Fiscal Year:	FY 2018	**Task Last Updated:**	FY 05/24/2018
PI Name:	Hammer, Bruce Ph.D.		
Project Title:	Study of Mammalian Pluripotent Stem Cells in Microgravity		
Division Name:	Space Biology		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	(1) Cell & Molecular Biology		
Space Biology Cross-Element Discipline:	(1) Developmental Biology		
Space Biology Special Category:	(1) Cell Culture		
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Zip Code:	55455-3007	**Congressional District:**	5
Comments:			
Project Type:	FLIGHT	**Solicitation / Funding Source:**	2014 Space Biology Flight NNH14ZTT001N
Start Date:	11/01/2014	**End Date:**	11/01/2018
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:**	NASA ARC
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Flight Program:	ISS		
Flight Assignment:	NOTE: Extended to 11/1/2018 per F. Hernandez/ARC (Ed., 10/21/16)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Dutton, James Ph.D. (University of Minnesota) Kidder, Louis Ph.D. (University of Minnesota)		
Grant/Contract No.:	NNX15AB38G		
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Task Description:	We propose to investigate the effect of gravity on fundamental properties of mammalian stem cells during differentiation of 3-D cultures of induced pluripotent stem (iPS) cells. Experiments aboard the ISS (International Space Station), STS (Shuttle), and ground-based simulations have demonstrated that microgravity influences gene expression, cell proliferation, and differentiation in stem cells. However, the mechanism behind these observations is not clearly understood. In this study we will investigate how exposure to microgravity fundamentally alters the regulation of Oct4, a transcription factor necessary to maintain pluripotency, and how these changes can affect the timing, progression, and outcomes of cell differentiation. Our laboratory has created an Oct4:CreER mTmG transgenic mouse that, for the first time, allows lineage tracing of Oct4 expression in stem cells and their progeny. We will use iPS cells derived from this model to determine the influence of microgravity on the loss of pluripotency and differentiation. During the Flight Definition Phase we will use magnetic levitation, a unique ground-based simulation of orbital free fall, to optimize execution of the Spaceflight Experiment Phase. This approach will maximize the success of space-based studies. We propose to investigate the effect of gravity on the timing and spatial arrangement of the loss of Oct4 expression in differentiating iPS cell aggregates. We will also examine the effect of gravity on gene expression in cohorts of Oct4 expressing and non-expressing cells during differentiation by comparing the results of ground-based experiments to those conducted on orbit. Finally, we will explore mechanisms behind the effect of microgravity on both Oct4 gene regulation and control of downstream gene expression by Oct4. This work will determine the effect of spaceflight on changes in Oct4 gene expression during differentiation of pluripotent stem cells and the consequences of these changes on differentiation outcomes. This will increase our understanding of fundamental stem cell behavior in microgravity.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Gravity likely influences organismal development but little is currently understood about its specific influence on stem cell differentiation. We propose to utilize a novel system to investigate how microgravity fundamentally changes the timing and spatial arrangement of the loss of Oct4 gene expression during the differentiation of stem cells. We expect this to have consequences on differentiation outcomes. Our results from this study will ultimately have a direct impact on improving the translation of human stem cell based treatments. Cell manufacturing in microgravity may speed-up the rate of iPSC (induced Pluripotency Stem Cell) differentiation, thereby reducing the time and cost to obtain a therapeutic dose of cells. If this can be done on-orbit and replicated on Earth with magnetic levitation, this will have significant commercialization possibilities.
Task Progress:	Due to delays in obtaining crew time aboard the ISS we have postponed full start of project to conserve resources. The flight definition plan was approved in year 1 and placed on temporary hold from January 2016 until January 2018 when ISS crew time was approved for the project. The first phase of the project focused on generating embryoid bodies (EBs) which are 200 micron spherical aggregates of iPSCs (induced Pluripotent Stem Cells) and developing freezing protocols so that EBs can be transported and stored at -95 C aboard the ISS until crew time is allocated to the project. We determined that EBs did not cryopreserve well and investigated the possibility of previously frozen stem cells self-assembling into EBs aboard the ISS. This procedure has been done successfully in a conventional incubator (1g) and when exposed to simulated microgravity via magnetic levitation in our laboratory. These self-aggregated EBs exhibit the same fluorescence patterns when tamoxifen treated as those grown on 96 well plates. A significant benefit of transporting frozen stem cells to the ISS for self-assembly avoids g-force and vibration of launch as well as ground and berthing delays which can damage fragile stem cells.
Bibliography Type:	Description: (Last Updated:)