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| **Fiscal Year:** | FY 2020 | **Task Last Updated:** | FY 08/03/2020 |
| **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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| **Zip Code:** | 02142-1019 | **Congressional District:** | 7 |
| **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:** | 1 |
| **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):** | Langer, Robert Sc.D. ( Mentor: Massachusetts Institute of Technology ) | | |
| **Grant/Contract No.:** | NNX16AO69A-P0401 | | |
| **Performance Goal No.:** | | | |
| **Performance Goal Text:** | | | |

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| **Task Description:** | POSTDOCTORAL FELLOWSHIP<br>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.<br><br>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. |
| **Rationale for HRP Directed Research:** | |
| **Research Impact/Earth Benefits:** | During this reporting period we have developed a key technology with significant impact beyond this project.<br>Impact: A bacterial intestinal localization device that has been validated for safety and function in a large animal model (swine).<br><br>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. |
| **Task Progress:** | During this reporting period, we have developed two key technologies with significant impact beyond this project.<br>Impact 1: A manufacturing method for microchambers compatible with the gastrointestinal (GI) tract.<br><br>For this project, this process is essential for the localization of microbes to target GI locations. Beyond this project, this approach enables the development of custom designed ingestible microfluidic devices. Traditionally, microfluidic devices are made from materials that are not compatible with translation to humans (glass polydimethylsiloxane (PDMS)). Our use of polyethylene (PETG) and polycarbonate (PC) membranes opens enables the development of microfluidic devices compatible with translation to humans.<br><br>Impact 2: A testing platform for microbial genetics in large animals.<br><br>During this reporting period, we laid the foundation for an easily implantable and retrievable system for microbes in pigs through the use of PEG-J tubes. For this project, this set up enables the transcriptional profiling proposed for Aim 2. This by itself should lead to a new set of validated genetic parts for developing microbial therapeutics. Beyond this project, this large animal testing platform also allows testing of new microbial therapeutic strain much earlier in the translational development process. Normally, researchers test genetic designs in ideal laboratory conditions (culture flasks). However, our platform enables direct testing in large animals early in the development process. Once complete, this platform is likely to enhance the likelihood that certain genetic designs will work in humans. |
| **Bibliography Type:** | Description: (Last Updated: 08/06/2024) |