Fiscal Year:	FY 2020	**Task Last Updated:**	FY 09/22/2021
PI Name:	Bodmer, Rolf Ph.D.		
Project Title:	The Effects of Microgravity on Cardiac Function, Structure and Gene Expression using the Drosophila Model		
Division Name:	Space Biology		
Program/Discipline:	SPACE BIOLOGY		
Program/Discipline--Element/Subdiscipline:	SPACE BIOLOGY--Cellular and molecular biology		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	(1) Animal Biology: Invertebrate		
Space Biology Cross-Element Discipline:	(1) Reproductive Biology (2) Developmental Biology (3) Musculoskeletal Biology		
Space Biology Special Category:	(1) Translational (Countermeasure) Potential		
PI Email:	rolf@sbpdiscovery.org	**Fax:**	FY
PI Organization Type:	NON-PROFIT	**Phone:**	858-795-5295
Organization Name:	Sanford-Burnham Medical Research Institute		
PI Address 1:	Development & Aging		
PI Address 2:	10901 N Torrey Pines Rd		
PI Web Page:			
City:	La Jolla	**State:**	CA
Zip Code:	92037-1005	**Congressional District:**	49
Comments:			
Project Type:	Flight	**Solicitation / Funding Source:**	2012 Space Biology NNH12ZTT001N
Start Date:	09/01/2013	**End Date:**	09/30/2020
No. of Post Docs:	5	**No. of PhD Degrees:**	2
No. of PhD Candidates:	2	**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA ARC
Contact Monitor:	Griko, Yuri	**Contact Phone:**	650-604-0519
Contact Email:	Yuri.V.Griko@nasa.gov		
Flight Program:	ISS		
Flight Assignment:	ISS NOTE: Extended to 9/30/2020 per NSSC information (Ed., 9/25/19) NOTE: Extended to 9/30/2019 per F. Hernandez/ARC; previously had been extended to 9/30/2018 (Ed. 9/21/18) NOTE: Extended to 9/30/2018 per F. Hernandez/ARC (Ed., 4/13/18) NOTE: Extended to 6/30/2018 per NSSC information (Ed., 10/10/17) NOTE: Extended to 9/30/2017 per NSSC information (Ed., 7/18/16) NOTE: Extended to 12/31/2015 per NSSC information (Ed., 2/18/16) NOTE: Extended to 10/31/2015 per NSSC information (Ed., 9/15/15)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Bhattacharya, Sharmila Ph.D. (NASA Ames Research Center) Ocorr, Karen Ph.D. (Burnham Institute for Medical Research)		
Grant/Contract No.:	NNX13AN38G		

Performance Goal No.:	
Performance Goal Text:	
Task Description:	The detrimental effects of spaceflight on the cardiovascular system are well known. It is believed that these effects may lead to clinically significant risks to astronauts on long duration space missions as well as to the success of these missions themselves. Current studies are limited primarily to human studies and rodent experiments. However, these model systems and human studies have significant limitations that may be addressed by using the well-established Drosophila model. Drosophila have previously been successfully launched into space and a ground-based Drosophila model for cardiac disease and function has been developed. However, the genetically versatile Drosophila model has yet to be used for studying the effects of spaceflight on the cardiovascular system. We flew 4 genotypes of Drosophila aboard the International Space Station (ISS) for approximately 30 days, along with identical 1-g ground controls. The Drosophila required minimal astronaut intervention, primarily transfer to an incubator and stowage within the ISS. The samples will be retrieved post-flight and analyzed using established methods. Heart function, including measurements of diastolic and systolic intervals, heart rate, heart diameters, contractility, and arrhythmias was recorded. Microscopic and immuno-histochemical evaluations of heart morphology was carried out. Messenger RNA (mRNA) expression by RNA Sequencing (RNA Seq) was conducted on both heart and brain tissue. The ultimate goal of this research was to obtain data on heart muscle function in low gravity while validating the Drosophila model for studying the effects of spaceflight on cardiac disease and function. Our studies identified disruption in metabolic gene expression and a dramatic increase in proteasome gene expression. This was confirmed in a subsequent flight with immuno-histochemical analyses. The increased proteasome numbers correlated with an increase in amyloid-like protein aggregations within the heart tissue and with increased myofibrillar disarray. We also documented a decrease in collagen fibers associated with the sarcomere Z-lines within myocardial cells.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Information about cardiac muscle function in microgravity is expected to provide insights on genetic and molecular changes that occur with muscle atrophy on Earth. For example, we identified an increase in misfolded muscle protein associated with aggregated proteasomes in the heart muscle cells. Similar alterations in protein processing may underlie the muscle atrophy that occurs during prolonged bed rest or muscle disuse in muscular dystrophies.
Task Progress:	Understanding the effects of microgravity on human organs is crucial to exploration of low-Earth orbit, the Moon, and beyond. Drosophila can be sent to space in large numbers to examine the effects of microgravity on heart structure and function, which is fundamentally conserved from flies to humans. Flies reared in microgravity exhibit reduced climbing ability, cardiac constriction with myofibrillar remodeling, and diminished cardiac output. Analysis of gene expression in isolated hearts revealed reduced expression of sarcomeric / extracellular matrix (ECM) genes and increased expression of genes encoding proteasome subunits (cellular garbage disposals). We further examined the role of proteasomes and protein misfolding on a second flight. We sent flies expressing fluorescently labeled proteins that we could monitor when returned to Earth for misfolding (as protein plaques). We were also able to use staining techniques to monitor proteasome numbers. We observed dramatic increases in protein plaque number and size in flies exposed to micro g and these were co-localized with large proteasome aggregates. Remarkably, in long-QT causing seizure (sei) / human ether-a-go-go (hERG) mutants, proteasomal gene expression was already lower than wildtype at 1g , but under micro g we still observed an increase compared to the 1g ground controls. Therefore, cardiac remodeling and proteostatic stress may be a fundamental response of heart muscle to microgravity. Our experiments validated the use of Vented Fly Boxes (VFBs) for fly experiments that require minimal space and astronaut input yet provide significant insights into organismal function under low gravity. One unexpected outcome from our second flight was excessive fungal contamination of samples stored in the Space Automated Bioproduct Lab (SABL) incubator. This information should assist future experiments that use this equipment to ensure that the experiments are not compromised by external contaminants. Nevertheless, the inclusion of fly boxes that were maintained as backup for the original flight permitted us to complete our analyses. The complete gene expression dataset is available on NASA's GeneLab database. Although not part of our original proposal we also developed an assay to measure both gene and protein expression from the same tissue source (brain) from the flies. Our analyses suggest that there are fundamental changes in proteins in metabolic pathways, circadian rhythm signaling, and the visual system that occur in micro g. This dataset is also available on GeneLab.
Bibliography Type:	Description: (Last Updated: 06/23/2023)
Articles in Peer-reviewed Journals	Walls S, Diop S, Birse R, Elmen L, Gan Z, Kalvakuri S, Pineda S, Reddy C, Taylor E, Trinh B, Vogler G, Zarndt R, McCulloch A, Lee P, Bhattacharya S, Bodmer R, Ocorr K. "Prolonged exposure to microgravity reduces cardiac contractility and initiates remodeling in Drosophila." Cell Rep. 2020 Dec 8;33(10):108445. ePub 2020. https://doi.org/10.1016/j.celrep.2020.108445 ; PubMed PMID: 33242407; PubMed Central PMCID: PMC7787258 , Dec-2020
Articles in Peer-reviewed Journals	Gilbert R, Torres ML, Clemens R, Hateley S, Hosamani R, Wade W, Bhattacharya S. "Spaceflight and simulated microgravity conditions increase virulence of Serratia marcescens in the Drosophila melanogaster infection model." npj Microgravity. 2020 Feb 4;6(1):4. https://doi.org/10.1038/s41526-019-0091-2 ; PubMed PMID: 32047838; PubMed Central PMCID: PMC7000411 , Feb-2020
Articles in Peer-reviewed Journals	Tahimic CGT, Paul AM, Schreurs AS, Torres SM, Rubinstein L, Steczina S, Lowe M, Bhattacharya S, Alwood JS, Ronca AE, Globus RK. "Influence of social isolation during prolonged simulated weightlessness by hindlimb unloading." Front Physiol. 2019 Sep 13;10:1147. https://doi.org/10.3389/fphys.2019.01147 ; PubMed PMID: 31572207; PubMed Central PMCID: PMC6753329 , Sep-2019
Articles in Peer-reviewed Journals	Iyer J, Mhatre SD, Gilbert R, Bhattacharya S. "Multi-system responses to altered gravity and spaceflight: Insights from Drosophila melanogaster." Neurosci Biobehav Rev. 2022 Nov;142:104880. https://doi.org/10.1016/j.neubiorev.2022.104880 ; PMID: 36126744 , Nov-2022

NASA Technical Documents	Ocorr K, Bodmer R, Battacharya S, Diop SB, James B, Rosa Campos A. "Correlated gene and protein expression in heads from Drosophila reared in microgravity." NASA GeneLab Data Systems/GLDS-207. , Nov-2018
NASA Technical Documents	Ocorr K, Diop S, Gan Z, Bodmer R. "HEART FLIES - effect of microgravity on heart function in Drosophila." NASA GeneLab Data Systems/GLDS-347. , Dec-2020