Fiscal Year:	FY 2022	**Task Last Updated:**	FY 01/19/2023
PI Name:	Langer, Robert Sc.D.		
Project Title:	Just in Time Medications from Gastrointestinal Resident Microbial Systems		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	TRISH--TRISH		
Joint Agency Name:		**TechPort:**	No
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:**	2020 TRISH BRASH1901: Translational Research Institute for Space Health (TRISH) Biomedical Research Advances for Space Health
Start Date:	04/01/2020	**End Date:**	03/31/2022
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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:	2	**Monitoring Center:**	TRISH
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Traverso, Carlo Ph.D. (Brigham and Women's Hospital)		
Grant/Contract No.:	NNX16AO69A-T0504		
Performance Goal No.:			
Performance Goal Text:			
Task Description:	Genetically engineered microbes (synthetic microbes) represent a promising approach for the space- and resource-efficient production of active pharmaceutical compounds during long-duration space flight. Microbes are already widely used industrially for the fermentation-based production of many high-value compounds from simple feed stocks. Furthermore, it has been proposed that during long-duration space flight microbes could be stored as small starter stocks and cultured to make fuels, food, and pharmaceuticals. Here we propose to develop an ingestible device that can be used for the modular production of medicines on demand via the use of integrated synthetic microbes.		

Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	During the entire project period we have developed several key technologies with significant impact beyond this project: Impact 1: Porous membranes for controlled release of bacteria. We developed a technology to tune the release rate of bacteria. This technology may have application generally for the controlled release of bacteria in therapeutics or other applications were controlled release may be required (e.g. plant probiotics). While there has been extensive work in developing technologies for controlling the release profiles of small molecules from different types of matrices, the technology described here fills a growing need to control the release of bacteria that are intended as therapeutics. Impact 2: Matrices for dosing and manipulating dry bacteria. Bacteria are traditionally handled as liquid suspensions, slurries or frozen pastes. All these modalities require a dedicated environment (e.g. wet bench laboratory) and expert personnel to handle. In contrast to these, commercially available bacterial pills (i.e. probiotics) present a tantalizing alternative. However, our previously funded Translational Research Institute for Space Health (TRISH) work demonstrated that a many of these commercial products do not have the viabilities promised and some have extremely poor recovery of viable bacteria. The technology developed during this project builds on our previously developed bacterial formulations, expanding them to incorporation of bacteria directly into easily handled matrices. Furthermore, we showed that the bacteria not only can be recovered with high viability but also that maximal enzymatic/metabolic activity is recovered in less than 1 hr. Such a simple medium for manipulating, aliquoting and dosing bacteria may have impacts beyond this project including streamlined manufacturing workflows of components that may use the incorporated bacteria for treating, sensing or controlling down stream components. Impact 3: Transfer of biosynthetic pathways to probiotic bacteria. In the proposed project we selected target molecules that are currently part of the NASA med kit and which have biosynthetic pathways previously established to differing degrees in bacteria. This strategic choice enhanced the likelihood of success achieving a traditionally challenging goal (i.e., biosynthesis of any molecule) in the abbreviated duration of the project. During this reporting period, we have established these biosynthetic pathways in a probiotic strain with a proven track record for use in humans. These strains may have impacts beyond this project by demonstrating and defining the challenges of biosynthesizing Food and Drug Administration (FDA) approved molecules in probiotic strains which are being actively used by commercial entities seeking FDA approval for microbial therapeutics. Impact 4: Ingestible micro-fermenter capsules. During this project we developed a prototype micro-fermenter capsule and validated its function and safety in a large animal model. This device may have applications generally for the rapid production of therapies on demand in low resource environments on earth. These devices may be of used to rapidly produce microbial medicines at the point of care without the need for traditional microbial culturing equipment or training.
Task Progress:	Genetically engineered microbes (synthetic microbes) represent a promising approach for the space- and resource-efficient production of active pharmaceutical compounds during long-duration spaceflight. Microbes are already widely used industrially for the fermentation-based production of many high-value compounds from simple feed stocks. Furthermore, it has been proposed that during long-duration spaceflight microbes could be stored as small starter stocks and cultured to make fuels, food, and pharmaceuticals. Here, we propose to develop an ingestible device that can be used for the modular production of medicines on demand via the use of integrated synthetic microbes. Specifically, our project aims to provide a countermeasure for a limited pharmacy during exploration space travel by using synthetic microbes to generate medicines just at the time of need, freeing related resources to increase the total variety and potential output of a microbe-based pharmacy. We developed a proof-of-concept microbial pharmacy as a countermeasure to current limits and lack of flexibility of a traditional pharmacy during exploration missions (i.e., limited doses and stability of medicines). Our microbial pharmacy is made of dry stabilized microbial paper that can be stored in the shape of a book with one medicine per page, and companion ingestible capsules fermenters that allow just-in-time production of a target medicine inside the body from a miniature portion of the microbial paper. None of the components need power nor refrigeration to function. By separating the instructions for making a medicine (i.e., engineered microbial therapeutics) from the generic raw feedstocks (i.e., body heat, nutrients) a microbial pharmacy would allow many more doses of just the right medicine to be made only at the time of need.
Bibliography Type:	Description: (Last Updated: 05/19/2020)