, Whitmire AM, Zwart SR, Smith SM, Huff JL. "Red risks for a journey to the red planet: the highest priority human health risks for a mission to Mars." NPJ Microgravity. 2020 Nov 5;6(1):33. <a href="https://doi.org/10.1038/s41598-020-19999-9">https://</a> ; PMID: 33298950; PMCID: PMC7645687, Nov-2020
<b>Articles in Peer-reviewed Journals</b>	Shelhamer M, Bloomberg J, LeBlanc A, Prisk GK, Sibonga J, Smith SM, Zwart SR, Norsk P. "Selected discoveries from human research in space that are relevant to human health on Earth." npj Microgravity. 2020 Feb 12;6(1):5. <a href="https://doi.org/10.1038/s41598-020-19999-9">https://</a> ; PMID: 32128361; PMCID: PMC7016134, Feb-2020
<b>Articles in Peer-reviewed Journals</b>	McGregor HR, Lee JK, Mulder ER, De Dios YE, Beltran NE, Kofman IS, Bloomberg JJ, Mulavara AP, Smith SM, Zwart SR, Seidler RD. "Ophthalmic changes in a spaceflight analog are associated with brain functional reorganization." Hum Brain Mapp. 2021 Sep;42(13):4281-97. <a href="https://doi.org/10.1002/hbm2.5111">https://</a> ; PMID: 34105833; PMCID: PMC8357001, Sep-2021
<b>Articles in Peer-reviewed Journals</b>	Smith SM, Zwart SR. "Nutrition as fuel for human spaceflight." Physiology (Bethesda). 2021 Sep 1;36(5):324-30. Review. <a href="https://doi.org/10.1152/physiol.00000.2021">https://</a> ; PMID: 34431417, Sep-2021

**NASA Technical Documents**

Smith SM, Zwart SR, Douglas GL, Heer M. "Human adaptation to spaceflight: The role of food and nutrition. Second edition." Houston, TX: NASA Lyndon B. Johnson Space Center, 2021. 255 p. NP-2021-03-003-JSC. <https://>, Apr-2021