MPLA as an innovative immune countermeasure

Active Technology Project (2018 - 2018)

Project Introduction

Spaceflight perturbs the human immune system. Among other manifestations, crewmembers may experience latent herpesviruses reactivation due to impaired lymphocyte function, as well as allergic/hypersensitivity reactions. Considering future space travel will be of longer duration (thereby increasing stress, exposure to radiation, etc…) with no rapid return option, it is of paramount importance to develop a countermeasure(s) to immune dysregulation. Monophosphoryl lipid A (MPLA) is a derivative of lipopolysaccharide (LPS), a potent inflammatory agent that can cause septic shock. MPLA possesses the immune-stimulatory effects of LPS without the adverse inflammatory effects. We hypothesize that treating immune cells with MPLA will boost their function enough to overcome the inhibitory effects of microgravity. While MPLA has been tested as an adjuvant extensively in mice and preliminarily for human vaccines, it has never been assessed for efficacy in microgravity.

Anticipated Benefits

An emerging paradigm in spaceflight immunology is a direct correlation between the amount of time spent in microgravity, the degree of immune system dysregulation, and the incidence of clinical sequelae. Given the next NASA objective is voyage beyond lower-Earth orbit -- and missions of unprecedented duration – it is reasonable to hypothesize the clinical risk to astronauts will be higher than ever before. Thus, our communal goal is to ensure the health and safety of prospective crewmembers. To this end, we must identify a set of countermeasures, offering broad coverage, that will obviate any clinical risks. This project leverages the validated cell culture techniques and immune measures of the JSC Immunology Laboratory, as well as the ground-based microgravity cell culture analog ('Clinostat') available in the laboratory, to define an innovative experimental approach to evaluate candidate immune countermeasures. MPLA is the first of a suite of compounds we will test.

Project Closeout - Executive Summary

We cultured immune cells in either static (1xG) or microgravity/clino-rotation conditions, with or without stimuli to induce cellular activation, and with or without the MPLA compound countermeasure. Using our standard measures of immune competency via multi-parametric flow cytometry, we expected to observe a normal robust response, the suppressive effects of microgravity culture, and the restorative effects of MPLA as a countermeasure. Unfortunately, MPLA treatment did not recover 6-hour cytokine production by T cells, nor their activation status after 24-hour stimulation, that were lost in the clinostat representing microgravity. While MPLA was not able to prevent T cell impairment, its mechanism of action suggests it will be effective at boosting the function of other immune cells; we will test its effect on monocytes and natural killer (NK) cells. Broadly, this project proves our laboratory method is optimal;

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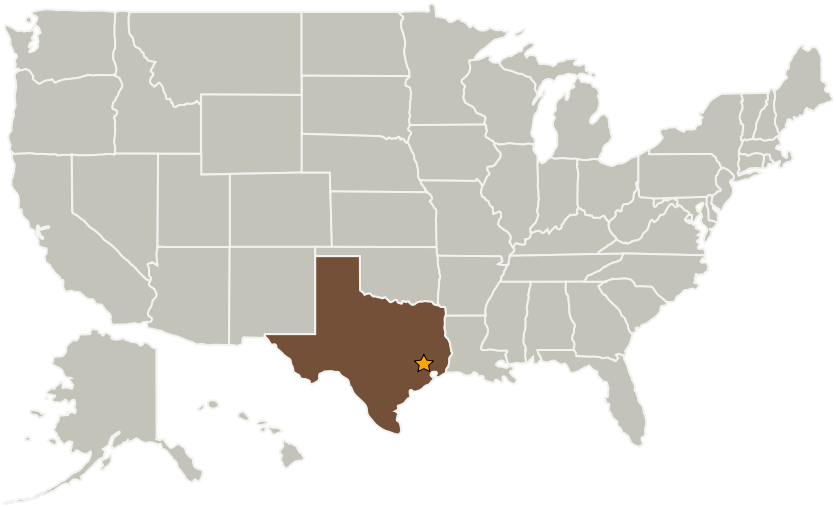
we are prepared to evaluate a suite of immune dysfunction countermeasure products. Once we identify an immune countermeasure in this setting, our goal is to perform similar assessments in a ground analog, such as Antarctica Winter-over, and ultimately with crewmembers onboard ISS.

Primary U.S. Work Locations and Key Partners



Organizations Performing Work	Role	Type	Location
★Johnson Space Center(JSC)	Lead Organization	NASA Center	Houston, TX

Primary U.S. Work Locations
Texas

Organizational Responsibility

Responsible Mission Directorate:

Mission Support Directorate (MSD)

Lead Center / Facility:

Johnson Space Center (JSC)

Responsible Program:

Center Independent Research & Development: JSC IRAD

Project Management

Principal Investigators:

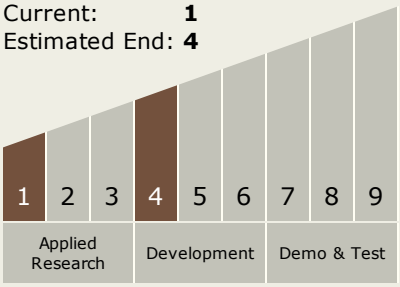
George Makedonas
Brian Crucian

Co-Investigators:

Stephanie S Krieger
Mayra A Nelman-gonzalez

Technology Maturity (TRL)

Start: **1**
Current: **1**
Estimated End: **4**



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Technology Areas

Primary:

- Human Health, Life Support, and Habitation Systems (TA 6)

Target Destination

Foundational Knowledge

Supported Mission Type

Push