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Hearing on

The Case for Space: Examining the Value

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Chairman Nelson, Ranking Member Vitter and distinguished Members of the Subcommittee, thank you for the opportunity to speak to you on the benefits and applications of space based research. I have the privilege of serving as the associate director of the National Space Biomedical Research Institute and also the chief scientist for Astrogenetix, which has supported the International Space Station National Laboratory Vaccine Pathfinder missions. For the hearing today, I was asked to address two areas: (i) the potential benefits and applications of my research, and (ii) what makes the space environment unique.

For the duration of my academic career, I have been involved in applying results gained from space based research to on-earth biomedical problems. My initial research experience with NASA based technology began in the early 1990's, with studies focused on three dimensional growth of human tumors, using the NASA-developed Rotating Wall bioreactor. This device was originally invented so that cells could be grown under conditions mimicking reduced gravity, and could be transported into space avoiding the harsh shear forces of launch and landing. The calm and quiescent culture environment provided by this device allows cells to assemble into large three dimensional aggregates, closely resembling the way cells grow within the human body. The three dimensional growth of tumor cells in this Rotating Wall bioreactor has proved to be remarkable for a number of reasons. As compared to the traditional means of growing cells flat, in a Petri plate, tumor cells cultivated in the bioreactor grow faster, are more biologically representative of native cancer tissue (that is, look and behave more like real human cancer) and are more aggressive, in that they become significantly more resistant to anti-cancer drugs. For example, the same dose of the chemotherapeutic agent taxol that kills breast or ovarian tumor cells in a Petri plate will not kill all the cancerous cells in these three dimensional clusters. The cancer cells in the three dimensional aggregates which are still alive following exposure to taxol then continue to grow, mirroring what happens in patients who fail chemotherapy. Ultimately, three dimensional growth of human tumor cells can be used as a way to more reliably test new drugs and other types of therapies before they are administered to patients, to give physicians a better first line of defense in determining which treatments will work for their patients.

Over the course of nearly two decades, the scientific literature has become filled with publications demonstrating the fidelity and usefulness of the Rotating Wall bioreactor for three dimensional culture of a wide variety of both normal and cancerous cells. However, taking a different perspective, if the Rotating Wall bioreactor is so effective at producing an environment which can replicate conditions in the body, is it necessary to conduct research on cells and tissue grown in space? One answer to this question can be found in the work of Dr. Leland Chung, the principal investigator for an experiment that launched on STS-107. The objective of this work was to characterize the interaction of prostate tumor cells and bone tissue by conducting a co-culture experiment in a bioreactor aboard the space shuttle. Although a tragic accident destroyed the crew and shuttle, data downlinked during the flight showed that within three days, the clusters of prostate cancer cells and bone had become the size of golf balls, relative to the same experiments conducted in the bioreactor on the ground, which showed three dimensional clusters one-eighth of an inch in diameter. An expert in prostate tumor biology, Dr. Chung maintains that this experiment had produced one of, if not *the*, best model of prostate cancer-bone interactions. This is an important accomplishment since advanced stages of prostate cancer commonly spread to bone making treatment options challenging and highly limited. Based upon the work of scientists like Dr. Chung, as well as my own personal experiences, I believe that we need experimentation in all types of environments, modeled microgravity, true microgravity and the 1G that we live in, to gain insight into how forces like gravity affect cell function and growth. We must utilize all options available for advancing the knowledge necessary to find new ways of treating devastating diseases, such as cancer. The International Space Station (ISS) is a critically important platform necessary to advance this science – there is no other means of conducting work in a sustained microgravity environment. ISS is the only laboratory of its kind.

Research in microgravity has also contributed to important advances in microbial biology. Previous space flight studies of the bacteria *Salmonella enterica* demonstrated that growth of this organism in the microgravity environment resulted in significantly enhanced virulence in mice when the space-grown bacteria were returned to earth and injected into the animals. Taking advantage of this knowledge, we reasoned that if the cause of the increased virulence could be identified, that is, targeted to a specific gene or set of genes, then a vaccine for this organism could potentially be developed. In order for a vaccine to be effective, it must be strong enough to induce an immune response in the host and strong enough to provide protection against future exposure to *Salmonella*, but weak enough to allow administration with no risk of illness, that is, it must not make the host sick. Working with the principal investigator for these studies, Dr. Timothy Hammond, we pursued development of a *Salmonella* vaccine using strains of the bacteria which were genetically altered to remove key genes associated with virulence, yet were still able to induce a good host immune response. A key factor for these investigations was the establishment of a host-pathogen model that would allow us to examine how the bacteria interact with, and infect, the host within the microgravity environment. For this, we developed an in-microgravity assay whereby the genetically altered bacteria are grown in the microgravity environment, then mixed with a tiny worm host, *Caenorhabditis elegans*. Interestingly, *C. elegans* exhibits many similarities with humans in their immune response to bacteria, making this a good model system. The model works

because *C. elegans* normally ingest bacteria as a food source. After the bacteria and worms interact on-orbit, the process is terminated and then returned to earth for determination of microbial virulence. If the bacteria are virulent, after being ingested by the *C. elegans* the bacteria kill the worm host, and continue to grow. If the bacteria are not virulent (that is, the removal of genes took away their ability to kill their host), the worms simply ingest the bacteria and the bacteria are removed from the system, so they cannot continue to grow. In post-flight analysis, altered bacterial strains not exhibiting virulence, due to the knock-out of specific gene(s), are potential targets for vaccine development. These investigations are made possible because of an extensive team effort, using the robust flight hardware and expertise provided by BioServe, under the leadership of Dr. Louis Stodieck and the funding provided by Astrogenetix.

To date, six flight studies have been conducted over a period of 18 months, and we are preparing for our next payload on STS-129 scheduled for launch in November of this year. We have successfully identified a gene target and a vaccine for *Salmonella enterica* is under development. This work has partnered academia and government with industry for the development of a commercial vaccine product based on results obtained in microgravity, and serves as a pathfinder mission to validate the use of ISS as a National Laboratory, that is, as a research and development platform, after station assembly is complete. As such, NASA has designated these flights as ISS National Laboratory Pathfinder missions and has provided a manifest on each of the remaining shuttle flights to enable iterative science to be conducted, as is necessary for tangible product development. Currently there is no *Salmonella* vaccine available for human use. Aside from being among the most common causes of food poisoning world-wide, *Salmonella* is a major cause of childhood death in third world nations.

A variety of medically important microbes have been tested in the *C. elegans* model and the system has worked well. Recently initiated follow-on experiments are focused on the use of microgravity to identify targets for the development of therapeutics for methicillin resistant *Staphylococcus aureus*, or MRSA. In the past decade, infection and mortality due to this organism has increased drastically, exceeding the death rate for HIV. In this country alone, MRSA is responsible for 100,000 cases of severe infections and 19,000 deaths annually. Although once predominantly confined to the hospital environment, this organism is fast becoming a major problem outside hospitals, and community acquired MRSA is on the rise.

To summarize the accomplishments of this work:

- The findings made in space are the product of fundamental research.
- Multiple successful spaceflight payloads have been conducted with industry support.
- A lead product, a vaccine for *Salmonella,* is in development based upon results obtained in microgravity.
- Work with additional microbes is ongoing, for future pipeline development.

The ability to support and maintain investments made in ISS will require an ongoing commitment but also comes with the expectation that significant gains and advantages will come about as a result of the resources allocated. One important question to ask regarding the development of therapeutics using ISS as a platform is how exactly can using space change drug development on earth? Currently, the research and development pipeline for a single agent may take years of work to allow identification of viable candidates for pharmaceutical applications. At the end of this period, the possibly exists that the candidate agent is not suitable for continued development. The time, money and resources expended getting to this point could be minimized by using a process which identifies promising agents or drug candidates earlier in the development pipeline, for quicker testing to evaluate downstream efficacy and market potential. Using space, years may be eliminated from research and development pipeline activities, to allow for fast-tracking of promising agents, and termination of unsuccessful agents at earlier time points. In this manner, ISS may be not only a one-of-a-kind laboratory resource for the development of new and sorely needed pharmaceutical and therapeutic products, but could facilitate the generation of an entirely new kind of biotechnology industry based upon discovery in microgravity.

Outside of my own research, in my role as associate director of NSBRI, I have the opportunity to facilitate the work of over 180 investigators at 60 institutions across the country. The research of these scientists is also aimed at making advances in the space environment and applying this knowledge to benefit life on earth. From new technologies for noninvasive health monitoring, to advanced training techniques in areas such as ultrasound, to enhanced lighting devices to counteract fatigue, this work leverages the academic resources of our Nation's top tier institutions and the federal funding of agencies such as the National Institutes of Health and the Department of Defense. The continued accomplishments of this body of work are strongly dependent upon the maintenance of ISS as a National research enterprise.

Mr. Chairman and Members of the Subcommittee, in closing, I want to again extend my appreciation for affording me this opportunity to discuss the benefits and applications of research conducted in the space environment. At this critical time when National resources are hard fought, I sincerely believe that investments made in the International Space Station will yield tremendous benefits for new discovery to enhance health on earth. Vital to these successes are the collaborations and efforts of academia, industry and government, working together with your strong support. I would be pleased to answer any questions that you may have.

Biography.

Jeanne L. Becker, Ph.D. is Vice President and Institute Associate Director of the National Space Biomedical Research Institute (NSBRI), a nonprofit research consortium. She holds faculty appointments in the Departments of Obstetrics and Gynecology, and Surgery, at Baylor College of Medicine in Houston. She has also been appointed as Chief Science Officer for Astrogenetix, Incorporated, a subsidiary of AstroTech, Incorporated. Dr. Becker is a member of the National Advisory Committee for the Women's Health Research Coalition, a Washington DC-based network of more than 600 leaders in academic medical, health and scientific institutions, and currently is Chair of the Coalition. Dr. Becker serves on the Executive Council for the newly formed Organization for the Study of Sex Differences. She also is on the Advisory Board of the Conrad Foundation, an educational foundation honoring astronaut Pete Conrad, dedicated to providing students with the tools, resources, and opportunities to innovate in science and technology. Dr. Becker is active in numerous NASA panels and committees, and is a recipient of NASA Space Life Sciences Directorate Professional Achievement Award. Her NSBRI responsibilities include oversight of the Institute's science and technology, and education, portfolios.

Dr. Becker's research has focused on the development of three dimensional models of human breast and ovarian cancer, using the Rotating Wall Vessel (developed by NASA). The three dimensional cellular constructs of breast and ovarian cancer developed in this model reproduce many aspects of cancer, by creating tissue-like architecture that exhibits rapid onset drug resistance as occurs in human disease. This work was selected as part of the suite of the first cell culture studies performed aboard the International Space Station (ISS), on Increment 3. As a result of the work conducted in the Rotating Wall Vessel, Dr. Becker has developed a companion technology, a novel three dimensional cell culture paradigm based upon diamagnetically stabilized magnetic levitation. Two patents have been filed on this technology, which has applications for anti-cancer drug testing. In other past notable work, Dr. Becker's laboratory published the first report linking chronic dioxin exposure with the development of endometriosis in rhesus monkeys. This observation led the Environmental Protection Agency to re-examine the effects of this environmental toxicant on the female reproductive system.

Dr. Becker is currently part of the research team developing a vaccine for *Salmonella enterica*. This initiative partners industry (Astrogenetix) with academia and government for the development of a commercial product, and serves as a Pathfinder mission to validate the use of ISS as a National Laboratory after assembly is complete. Furthermore, these studies have resulted in the development of a novel in-flight method to assess host-pathogen interactions and microbial virulence in microgravity. Newly initiated work is focused on using microgravity to identify targets for the development of therapeutics for methicillin resistant *Staphylococcus aureus*. Dr. Becker recently provided an invited briefing on the Pathfinder work to NASA Administrator Charles Bolden and Deputy Administrator Lori Garver.