Fiscal Year:	FY 2021	**Task Last Updated:**	FY 07/22/2021
PI Name:	Kaplan, David L. Ph.D.		
Project Title:	Silk Composite Biomaterials for Shielding Medications in Space		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	TRISH--TRISH		
Joint Agency Name:		**TechPort:**	Yes
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2018 TRA BRASH1801: Translational Research Institute for Space Health (TRISH) Biomedical Research Advances for Space Health
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No. of Post Docs:	2	**No. of PhD Degrees:**	0
No. of PhD Candidates:	1	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
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Contact Monitor:		**Contact Phone:**	
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Key Personnel Changes/Previous PI:			
COI Name (Institution):	Kluge, Jonathan Ph.D. (Vaxess Technologies)		
Grant/Contract No.:	NNX16AO69A-T0411		
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Task Description:	The goal is to utilize silk protein, an US Food and Drug Administration (FDA) approved protein biomaterial, in composite material formats, to shield and protect a range of medications -- addressing topic #5 in Biomedical Research Advances for Space Health (BRASH) 1801 - New materials for shielding medications. We will utilize novel formulations of the silk protein in composite formats with inorganic particles, as both pouch and as part of the material, to demonstrate broad protection of a range of drugs during exposure to environmental extremes using accelerated testing, mechanistic insights and modeling, and functional assessments. The outcome will be new composite material systems that provide broad-ranged protection, a preliminary model for predictive outcomes, and publications.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Silk and the additives have potential to provide protection for medications against environmental stresses, such as elevated temperature and radiation. Such protection would ensure that medications retain bioactivity and are safe to use by the space crew during long duration mission missions. Silk also provides a versatile material that can be morphed into useful applications (e.g., other material formats) for space missions, while also serving as a backup protein source if needed.
Task Progress:	The medications needed to keep a crew healthy during a deep space exploration missions must remain effective while enduring more than a year in deep space, which includes exposure to space radiation. Medications must be stored in containers that are resilient to such conditions, which is the goal of our project. The objective is to utilize silk protein composite materials to protect these compounds. Silk protein is a biomaterial that has previously been approved by the US Food and Drug Administration for various medical products. In the study for NASA, formulations including silk proteins will be used with inorganic particles and additives to shield a variety of drugs from exposure to environmental extremes. The protective ability of the materials and mechanisms underlying this protection will be explored and optimized through a combination of experimental testing and molecular modeling. The specific objectives are: 1. Preparation and Characterization of Protective Silk-Based Composite Materials 2. Assessment of Stability of Medications in the Protective Materials 3. Mechanisms of Stabilization Experimental Approaches - Year 2 We focused the Year 2 on silk films loaded with drugs. For the study, two drugs were selected: Ampicillin (known to be stable to radiation), and Clavulanate (known to be unstable to radiation). Silk films were irradiated under different conditions: X-rays (0.1 and 1 kGy), Protons (1.0 and 200 kGy), Solar Particles Event (SPE) simulation (SPE, 1.0 Gy), and Galactic Cosmic Radiation (GCR, 0.5 Gy). X-ray and proton radiation exposures were conducted at Columbia University (NY) with the help of Dr. Guy Garty and Dr. David Brenner, SPE and GCR were run at the NASA national radiation lab (Brookhaven, NY) with the help of Dr. Afshin Beheshti. High Pressure Liquid Chromatography (HPLC) is being used to quantify the recovery and to analyze the stability of the medications being studied, while Fourier Transform Infrared Spectroscopy (FTIR) is used to evaluate changes in the silk structure. Films were modified with the addition of inorganic or organic compounds to further enhance their protective properties, such as to increase mechanical toughness and free radical scavenging capabilities. The radiation had a minimal effect on silk structures at the exposures utilized in the experiments, demonstrating suitable stability of this protein matrix. With the addition of SiO2, the dissolution of silk to enable the recovery of the sequestered drugs, and the recovery of the drugs, were minimal, demonstrating the need to further study the interactions of the drugs with SiO2. Finally, it was also observed that the most significant environmental impact on drug recovery and silk dissolution was the humidity. The crystallinity of the silk increased at the higher humidity, due to chain dynamics and thus beta sheet formation (by FTIR), preventing the dissolution of the films in aqueous systems, hence the poor recovery of drug. Under low humidity, 100% of the ampicillin was recovered when embedded in silk films, and increased recovery of clavulanate was also obtained compared to the free powder (control) with GCR exposure. These results demonstrate the efficiency of silk as a stabilizing matrix to some space-related radiation. Modeling Approaches - Year 2 Atomistic modeling of the effect of silk proteins on the reactivity of several commonly-used drug molecules was performed using the combination of molecular dynamics (MD) and density-functional theory (DFT) calculations. More specifically, equilibrated configurations of selected drug molecules (ibuprofen, ampicillin, and clavulanate) binding to silk proteins were identified from MD results and then fed as input to the conceptual DFT calculations of their reactivity descriptors. The comparison between the reactivity descriptors of (i) free-standing drug molecules and (ii) drug molecules bound to the residues in silk proteins can help us understand how the presence of silk materials affects the reactivity of drugs, as well as their susceptibility to space radiation. Next Steps - Future work would include the study of the interaction between SiO2 and the drug to elucidate the mechanisms involved. Additional beam time (GCR and SPE) would be helpful to obtain better insight into the effect of radiation on drugs and silk. All the samples would be prepared under controlled humidity to evaluate the range of stability or crystallization outcomes. Finally, we would like to study edible patches such as their dissolution in the gastrointestinal track for future uses, where even with the humidity-induced crystallization and thus poor drug recovery from the silk matrix, the systems would still be useful as edible reservoirs for the drugs. The design of alternative silk sequences that interact (and protect) specially with the reactive areas of the sensitive regions of the structures of the drugs would be another direction to pursue. In work that we could not finish, we planned to perform a parameter study based on the existing modeling approach to find the density of silk fibroin and the threshold spacing between silk and drugs to make the drugs less reactive in the presence of silk materials. We will also implement the atomistic model to investigate the interaction between drugs and inorganic particles such as SiO2.

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