

Fiscal Year:	FY 2021	Task Last Updated:	FY 07/13/2022
PI Name:	Jimenez, Miguel Ph.D.		
Project Title:	In Situ Expression Analysis of Therapeutic Microbes with Gastrointestinal Devices		
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:	2019 TRISH RFA-1901-PD Translational Research Institute for Space Health (TRISH) Postdoctoral Fellowships
Start Date:	08/01/2019	End Date:	04/30/2021
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:	0
No. of Bachelor's Candidates:	1	Monitoring Center:	TRISH
Contact Monitor:	Contact Phone:		
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date changed to 04/30/2021 per E. Urquieta/TRISH (Ed., 6/2/21)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):			
Grant/Contract No.:	NNX16AO69A-P0401		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	<p>POSTDOCTORAL FELLOWSHIP</p> <p>Genetically engineered therapeutic microbes (synthetic microbes) represent a promising approach to modulating the gut microbiome and enhancing human health. In particular, this new therapeutic modality has the potential to mitigate several risks defined by the Human Research Program, such as restricted pharmacy resources, altered astronaut immune response, inadequate nutrition, host-microorganism interactions, and adverse cognitive disorders. Ingested synthetic microbes provide the opportunity to carry out therapeutic and prophylactic functions on-demand, directly in the gut while minimizing personnel, equipment, and space requirements beyond those for food supply. However, there are two major challenges to implementing synthetic microbes in humans: stable, long-term delivery or administration, and effective genetic parts that function in the gut.</p> <p>This proposal focuses on overcoming the latter challenge. In this proposed work, we hypothesize that gastrointestinal (GI) polymeric devices can be used to uncover GI location-specific genetic promoters. If successful, this work will generate a reference toolbox of genetic parts that can be used by the field to develop effective interventions based on genetically engineered microbes. The specific aims of this proposal are (1) to develop a device that can stably localize microbes in the GI tract and (2) to deploy this device in swine to profile the set of microbial genes that are expressed and repressed in each GI location.</p>
Rationale for HRP Directed Research:	<p>During this reporting period we have developed a key technology with significant impact beyond this project. Impact: A bacterial intestinal localization device that has been validated for safety and function in a large animal model (swine).</p> <p>For the goals of this project, this device allows the expression profiling of microbes. Beyond this project, for the wider scientific community, this device represents a platform technology to study any microorganism directly in the milieu of the GI tract while retaining the ability to retrieve it directly. This may be an essential tool for dissecting key mechanisms within the GI microbiome as well as culturing key microbiome species in their native environment. Finally, as this device closely mimics jejunal feeding tubes commonly placed in humans, it may also be further developed into a clinical device to monitor (bacterial sensors) or treat (bacterial therapeutics) disease in those patients that already have jejunal extension tubes placed for multi-month periods as part of their normal treatment.</p>
Task Progress:	<p>Genetically engineered therapeutic microbes (synthetic microbes) represent a promising approach to modulating the gut microbiome and enhancing human health. In particular, this new therapeutic modality has the potential to mitigate several risks defined by the Human Research Program, such as restricted pharmacy resources, altered astronaut immune response, inadequate nutrition, host-microorganism interactions, and adverse cognitive disorders. Ingested synthetic microbes provide the opportunity to carry out therapeutic and prophylactic functions on-demand, directly in the gut while minimizing personnel, equipment and space requirements beyond those for food supply. However, there are two major challenges to implementing synthetic microbes in humans: stable, long-term delivery or administration, and effective genetic parts that function in the gut.</p> <p>This proposal focuses on overcoming the latter challenge. In his proposed work, we hypothesize that gastrointestinal (GI) polymeric devices can be used to uncover GI location-specific genetic promoters. If successful, his work will generate a reference toolbox of genetic parts that can be used by the field to develop effective interventions based on genetically engineered microbes. The specific aims of his proposal are to (1) develop a device that can stably localize microbes in the GI tract and (2) to deploy this device in swine to profile the set of microbial genes that are expressed and repressed in each GI location.</p>
Bibliography Type:	Description: (Last Updated: 08/06/2024)
Articles in Peer-reviewed Journals	Inda-Webb ME, Jimenez M, Liu Q, Phan NV, Ahn J, Steiger C, Wentworth A, Riaz A, Zirtiloglu T, Wong K, Ishida K, Fabian N, Jenkins J, Kuosmanen J, Madani W, McNally R, Lai Y, Hayward A, Mimeo M, Nadeau P, Chandrakasan AP, Traverso G, Yazicigil RT, Lu TK. "Sub-1.4 cm3 capsule for detecting labile inflammatory biomarkers in situ." Nature. 2023 Jul 26. https://doi.org/10.1038/s41586-023-06369-x ; PMID: 37495692 , Jul-2023
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Articles in Peer-reviewed Journals	Jimenez M, L'Heureux J, Kolaya E, Liu GW, Martin KB, Ellis H, Dao A, Yang M, Villaverde Z, Khazi-Syed A, Cao Q, Fabian N, Jenkins J, Fitzgerald N, Karavasili C, Muller B, Byrne JD, Traverso G. "Synthetic extremophiles via species-specific formulations improve microbial therapeutics." Nat Mater. 2024 Jul 5. https://doi.org/10.1038/s41563-024-01937-6 ; PMID: 38969782 , Jul-2024
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Papers from Meeting Proceedings	Liu Q, Riaz A, Zirtiloglu T, Inda ME, Jimenez M, Lai Y, Steiger C, Diamond E, Traverso G, Lu T, Chandrakasan A, Nadeau P, Yazicigil RT. "Zero-Crossing-Based Bio-Engineered Sensor." 2021 IEEE Custom Integrated Circuits Conference (CICC) 1–2 (2021), April 25-30, 2021. 2021 IEEE Custom Integrated Circuits Conference (CICC) 1–2 (2021), April 25-30, 2021. https://doi.org/10.1109/CICC51472.2021.9431409 , Apr-2021

