Space: The Next Frontier for Next Generation Life Science Research

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Since mankind's first voyage into space, research and discovery have continued to unlock the mysteries and potential of this vast frontier beyond earth's borders. Today, scientific exploration continues to evolve, unveiling new opportunities to enhance and expand the scope of life science through microgravity studies made available by CASIS, the Center for the Advancement of Science in Space.

Free-fall or zero-gravity environments provide an advantageous context for

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research that simply cannot be faithfully replicated on earth. From drug development and the study of disease progression to understanding how materials react to extreme conditions, notable opportunities have surfaced in recent decades, yielding results that are positively impacting human life.

Microgravity environments provide weightless conditions that can significantly impact the pace of research for some diseases because of the physiological impact of this unique environment on progression of disease from onset to clinical symptoms. These symptoms have been well characterized in humans and animal models in microgravity for diseases that affect muscle and bone strength. For example, studies of muscle wasting and bone weakening in rodents help us understand human disease because microgravity accelerates disease progression. In addition, microgravity research has proven advantageous for producing higherquality protein crystals for structure-based drug design and testing of new drugs in animal models of disease.

The good news is that access to space for research is easier now than at any previous time in history because of the International Space Station (ISS) U.S. National Laboratory managed by CASIS. Organizations ranging from academic and government research institutions to established pharmaceutical companies, new business start-ups and medical device manufacturers have access to the only National Lab where gravity does not apply.

Bigger Crystals for Better Data

Protein crystallization has long been recognized as an ideal technique for providing a clear picture of a protein's physical structure that enables scientists to design and optimize drugs. While the growth of three-dimensional protein structures happens on Earth, many proteins are difficult to crystallize in normal gravity. Microgravity helps scientists achieve more detailed road maps of proteins for drug development.

Microgravity can be very beneficial for making large crystals required for highresolution crystallography using neutron diffraction. A recent experiment sponsored by CASIS was published in 2015 in the Acta Crystallographica: Structural Biology and Crystallization Communications <u>describing</u> [1] the use of space-grown crystals to generate larger, more homogenous protein crystals for neutron diffraction. A more enhanced method for revealing the detail of a protein's structure than traditional X-rays, neutron diffraction holds great promise for improving drug design by enabling scientists to make better maps of proteins with more detail.

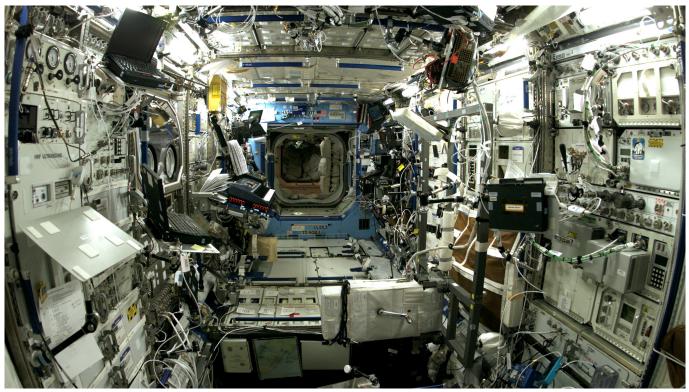
The challenge for advancing this method has been the need for larger protein crystals with well-ordered lattice structures. In this area, microgravity has been proven to deliver a less variable distribution of crystals formed over time, creating a more uniform structure that lends to better data.

Lead researcher and author of the paper Dr. Joseph Ng of iXpressGenes, Inc., noted in his analysis: "Microgravity may play a critical role in obtaining protein crystals suitable for [neutron diffraction] that would not otherwise be possible on earth."

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It's not the first time the biotechnology industry has leveraged microgravity for protein crystallization. A joint research effort between the Japanese Space Agency and Russian federal space agency Roscosmos resulted in the improved drug design of an inhibitor of human hematopoietic prostaglandin D2 synthase (HQL-79), a drug target in patients with Duchenne's muscular dystrophy. If conducted on earth, it is estimated that the timeframe for the study could have been extended by three to five years. [2]

Understanding Disease Through Space-Based Animal Models of Human Disease



Astronauts face a number of health-related challenges while living in space. Most of these effects are understood and can be addressed by countermeasures including lots of exercise and a good diet. In fact, study of these challenges to life in space revealed that microgravity can accelerate the onset of some chronic diseases associated with normal aging on Earth, including muscle atrophy (or weakness) and osteoporosis. This phenomenon offers a unique environment for study using animal models like mice or rats that share many of the same genes with humans.

Combined with data from human studies, animal models help us understand the causes of disease and how to most effectively diagnose, prevent, treat or cure them. When used in microgravity, animal models like mice develop disease symptoms similar to the crew but at an even more accelerated rate because of their shorter life span. This allows researchers to generate data from bone and muscle loss studies more rapidly than models on Earth. The end result offers a much more expansive view of disease mechanisms, lending to better identification of potential new drug targets and enabling preclinical evaluation of drug effectiveness for disease treatment.

Pharmaceutical company Amgen leveraged animal research models for use in

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microgravity on the Space Shuttle to support development of Prolia (denosumab), a drug to treat osteoporosis. By sending mice into space, the company was able to test the effectiveness of the drug, which was first approved by the FDA for postmenopausal women at risk of bone fractures due to osteoporosis and later for men at <u>high risk of fracture.</u> [3] These same animal models can now be used on the International Space Station with the added advantage that they can be exposed to microgravity for weeks to months rather than just days.

Novartis, another leading pharmaceutical company, is also using a "mice in space" study to better understand muscle development and muscle atrophy. In a study just completed last year on the ISS National Lab, Novartis scientists used a mice with a specific genetic pathway knocked out—one that made it <u>resistant to muscle loss</u>. [4]

The mice flown in space are compared against littermates who live in identical habitats on Earth under normal gravity. By comparing the rate of muscle atrophy in the mice living in microgravity against those on Earth, the company hopes to increase understanding of the pathway and its potential as a target for drug therapies to help reduce the effects of muscle loss associated with aging.

Improving Devices for Better Scientific Discovery

The accelerated pace of medical discovery in microgravity is not just limited to protein crystals and animal models for drug testing. Another active area of research that benefits from this unique environment is materials research. Recognizing the potential of space-based research, Ras Labs has initiated a study aboard the ISS National Lab to improve materials for use in prosthetics to replace missing limbs or in robotics for space missions that are too difficult or dangerous for humans. This innovative new startup company is testing its own synthetic muscle material to provide improved mobility for amputees on Earth and improved radiation resistance in robotics systems for space. The impact of the research is expected to enhance the organization's development of robust electroactive polymers (EAPs) that contract and expand, lending life-like motion that could transform robotics and prosthetics.

With the ISS National Lab, it's the dawn of new day for life science research. In fact, it is several new dawns. Every day, the crew of the International Space Station is witness to 15 sunrises and sunsets while they operate experiments in space for the benefit of Earth. As each day unfolds new discoveries emerge from just beyond the horizon.

• CONFERENCE AGENDA ANNOUNCED:

The highly-anticipated educational tracks for the 2015 R&D 100 Awards & Technology Conference feature 28 sessions, plus keynote speakers Dean Kamen and Oak Ridge National Laboratory Director Thom Mason. Learn more. [5]

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