Fiscal Year:	FY 2025	**Task Last Updated:**	FY 02/03/2025
PI Name:	Christenson, Lane Ph.D.		
Project Title:	Female Reproductive Health: Space Flight Induced Ovarian and Estrogen Signaling Dysfunction, Adaptation, and Recovery--80NSSC24M0072 ; NNX15AB48G		
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 (2) Animal Biology: Vertebrate		
Space Biology Cross-Element Discipline:	(1) Reproductive Biology (2) Developmental Biology		
Space Biology Special Category:	(1) Translational (Countermeasure) Potential		
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Zip Code:	66160-0001	**Congressional District:**	3
Comments:			
Project Type:	Flight	**Solicitation / Funding Source:**	2014 Space Biology Flight NNH14ZTT001N
Start Date:	01/25/2018	**End Date:**	01/31/2026
No. of Post Docs:	1	**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:**	2
No. of Bachelor's Candidates:	2	**Monitoring Center:**	NASA ARC
Contact Monitor:	Klotz, Rebecca	**Contact Phone:**	650-604-1119
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Flight Program:	ISS		
Flight Assignment:	NOTE: End date changed to 1/31/2026 per F. Hernandez/NASA-ARC (Ed., 2/12/25). NOTE: New grant number (80NSSC24M0072) per NSSC information (Ed., 2/3/25). NOTE: End date changed to 1/31/2024 per NSSC information (Ed., 11/6/2023) NOTE: End date changed to 1/31/2023 per NSSC information (Ed., 1/24/2022) NOTE: End date changed to 1/31/2022 per NSSC information (Ed., 1/22/2021) NOTE: End date changed to 1/31/2021 per F. Hernandez/ARC (Ed., 2/3/2020) NOTE: End date changed to 1/31/2020 per NSSC information (Ed., 3/12/19)		
Key Personnel Changes/Previous PI:	We have added Dr. Stephanie Puukila from the NASA Ames Research Center as a CoI in June of 2023. Dr. Puukila was added due to expertise in behavioral analyses and due to our addition of a study looking at the behavior of the offspring born to the Flight (FLT) females. This work is a natural extension of Aim 3 Specific Aim, where we are evaluating fertility of the FLT mice, to now include whether those mice born to FLT mice are normal with respect to behavior.		

COI Name (Institution):	Ronca, April Ph.D. (NASA Ames Research Center) Alwood, Josh Ph.D. (NASA Ames Research Center) Puukila, Stephanie A (NASA Ames Research Center)
Grant/Contract No.:	80NSSC24M0072 ; NNX15AB48G
Performance Goal No.:	
Performance Goal Text:	
Task Description:	Continuation of "Female Reproductive Health: Space Flight Induced Ovarian and Estrogen Signaling Dysfunction, Adaptation, and Recovery" with the grant number NNX15AB48G and Principal Investigator (PI) Lane K. Christenson, Ph.D. (Previous PI was Joseph Tash, Ph.D.). In view of NASA's plans to conduct multigenerational studies on rodents in long-term spaceflight, these observations raise important fundamental questions on maintenance of female reproductive health that need to be addressed prior to conducting complex multigenerational studies in mammals under spaceflight conditions. As a result of our previous findings, specific important knowledge gaps now exist regarding the impact of spaceflight on female reproductive health. The central hypothesis that we will test is that spaceflight elicits direct and/or indirect effects at the ovarian level to cause infertility in adult female mice. This grant application combines the expertise of Dr. Christenson in ovarian physiology, and Dr. Ronca in pregnancy and early development, to address this central hypothesis. Additionally, these studies will address an important secondary hypothesis that the loss in uterine estrogen receptor expression will also occur in bone and this may exacerbate the observed bone mass loss during spaceflight (Dr. Alwood as collaborator). To address these hypotheses the following specific aims are proposed: Aim 1. Determine whether short-term (~10 d) spaceflight-disrupted ovarian function is due to a direct effect at the ovarian level. The working hypothesis, based on our preliminary data, is that disrupted ovarian function is due to a failure of the periovulatory follicle to ovulate and form a functional corpus luteum. To test this hypothesis, mice will undergo a timed follicular stimulation protocol followed by evaluation of established temporally expressed ovarian markers, ovulation, and luteal development. This study will for the first time determine if space induced loss of ovarian function is due to an intrinsic ovarian defect or is a problem with hypothalamic/pituitary support. Aim 2. Determine if adult female mice recover ovarian function during extended (~60 d) flight time. Currently, it is unknown whether females will recover fertility following long-term (i.e., ~60 d) acclimation to spaceflight, or will they remain infertile or exhibit more pronounced defects in ovarian/uterine function. To address this question, mice will undergo a similar follicular stimulation and ovulatory protocol in flight but after ~60 d, as described in Aim 1, and fertility and tissue biomarkers will be evaluated. Aim 3. Determine if adult female mice exposed to spaceflight are fertile upon return to Earth. The working hypothesis for this aim is that upon return to Earth, fertility will return. To test this hypothesis, flight mice will be exposed to male mice during a recovery period upon return to Earth, and regain of mating reproductive behavior, estrous cyclicity, early embryo implantation, and health and development of F1 offspring will be evaluated. These studies will provide the first ever examination of long-term space exposure on the female reproductive behavior/physiology, and germ-line stability. In all 3 specific aims, collection of uterine and bone (femur) tissues will allow us to address our secondary hypothesis by determining long-term spaceflight effects on estrogen receptor expression. Ultimately, findings of the proposed studies will provide critical foundational data to support multigenerational mammalian studies in space, and importantly, aid in our understanding of the impact spaceflight has on female astronaut health.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Fertility is a general measure of fitness of a species on Earth. Disruptions to fertility have both short- and long-term effects on the health on the individual or the ability of a species to maintain critical numbers, respectively. Earth species have adapted to changes in environment over millennia; these adaptations allow species to survive and flourish on Earth. The reproductive systems of both female and male mammals are well tuned to sense environmental changes. These environmental responses can then either increase or decrease fertility appropriately. The effects of weightlessness on female ovarian function we currently are studying are critical as we consider longer-term flights and the overall health of these individuals upon return to Earth. The fact that ovarian estrogen plays a key metabolic role in almost all tissues of the body also highlights the importance of understanding how female fertility is influenced by exposure to space. The Earth benefits of this research may yield new, yet undiscovered mechanisms controlling ovarian function, steroidogenesis, and female fertility. Our research has led us to adapt an approach to monitor estrous cyclicity in rodents; we believe this methodology has the potential to impact all female based NASA flight research projects due to our ability to accurately determine the stage of the estrous cycle and thus predict ovarian estrogen levels.
Task Progress:	Rodent Research-20 launched on November 9, 2023 and half of the females returned from the International Space Station (ISS) on December 23, 2023. Following return, female mice were bred to male mice and all females had litters following return, indicating that spaceflight did not render the females sterile; litter size was, however, slightly reduced, indicating some reduction in fertility. Following 55 to 60 days of spaceflight, ovarian function of the other half females that remained on the ISS was evaluated and no differences in ovulation rate was observed when compared to ground control females. Experiments examining the offspring of return flight females were initiated in June of 2024, with behavioral studies being completed in July of 2024; metabolic studies completed on December 12, 2024; and reproductive studies on January 17, 2025. Evidence of changes in behavioral and metabolic differences were noted in both male and female offspring. Ongoing studies are elucidating the molecular, biochemical, genetic, and epigenetic causes that might explain these differences.
Bibliography Type:	Description: (Last Updated: 02/24/2025)

Abstracts for Journals and Proceedings	Siceloff SI, Chauhan S, Hong X, Morris EM, Christenson LK. "Impact of long-term microgravity on offspring of female Mice following 42 days on the International Space Station." 40th Annual Meeting of the American Society for Gravitational and Space Research, San Juan, Puerto Rico, December 3-7, 2024. Abstracts. 40th Annual Meeting of the American Society for Gravitational and Space Research, San Juan, Puerto Rico, December 3-7, 2024. , Dec-2024
Abstracts for Journals and Proceedings	Christenson LK, Nies P, Stoltz A, Puukila S, Ronca AE, Alwood JS, Choi S, Teate A. "Impact of spaceflight and exposure to the International Space Station environment on the female reproductive system and fertility in mice." 40th Annual Meeting of the American Society for Gravitational and Space Research, San Juan, Puerto Rico, December 3-7, 2024. Abstracts. 40th Annual Meeting of the American Society for Gravitational and Space Research, San Juan, Puerto Rico, December 3-7, 2024. , Dec-2024
Abstracts for Journals and Proceedings	Puukila S, Frazier A, Hong X, Ronca AE, Alwood JS, Christenson LK. "Behavioral changes in adult mouse F1 offspring born to dams that experienced spaceflight." 40th Annual Meeting of the American Society for Gravitational and Space Research, San Juan, Puerto Rico, December 3-7, 2024. Abstracts. 40th Annual Meeting of the American Society for Gravitational and Space Research, San Juan, Puerto Rico, December 3-7, 2024. , Dec-2024
Abstracts for Journals and Proceedings	Higgins LA, Juran CM, Almeida EAC, Christenson LK, Chakravarthi P. "Impact of microgravity on ovarian follicle counts in mice." 40th Annual Meeting of the American Society for Gravitational and Space Research, San Juan, Puerto Rico, December 3-7, 2024. Abstracts. 40th Annual Meeting of the American Society for Gravitational and Space Research, San Juan, Puerto Rico, December 3-7, 2024. , Dec-2024
Abstracts for Journals and Proceedings	Chauhan S, Hong X, Morris EM, McCoin C, Christenson LK. "Offspring of Rodent Research-20 International Space Station female mice exhibit impacted metabolic measures." 21st Annual Gilbert S. Greenwald Symposium on Reproductive and Developmental Sciences, Kansas City, Kansas, November 7-8, 2024. Poster. Abstracts. 21st Annual Gilbert S. Greenwald Symposium on Reproductive and Developmental Sciences, Kansas City, Kansas, November 7-8, 2024. , Nov-2024
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Books/Book Chapters	Puukila S, Alwood JS, Christenson LK, Ronca AE, Steller JG. "Women's health in spaceflight." in "Precision Medicine for Long and Safe Permanence of Humans in Space." Ed. C. Krittanawong. Academic Press; 2025. p. 137-50. https://doi.org/10.1016/B978-0-443-22259-7.00038-2 , Jan-2025