JOURNAL OF
EMERGING INVESTIGATORS

Special Edition

# Genes in Space 2024 Finalists

**Marc Bliss**[1]
[1] Genes in Space Program Lead

## INTRODUCTION

If you haven't been following space news, you may not be aware that we are in a golden age of innovation and exploration. New rockets and vehicles are being tested for extended missions to the moon and beyond, and next-generation space stations are in active development. As we embark on this new era, the challenges of long-duration spaceflight and extraterrestrial settlement loom large, and many of these challenges are biological in nature. Understanding the effects of space environments on living organisms is crucial to ensuring the health and well-being of future astronauts and space colonists.

The Genes in Space program is an annual STEM competition that empowers young scientists to address these important biological challenges by providing them with the opportunity to design space biology experiments. Each year, one winning entry is selected to be sent as a flight-ready payload to the International Space Station (ISS) and is conducted by astronauts. Since its inception in 2015, the program has received proposals from over 10,000 students and has launched eleven winning projects. Each of these experiments has pushed our collective understanding of how life in space works and has opened the door for future research to build on their successes.

The abstracts featured on the following pages represent the top five proposals from the 2024 Genes in Space competition. Of the 945 students who entered this year's competition, these proposals were selected for their innovative ideas and rigorous scientific approaches. These talented young researchers have explored a diverse range of topics, including studying phage-host interactions in microgravity, detecting airborne silicone using fluorescence, using nanoparticles for drug delivery, investigating blood clotting mechanisms in microgravity, and utilizing liquid-liquid phase separation to observe brain aging in space. Each of these novel ideas has the potential to significantly contribute to our understanding of space biology and inform future space missions.

We invite you to delve into the following pages and discover the exciting research conducted by these promising young scientists.

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# Using Liquid-liquid Phase Separation to Understand Neurodegeneration in Space

**Megan Chiu[1], Michael Richard Das[2]**
[1] Bryn Mawr School, Baltimore, Maryland
[2] Massachusetts Institute of Technology, Cambridge, Massachusetts

## ABSTRACT

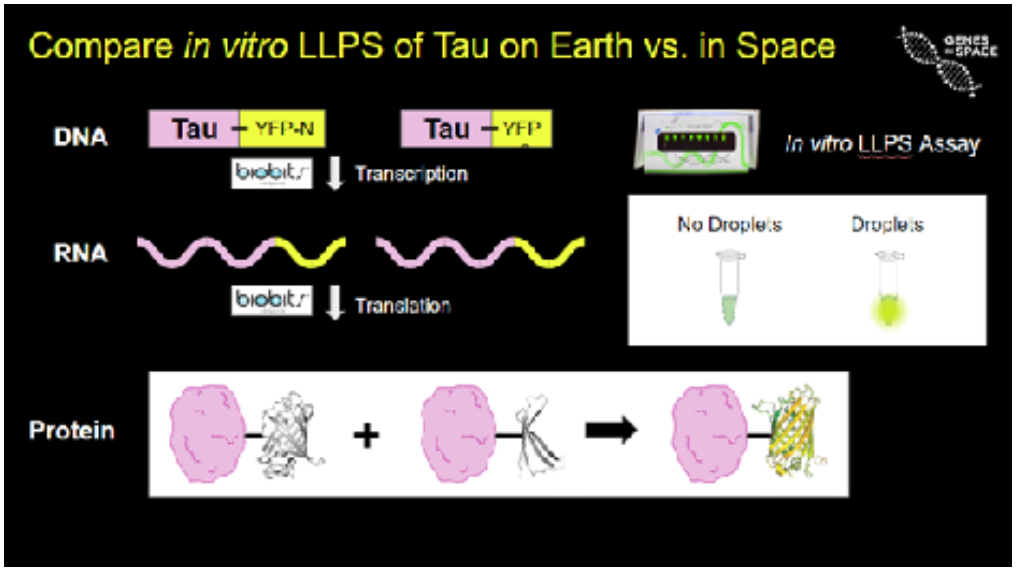
As we begin to expand humanity's presence beyond the Earth, we must carefully consider our physiological well-being in this new environment. For example, prolonged exposure to space has been suggested to increase the risk of brain diseases such as Alzheimer's Disease, which is an example of a neurodegenerative disease that is caused by the formation of protein aggregates.

Our experiment aims to investigate how exactly space affects Alzheimer's Disease by studying the intracellular process of liquid-liquid phase separation (LLPS). LLPS is where a variety of proteins concentrate into a liquid droplet that is separate from the rest of the cell contents. These droplets make it easier for biochemical reactions to occur between the proteins in the droplets. However, incorrectly assembled droplets can accelerate the formation of protein aggregates.

We will investigate how LLPS is affected by the environmental differences in space by studying a neuronal protein called Tau, which is an aggregating protein that contributes to Alzheimer's Disease. We hypothesize that Tau will undergo abnormal LLPS faster in space due to the lack of gravity or other external factors, which could explain observations of increased likelihood of brain disease with space exposure.

To test our hypothesis, we will compare the in vitro phase separation of Tau on Earth versus in space using mVenus, which is a yellow fluorescent protein (YFP). By binding the N-terminus of mVenus to half of the Tau protein population and binding the C-terminus of mVenus to the remaining Tau proteins, we can determine the amount of aggregation that occurs. When Tau aggregates, the split halves of the Venus protein will bind together and fluoresce. Therefore, we can use the fluorescence viewer to quantify the fluorescence of each sample and determine the amount of aggregation that forms.

If exposure makes it easier for abnormal LLPS to occur, abnormal LLPS formation may be a causal factor for the increased risk of neurodegeneration in space. Our experiment will be a step towards understanding how to reduce the risks of space travel and could have significant implications surrounding the safety of astronauts in future space exploration.



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# The Real-time Tracking of Phage Production and Lysis in Space

**Isabelle Chuang[1]*, Julia Gross[1]*, Kayleigh Ingersoll Omdahl[2]**
[1] The Nightingale-Bamford School, New York, New York
[2] Harvard Medical School, Boston, Massachusetts
* These authors contributed equally

GENES IN SPACE

2024 GIS Winner

## ABSTRACT

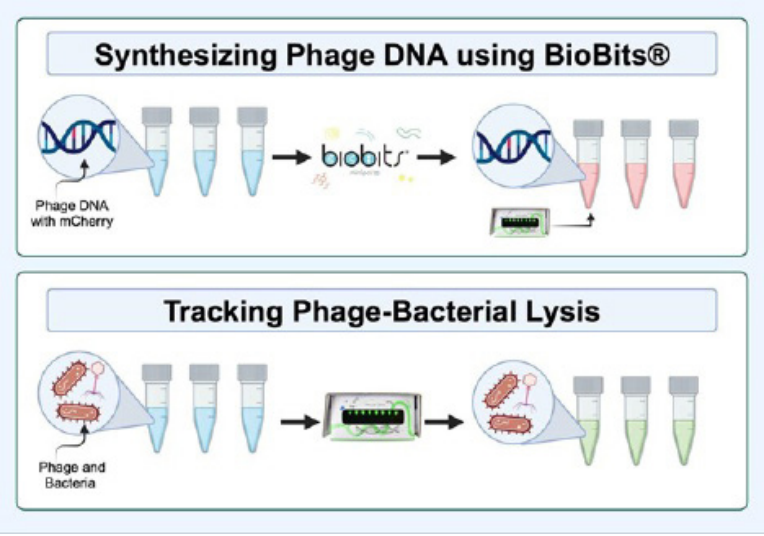
Cosmonaut Yuri Romanenko once experienced an excruciating bacterial dental infection for more than two weeks while in space; he was treated only after returning to Earth. Studies have shown that bacteria thrive in space with increased growth and virulence. Additionally, antibiotics have been shown to lose efficacy in space, perhaps due to increased antibiotic resistance or the antibiotics not reaching the bacteria. The inability to treat bacterial infections is an even more relevant problem due to the increased chance of bacteria spreading within the confinement of a spacecraft, where air and water are recirculated and particles may be suspended.

Bacteriophages, or phages, are viruses that target bacteria. Phage therapy uses phage to lyse, or kill, bacteria and is a possible alternative to antibiotics. We aim to test the effectiveness of phages in microgravity, in order to determine the potential of using phage therapy in space. Our experiment has two objectives: 1) to determine the potential of cell-free phage synthesis and 2) to track the kinetics of phage lysis in real-time. These objectives would be achieved in orbit for the most accurate results.

We propose using BioBits™ as a novel method to synthesize phages. The phages will have an integrated fluorescent marker called mCherry to help track phage production. Once the phages are produced, we will track how quickly they can lyse bacteria. Next, we will use SYTOX green to stain bacterial DNA, and because SYTOX green is membrane impermeable, we should only see fluorescence increase once phages break down the bacterial membrane and the DNA is released.

We hypothesize that cell-free phage synthesis will be slower than on Earth but still produce functional phages as Genes in Space 9 showed that GFP synthesis using BioBits™ in space was comparable to Earth. We also predict the rate that phage lyse bacteria will also be slower in space due to a previous study showing decreased interactions between phage and bacteria in space.

In order to plan long-term space missions for the future, we must consider effective bacterial treatment options. Our experiment will provide valuable insight into the development of on-demand therapeutics in space.



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# Monitoring the Rate of Fibrin Clot Development Under Microgravity Conditions

**Minjun Kim[1]*, Daniel Syed[1]*, Aleksandar Radakovic[2], Marissa Morales[3]**
[1] International Academy Central, Bloomfield Hills, Michigan
[2] The University of Chicago, Chicago, Illinois
[3] Massachusetts Institute of Technology, Cambridge, Massachusetts
* These authors contributed equally

## ABSTRACT

Proper blood clotting occurs through a complex series of protein interactions known as the coagulation cascade. In brief, the protein thrombin cleaves the protein fibrinogen, causing fibrinogen to polymerize into an insoluble fibrin mesh. This mesh secures a platelet plug to sites of injury. In microgravity, the irregular blood flow heightens the risk of adverse blood clotting events. Additionally, the lack of knowledge in the kinetics and dynamics of these clotting protein interactions causes a 30% increase in life-threatening events like embolisms, limiting treatment capacity and prevention of diseases. Previous studies indicated increased protein aggregation and reduced platelet counts in microgravity. Therefore, we hypothesize that clot formation will be faster and the formed clot will be more fluid, leading to abnormal clot movement and integrity.

To test clot formation kinetics, we will use Thioflavin T, which fluoresces upon fibrin aggregation. Recombinant fibrinogen, created by the Biobits Cell-Free System, will be cleaved with the addition of thrombin in an in-vitro based assay. Upon fibrinogen cleavage, beta-sheet-rich fibrin aggregates, reveal binding sites for the indicator. Comparing the timing of this process in Space and Earth helps us elucidate the magnitude of microgravity's impact on the kinetics of fibrin aggregation. To test clot integrity we will use the microscopy technique Fluorescence Recovery After Photobleaching (FRAP) after attaching the fluorescent dye FITC onto the lysine residues of the fibrinogen. By eliminating fluorescent signals from one region of a fibrin clot through photobleaching and then timing the recovery rate, we can evaluate microgravity's impact on clot dynamics.

Our experiments will improve our understanding of blood clotting mechanisms in microgravity by identifying which proteins in the coagulation cascade are most affected. This work may further allow for the development of specific treatments. More importantly, we will be able to pave the way for safer journeys into the cosmos.

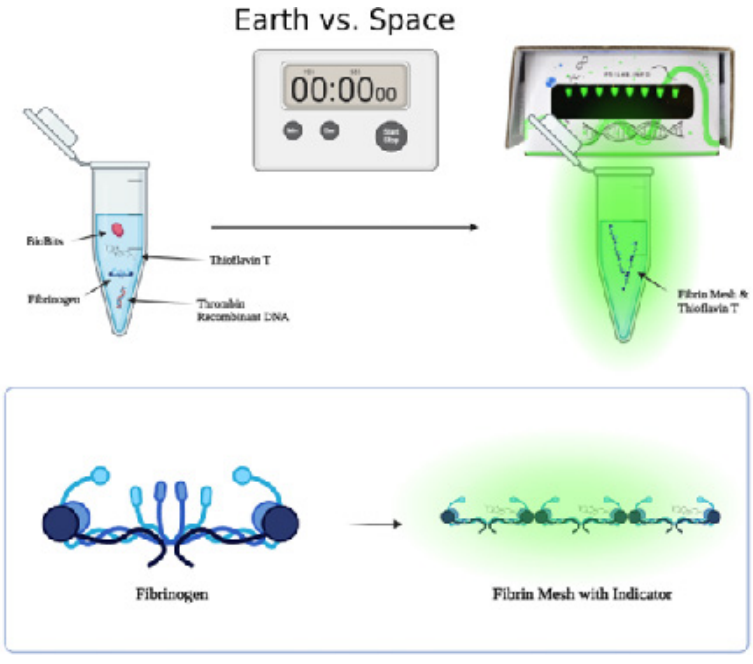


Figure created in BioRender.com

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# SilicoSensor: Detecting and Degrading Airborne Silicone Compounds in Space Using a Fluorescent Biosensor System

**Sean Lee[1]*, Vedant Mehta[1]*, Julie McDonald[2], Catherine Sharer[1], Janet Standeven[1]**
[1] Lambert High School, Suwanee, Georgia
[2] Massachusetts Institute of Technology, Cambridge, Massachusetts
* These authors contributed equally

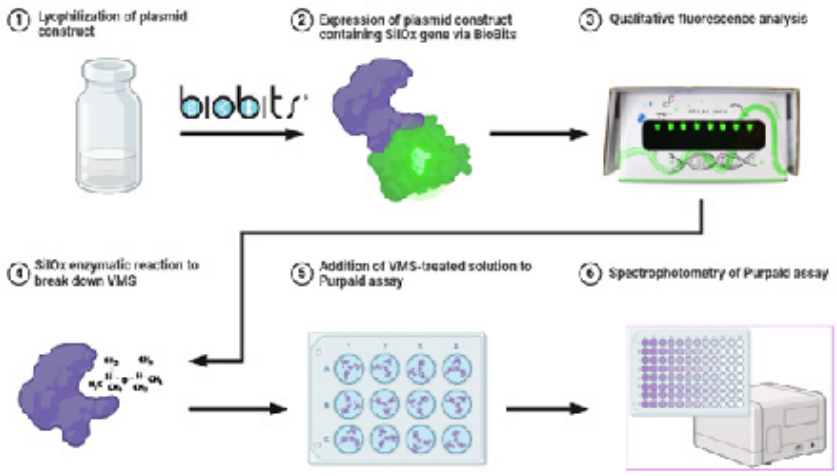
## ABSTRACT

In space, astronauts are often exposed to volatile methylsiloxanes (VMS), harmful compounds that are linked to various respiratory issues like asthma and lung cancer. VMS particles are released from materials aboard spacecraft through outgassing, which occurs when silicone materials come into contact with thermal pollution. Current efforts to reduce VMS levels are insufficient and allow VMS to persist in enclosed space environments. For example, the VMS concentrations on the International Space Station (ISS) reach up to 400,000 times higher than on Earth despite current efforts, which is a critical issue for astronaut health.

To counter this issue, we developed SilicoSensor to both detect and inhibit the activity of VMS. This fluorescence biosensor system relies on Siloxane Oxidase (SilOx), a synthetic enzyme engineered through directed evolution, to break harmful silicone-carbon bonds. The BioBits cell-free kit will be used to express SilOx in vitro, from which successful synthesis of the enzyme is verified by fluorescent emission from a GFP tag. The Purpald assay will then be used to detect formaldehyde, a byproduct of SilOx's enzymatic activity, to confirm the function of SilOx.

We hypothesize that if SilicoSensor is introduced to VMS concentrates aboard spacecraft, harmful silicone compounds will be broken down into less toxic substances. The efficacy of the system can be traced using the Purpald assay, as a deeper purple color indicates greater breakdown of VMS particles. Computational models suggest that SilicoSensor will have a high efficiency in space, with our simulation predicting that SilOx will efficiently break down up to 98% of VMS particles within five hours.

If SilicoSensor were to be launched aboard the ISS, it would serve as the first potential treatment for VMS in space environments. Through our dual-pronged approach, we hope to reduce exposure to VMS, protecting astronauts and improving the sustainability of space travel.



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# Leveraging Altered Mechanobiology in Space for improved Nanoparticle-mediated Gene Delivery

**Aarush Tutiki[1]*, Dhruv Grandhe[1]*, Marissa Morales[2], Achraf Noureddine[3]**
[1] Albuquerque Academy, Albuquerque, New Mexico
[2] Massachusetts Institute of Technology, Cambridge, Massachusetts
[3] University of New Mexico, Albuquerque, New Mexico
* These authors contributed equally

## ABSTRACT

One of the major barriers to long-term space travel is the genomic dysregulation that results from extensive exposure to spaceflight conditions. This dysregulation increases astronauts' risk for life-threatening diseases such as atherosclerosis due to PCSK9 upregulation. Simultaneously, altered anatomical conditions in spaceflight increase side effects associated with traditional treatments such as statins. Developing technology to transiently modify gene expression could reduce the impact of genomic dysregulation for astronauts on long-term missions.

We intend to solve this problem by improving existing liposome delivery systems to introduce siRNA, a transient nucleic acid, into cells. We believe that the altered physical conditions of spaceflight can be leveraged to improve efficiency for two reasons: 1) Altered fluid flow in microgravity reduces internal convective stress while increasing liposomal fluidity, improving the loading of genetic material, and 2) reduced cytoskeletal density due to lowered stress on the cell, will shift the nanoparticle internalization pathway to membrane fusion, preventing endosomal degradation of siRNA.

We will first load our liposomal system with RFP siRNA to quantify the knockdown in fluorescence of RFP-expressing endothelial cells, compared to knockdown on Earth. Phase one will consist of testing liposomes with varying concentrations of cholesterol to identify an optimal level for nanoparticle permeability, and siRNA loading, which will be quantified with the Ribogreen Assay. The loaded liposomes will then be used to treat RFP-expressing endothelial cells.

In phase two, we will enhance the cytoskeletal density of cells by treating them with the protein filamin. We will then treat these cells with the RFP siRNA-loaded liposomes to see whether microgravity induced dysregulation has been reverted. This will yield insights into how cytoskeletal density changes uptake routes of nanoparticles in space. These advancements will further development of drugs such as PCSK9 inhibitors in space, preventing disease after long-term spaceflight.