OCT Emerging Space Office

ESO Commercial Microgravity Case Study 1:

Novice Commercial Users (Medical)

Vivo Biosciences Inc. – A Small Business Perspective

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This case study was conducted in FY 2013 by the Emerging Space Office (ESO) to begin characterizing the kinds of opportunities and challenges encountered by small high-tech businesses who have never done R&D in space and who serve terrestrial versus space markets, but who have legitimate business reasons for considering space research and development for generating novel or improved products.

The primary motivation for ESO's interest in this investigation was to gain insight, through direct support of an emerging commercial space project as a case study, into the conditions important for the successful maturation of the International Space Station (ISS) into a multi-faceted, multi-user National Laboratory for providing social and economic benefits to the U.S. The ISS is the core of the human spaceflight economic ecosystem in orbit and is the primary test-bed for investigating and understanding how to productively work and live in space.

Other than providing funding for the $50K grant, NASA was not involved in any part of this study except as an observer. The entire effort was conducted by Vivo Biosciences Inc. (the small business customer) and BioServe Space Technologies (the space services provider).

Credits and Acknowledgements

This report was made possible through the generous contributions of many people who gave their time and expertise to the development, validation, review and editing of this document. Their efforts are deeply appreciated and were essential to the accuracy and utility of this study.

Programmatic direction and guidance on the value proposition of this work was provided by Mr. Alexander MacDonald, Program Executive for the Emerging Space Office.

Scientific and technical reviewers of the Vivo Biosciences unsolicited proposals included Dr. Todd Meyerrose, co-founder of PathDrugomics and Consulting Associate Professor of Structural Biology at Stanford University. Reviews and earlier discussions about the potential of Vivo Biosciences technologies and need for space were provided by Nobel Laureate Baruch Blumberg. Both reviewers agreed with the bottom line conclusion of this report: In order to determine the value of microgravity for advancing this kind of potentially life-saving research, the experiment must be done, and done correctly in space, and likely many times before a breakthrough is realized.

Review of the science content was provided by Dr. Raj Singh, CEO of Vivo Biosciences; Dr. Timothy Hammond, Professor of Medicine, Duke University School of Medicine and Senior Medical Officer, Department of Veterans Affairs Office of Research & Development; and Dr. Ioana Cozmuta, Discipline Scientist, Science and Technology Corporation.

Programmatic and technical reviews were provided by Ms. Carol Carroll, Deputy Director for Science, NASA Ames Research Center and Mr. Sidney Sun, Chief of the Space Biosciences Division, NASA Ames Research Center.

Information and review for commercial space insights were provided by Dr. Daniel Rasky, Director of the Space Portal at the NASA Ames Research Center; Mr. Mark Newfield, Deputy Director of the Space Portal; and Mr. Bruce Pittman, Executive Vice President of the National Space Society, Chair of the AIAA Commercial Space Group, and Director of Flight Projects for the Space Portal.

A special thanks goes to Mackenzie Harper and Christopher Harper for editorial support and guidance on how to improve readability.

Table of Contents

Executive Summary 4

ESO Case Study Report 1: Novice Users – A Small Business Perspective

Purpose and Rationale 10

Commercial Motivation for Space Research. 11

Scope of Case Study 15

Science of 3-D Tissue Cultures 16

Results and Findings 20

Conclusion and Recommendations 26

References 29

Image Captions 33

Appendix I: Vivo Biosciences Proposal Link 34

Appendix II: Vivo Biosciences Technical Review Link 34

Appendix III: Vivo Biosciences Final Report 34

Appendix IV: Vivo Biosciences Presentation to Tricon on results of blind studies for cancer research with Champion Oncology and Novartis Genomic Institute 34

Executive Summary

Why Does a Biotech Company Want to do Research in Space?

Vivo Biosciences Inc. (VBI) is an award winning company with a customer base that includes major pharmaceutical companies. *(Page 11)*

Their unique product (HuBiogel™) and 3-D tissue and tumor culture system was named by The Scientist Magazine as one of the Top Ten Innovations of 2012. HuBiogel™ is used in the Rotary Cell Culture System, which is a NASA spinoff now produced and marketed by Synthecon, that has some of the low shear and turbulence features of microgravity that are important in 3D tissue cultures. VBI's HuBiogel™ system is used to grow tissues and tumors for cancer research and is now also a leading new candidate for use in the selection of chemotherapy drugs for cancer patients. *(Pages 12-14)*

However, despite a continuing series of successes, VBI believes that they are about at the limit of the performance their product can achieve on Earth and gravity is the problem.

To develop better life-saving therapeutic options, VBI needs 3-D tissues and tumors that are both bigger than what they can achieve on Earth and of higher fidelity to disease processes in a patient. Reluctantly, VBI concluded that space might be the best place, and perhaps the only place, to get the improvements in performance they need.

Although gravity negatively affects their product's performance on Earth, VBI does not know whether growing tumors in space will improve outcomes. But if it does, the results would be important to many research areas, including selecting the right chemo-therapy options for patients. This is potentially life-saving research that could offer significant near-term benefits to the public.

Purpose of Case Study

Vivo Biosciences Inc. (VBI) submitted an unsolicited proposal to the Emerging Space Office (ESO) in 2012 and was selected for a case study in FY 2013. *(Page 15)* From ESO's perspective, the purpose of this study was to understand the kinds of options, motivations and difficulties encountered by small high tech companies that have legitimate business reasons for using space to improve existing products or develop new ones for a terrestrial market; especially those with no prior space experience. *(Page 10)*

VBI needed to know if they could grow tumor cells on HuBiogel™ in existing flight hardware well enough to make a flight investigation worth the effort and expense and obtain answers within the next three to five years.

Opportunities for Public Benefits

In 2013, while this Case Study was underway, VBI conducted a landmark study with Champion Oncology to address the selection of chemotherapies for two types of cancer: a drug sensitive colon cancer and a drug resistant colon cancer. *(Pages 11-14)*

Champions Oncology provides diagnostic support to physicians in the selection of chemotherapies. They take cancers cells directly from a patient, grow that patient's tumor in a mouse, then test a variety of different chemotherapeutic agents to see which drugs work on that patient's specific type of cancer.

The problem is that it takes 20-30 weeks to grow the tumors in the mouse and Champions Oncology was seeing too much variability in the results.

In addition, colon cancer is a very aggressive cancer. Thirty weeks can be too long to wait before starting cancer therapy. This is where Vivo Biosciences offers a potentially significant improvement.

Executive Summary

continued

Chemotherapeutic agents are poisons that significantly weaken the patient.

They are used because cancer cells are often weaker than healthy cells to certain chemicals and the goal is to eradicate the cancer before killing the patient.

Treating a patient with the wrong chemotherapeutic agent not only will not work to destroy the cancer cells, it will also further weaken an already seriously ill person.

In a blind study using VBI's technology, patient tumors provided by Champions Oncology were grown in HuBiogel™ at VBI and treated with known drugs along with control samples.

In the very first study performed, HuBiogel™ tests were correct in 70-80% of the cases, but it only took 2-3 weeks to get the results and not 30 weeks.

This speed can make a critical difference for a patient suffering from colon cancer and other aggressive cancers.

The goal now is to predict and achieve >90% accuracy in 2 week analyses. *Achieving this accuracy is where VBI believes that space research could make the difference.*

The High Cost of Learning

VBI was highly motivated to make the flight hardware evaluation test work.

The insights gained from their successes and problems are useful for understanding where NASA and CASIS can play critical roles in achieving better outcomes for public benefits from both the ISS and the emerging commercial space transportation and services companies. *(Pages 20-25)*

$50K was provided via an ESO grant to VBI to determine whether they could grow tumors in existing flight hardware.

Of the $50K ESO funding:

- $28K supported the Vivo Biosciences Principal Investigator and a part time temporary research assistant for preparation and analyses of samples;
- $11K went to BioServe Space Technologies for leasing the flight test unit (BioCell) and design services; and
- $11K went for tissue culture supplies and reagents used to grow and analyze the samples.

The test required successfully managing the culture conditions and fixation strategies for 4-6 weeks in the flight hardware under anticipated space flight conditions.

Then VBI evaluated the adequacy of tumor growth and function in the BioCell using imaging and biochemical analyses. *(Appendix III)*

The results determined whether a flight investigation had a high probability of yielding new important insights for project improvement.

After six months, Vivo Biosciences concluded that some but not all of their technical goals could be met because the culture chamber was too small.

However, they did determine that there were no fundamental biocompatibility issues with the BioCell materials and that they could manage the tissue growth environment for the necessary 4-6 weeks.

With a minor redesign of the flight hardware, this experiment could be conducted in space within a year … *if funds were available to support it.*

Which as of this writing, there are not.

Executive Summary

continued

Pitfalls and Pathfinders

Nobody does biotech research on earth the way it must be done in space. The procedures are not even close. Terrestrial labs do not have to manage launch stresses, unwanted and non-intuitive effects of microgravity, re-entry stresses, and post-flight recovery delays.

In fact, laboratory research in microgravity is so different from anything a typical laboratory scientist would experience on Earth that it is akin to pursuing a graduate degree in a new technical subject.

Novice investigators need considerable help to succeed, especially if flight research is only a minor part of their business model. *(Pages 20-26)*

Like Vivo Biosciences, commercial biotech research will seek specific research outcomes that are likely to require changes in flight hardware.

Few companies, even large companies, can afford to spend $50K and six months of their own resources to determine that the flight hardware is not adequate for their investigation; wait six months or more for a re-design; then spend an additional $50K (or more) to test the new hardware again before committing to a flight (costing in excess of $200K) that may or may not yield a productive outcome. For large companies, this is unattractive. For small companies, it is prohibitive.

However, these small companies are often the pathfinders for new capabilities in high tech industries and they offer the innovative culture that can pioneer important new uses for the ISS National Laboratory, serving both the nation and NASA's interest well.

The Vivo Biosciences flight concept:

- Addresses an important public need (cancer research and applications),
- Serves a terrestrial rather than flight market,
- Requires space to achieve it's goals (currently, accuracy is limited by tumor size and characteristics which are limited by gravity),

If successful, this study could result in an important breakthrough. But success is by no means assured.

This is an exploratory commercial applications proposal for a terrestrial market, rather than space biology basic research, space technology development, or space biomedical research.

Although Vivo Biosciences is a small business, VBI does not address a space market and so is not eligible for NASA's SBIR/STTR funding.

As such, this proposal falls through the cracks of NASA's R&D portfolio and the high risk nature of the space element makes it unattractive to most private investors.

Parts That Work

Flight accommodations as currently configured are not customer-friendly for novices, although BioServe Space Technologies provided excellent support to Vivo Biosciences throughout the study. *(Pages 26-32)*

In fact, the role of a mentor or guide (like BioServe) who provides a bridge between the needs of a novice flight investigator and the accommodations and constraints of space flight is the single most essential element in crafting a successful research experience for new entrants into space laboratories.

Executive Summary

continued

From VBI's commercial perspective, that the International Space Station (ISS) is immediately and permanently available for iterative research, and that SpaceX Dragon can provide the critical return of samples to earth as well as payload transportation to the ISS, were all essential to VBI even considering trying to improve their product in space. In this case, sample return is a deal-maker.

Conclusion: *(Pages 26-32)*

For any company, time is money.

During the six months that Vivo Biosciences conducted the ESO Case Study, it also completed two landmark studies for paying customers, which illustrates another point.

The priority of companies, especially small companies, must be to support their paying customers while the space flight investigations are being developed. Often they won't have the resources to do both with internal funds.

The amount of time it takes to do a space flight investigation (years) is significantly out of scale with a commercial laboratory investigation on Earth (days to weeks).

Vivo Biosciences believes that removing gravity to obtain larger, better-quality tumors is one of the few, and perhaps the best, option it has for improving research and cancer treatment outcomes with their product. *(Pages 16-19)*

But it still might not work and they can't afford to fund the wrong strategy.

Unfortunately, three outcomes are possible with this investigation and, from a company's perspective as a potential paying customer, two of them are bad.

First, the experiment might not work at all, either because microgravity doesn't help achieve the desired results or because of mechanical problems, operational issues or simply bad experiment design resulting from inexperience with space flight realities.

Alternatively, there may be some improvements from space but either they are not significant enough or their value is diminished by other negative effects of growth in microgravity and the outcome turns out not to be worth the cost.

Third and best, the space flight results are what the commercial researcher hoped to achieve. In which case, the company will need to fly the experiment again to confirm it and then many more times to develop sufficient reliability and confidence for a marketable product. This is a very expensive, likely prohibitively expensive, undertaking for a small company.

Unfortunately, there is no way to develop, or even to determine, the value of removing gravity for advancing this type of potentially life saving research without doing the experiments in space.

Recommendations: *(Pages 26-32)*

Nationally, there are insufficient funds for early stage exploratory applications research, like VBI's, that investigates unproven but promising microgravity techniques and addresses a terrestrial versus space market.

In fact, if the government does not help this new field of laboratory sciences to grow, it is unlikely to develop the critical mass of talent and ideas necessary to achieve the number and kinds of breakthroughs that can offer important new outcomes for the taxpayers' investments. Alone, CASIS' funding is insufficient to realize the potential this type of research offers.

Executive Summary

continued

The ISS and commercial space synergy are capable of delivering even more value to the public than the many contributions they have already achieved.

Therefore, it is strongly recommended that NASA establish funded solicitation mechanisms to encourage worthy applications R&D in space, at least through the initial flight test, when such studies have the potential to yield important public benefits, even if they don't provide a NASA application or fit within standard programmatic boundaries.

Mentors, advisors, guides and integrators (MAGIs) who can help a novice craft a successful flight experiment – like those at Bioserve Space Technologies, Dr. Lawrence DeLucas at University of Alabama, Nanoracks, and investigator flight support groups at NASA Centers – are essential to the development of the ISS National Laboratory and the commercial microgravity laboratory market that could become important to emerging space companies.

Because they play such essential roles in delivering value back to the public from spaceflight, it is recommended that the MAGIs be supported to maintain critical staff expertise during the intervals between funded flight developments.

Novel research of the kind that can lead to breakthroughs will almost always require hardware modification.

Some mods will be relatively easy and cheap, like those required by Vivo Biosciences.

But some that are important for opening new markets – like onboard analyses and the ability to handle sensitive biological samples on the launchpad, through the launch interval, and during return to Earth – may need funding in the $5M-$10M category.

However, given the magnitude of taxpayer investments to build the ISS and the billions of dollars per year spent in operating it, increasing funding to support more space research for public benefit and increasing the investment in infrastructure that makes more breakthroughs possible is a sound and worthy strategy, even with the challenges of sequestration.

The Vivo Biosciences flight concept is worth doing. It will offer valuable information to NASA and the emerging space community on the challenges facing new commercial entrants into the field of space research – *whether VBI succeeds in meeting its research objectives or not.*

Therefore, it is strongly recommended that both NASA and/or CASIS continue to support VBI's investigation through flight and that ESO monitor its progress because of its:

- **Potential benefit to public health;**
- **Utility as a Case Study for this class of commercial biotech research in space for a terrestrial (rather than space) market; and**
- **Value in understanding the customer perspective and developing the commercial research and applications potential of the ISS and the commercial space transportation and service providers that are evolving with the ISS National Laboratory.**

Finally, it is strongly recommended that NASA and CASIS continue their wise practice of encouraging and supporting exceptions to standard plans and procurement strategies for flight studies when "out of the box" and "out of the blue" proposals offer the potential for exceptional outcomes that could serve the public in important ways.

Themes

"Governments will always play a huge part in solving big problems. They set public policy and are uniquely able to provide the resources to make sure solutions reach everyone who needs them. They also fund basic research, which is a crucial component of the innovation that improves life for everyone."

Bill Gates

"Biotech is all about picking the exception."

Bob More, general partner with Frazier Healthcare Ventures.

"Experiments conducted in the microgravity environment of space are not typically at the forefront of the mind of a cancer biologist. However, space provides physical conditions that are not achievable on Earth, as well as conditions that can be exploited to study mechanisms and pathways that control cell growth and function. Over the past four decades, studies have shown how exposure to microgravity alters biological processes that may be relevant to cancer."

Jeanne L. Becker and Glauco R. Souza, Nature Reviews|Cancer. Volume 13. May 2013.

People's view of cancer will change when they have their own relationship with cancer, which everyone will, at some point.

Laura Linney

"A new survey of cancer researchers <in 2013> by the American Society of Clinical Oncology shows that the multiyear stagnation in federal cancer research funding, on top of this year's automatic budget cuts required under sequestration, is having a profound impact on the U.S. cancer research enterprise.

A large majority, 75 percent, of survey respondents reported that the current federal funding situation is having a direct impact on their ability to conduct cancer research, in many cases triggering "devastating" changes. Delayed clinical trials, the elimination of research staff positions, and the halting or slowing of promising research that could lead to new therapies for cancer were cited as specific results of stagnant funding."

American Society of Clinical Oncology

ESO Commercial Microgravity Case Study 1 – Novice Users – A Small Business Perspective

Purpose and Rationale

Image 1

This case study was conducted in FY 2013 by the Emerging Space Office (ESO). The purpose was to begin characterizing the opportunities and challenges encountered by small high-tech businesses whose primary markets are not related to space, but who have legitimate business reasons for considering space research and development for generating novel or improved products.

A biotech company was chosen for this case study because their product offers direct benefits to the public, addresses a mature and growing $93B U.S. industry, and because while there is strong evidence that space flight can offer important advances in this field, there is not yet sufficient proof to attract a wide range of paying customers for space research services.

The primary motivation for ESO's interest in this investigation was to gain insight, through direct support of an emerging commercial space project as a case study, into the conditions important for the successful maturation of the ISS into a multi-faceted, multi-user National Laboratory that provides increasing social and economic benefits to the U.S. economy.

The International Space Station (ISS) is the core of the human spaceflight economic ecosystem in orbit and is the primary test-bed for investigating and understanding how to productively work and live in space.

Achieving the fullest possible commercial utilization of the ISS is vital to delivering a return to the American taxpayers for their investment in the ISS, as well as vital to NASA as it develops long-term sustainable spaceflight and space exploration in Earth orbit and beyond.

Ensuring the full utilization of the ISS requires understanding the needs of emerging commercial entities as they develop spaceflight projects for the first time, as well as understanding the challenges that spaceflight presents for commercial participants, and what NASA can do to help to ensure that as many worthy U.S. organizations as possible are able to surmount these challenges.

The insights gained in this study is also relevant to emerging space companies like SpaceX, Orbital Sciences, and Bigelow Aerospace, who may be looking to attract this type of high tech customer.

This report is not written for bioscientists but rather for knowledgeable professionals in other technical disciplines who may have to make decisions regarding support for these types of commercial space biotech investigations.

The following insights have been derived from direct engagement with the researchers involved in this particular case study but with no other NASA role except that of observer.

ESO Commercial Microgravity Case Study 1 – Novice Users – A Small Business Perspective

Commercial Motivation for Space Research

Image 2

The Case Study focused on Vivo Biosciences Inc. (VBI), an award-winning small biotech business concentrated on 3-D tissue engineering primarily for cancer research, treatment selection, and testing. *(Ref 1, 2)*

VBI customers include pharmaceutical giants such as Merck, Johnson&Johnson, Astellas, Janssen, Roche, and Novartis, as well as smaller but highly respected cutting-edge cancer research companies including Molecular Response and Champion Oncology. *(Ref 3)*

Vivo Biosciences' product HuBiogel™ *(US Patent: 7,727,750, 2010: Novel human biomatrix scaffold for normal & disease models)* addresses important medical topics including cancer and stem cell research and is now beginning to emerge as one of the leading candidates for the selection of chemo-therapies for certain forms of cancer. *(Ref 4)*

Why Microgravity?

The CEO of Vivo Biosciences, Dr. Raj Singh is concerned that VBI may be approaching the limits of what their product can offer medical research and treatment selection, and that the limitation in product performance is caused by gravity. He does not know if research in microgravity can help, but it is one of the only options his company has to overcome negative gravitational effects. *(Ref 5)*

Their primary product line is used in conjunction with the NASA developed rotary cell culture system, now marketed by Synthecon, which mimics a number of microgravity features important for producing high quality 3-D cell cultures. *(Ref 6)*

Prior space flight results and the exceptional performance of the Synthecon Rotary Cell Culture System with its features of low shear and turbulence (features that are even more effective in microgravity) led the CEO of Vivo Biosciences, Dr. Raj Singh, to consider using space microgravity to improve the performance of his product for cancer research and clinical applications. *(Ref 7)*

VBI is looking to develop larger 3-D tissue models that more accurately simulate the behavior of the disease in the human body and believes that space may be the way to achieve it.

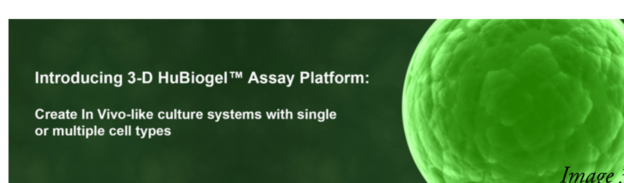


Image 3

ESO Commercial Microgravity Case Study 1 – Novice Users – A Small Business Perspective

Commercial Motivation for Space Research

continued

"The development and validation of reliable in vitro methods alternative to conventional in vivo studies in experimental animals is a well-recognized priority in the fields of pharmaco-toxicology and food research. Conventional studies based on two-dimensional (2-D) cell monolayers have demonstrated their significant limitations: the chemically and spatially defined three-dimensional (3-D) network of extracellular matrix components, cell-to-cell and cell-to-matrix interactions that governs differentiation, proliferation and function of cells in vivo is, in fact, lost under the simplified 2-D condition. Being able to reproduce specific tissue-like structures and to mimic functions and responses of real tissues in a way that is more physiologically relevant than what can be achieved through traditional 2-D cell monolayers, 3-D cell culture represents a potential bridge to cover the gap between animal models and human studies. (Ref 8)

Modelling tissues in 3D: the next future of pharmaco-toxicology and food research? Giovanna Mazzoleni, D. Di Lorenzo, and N. Steimberg

3-D tissue engineering of the kind that VBI's primary product supports is about growing larger and/or better tissues, where the size (*multicellular construct*) is essential to higher quality for medical research.

"*Better*" is specific to the disease biology being studied, changes with each disease, and is the metric of value.

The most important data from *in vitro studies are whether the tissues in culture exhibit characteristics found in patients suffering from a disease with enough fidelity to:**

- **Determine what causes a disease**
- **Understand how a disease progresses**
- **Identify therapeutic targets to interrupt or stop the disease process**
- **Enable very high fidelity testing of treatments.**

Using this information, researchers can determine what can be done to interrupt the disease cycle sufficiently well to mitigate or cure it, and with as few side effects as possible. *(Ref 9)*

High quality tissues that behave as a patient's tissues do *in vivo*** can also be used to test therapeutic strategies.

The quality of the results depends entirely upon how well a tissue mimics what happens in the body (*in vivo).*

This year VBI demonstrated that microtumors grown in its product behaved as they did in certain cancer patients. *(Ref 10)*

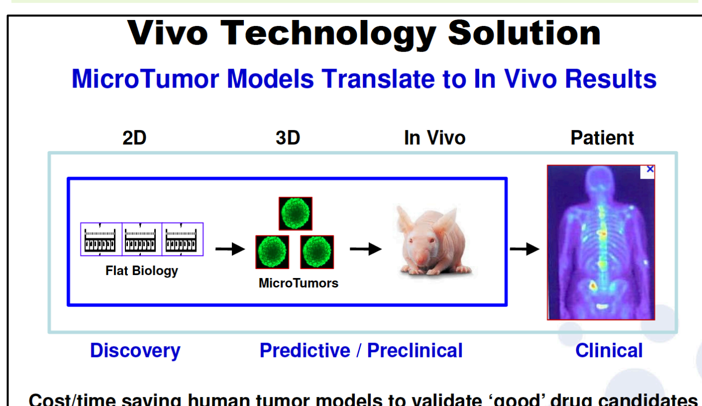


Image 4

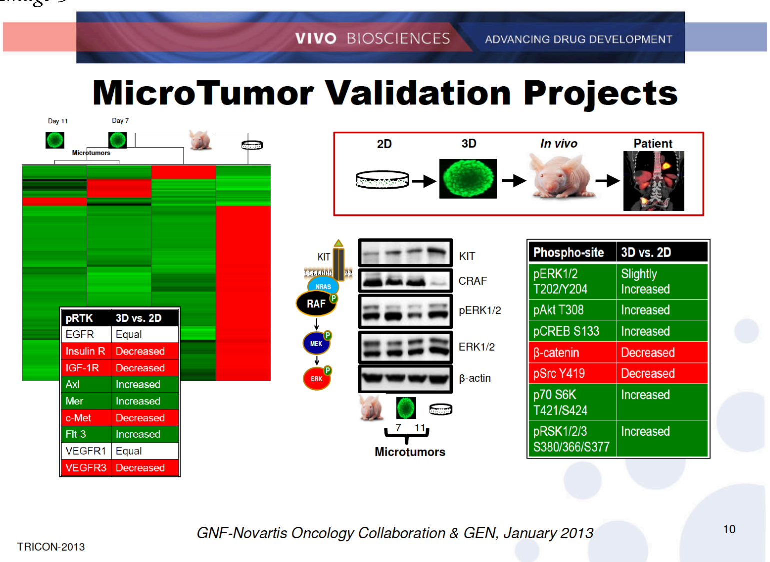
** in vitro is defined as "outside the living body and in an artificial environment" e.g., 3-D tissue cultures*
*** in vivo is defined as "in the living body of a plant or animal," e.g., in the patient's body*

ESO Commercial Microgravity Case Study 1 – Novice Users – A Small Business Perspective

Commercial Motivation for Space Research

continued

Image 5



One important reason that researchers are interested in growing larger tissues with the right characteristics is to study the "ecology" of the spread of a disease, i.e. how the environment around the tumor or infection inhibits or enhances virulence. If there are no effective therapeutics to attack a disease directly, researchers are looking for ways to affect the environment surrounding the affected tissue to inhibit its spread. *(Ref 12)*

Genomics Institute of the Novartis Research Foundation

In a recent R&D collaboration with **Novartis Genomic Institute**, VBI produced hundreds of 3-D human tumors and compared drug response and gene expression profiles with 2-D cultures and *in vivo* studies. Results from five independent projects, validated that 3-D tumor biology and gene targets matched with *in vivo* data but not with 2-D assay outcomes. This further highlights the physiological relevance and prediction value of HuBiogel™ technology. *(Ref 11)*

A factor limiting the size and quality of 3-D tissue and organ cultures on Earth is gravity. Regardless of the tissue culture strategies used to overcome gravitational effects on Earth, when the tissues grow to a size that allows important new insights to be gained, the techniques used to prevent the tissues from settling to the bottom of a culture system are increasingly perturbing, eventually damaging the tissues to the point that they become too unreliable for research. *(Ref 13)*

Image 6

Commercial Motivation for Space Research

continued

While the Case Study was underway, **Champions Oncology** partnered with Vivo Biosciences to use HuBiogel™ to address the selection of chemotherapies for two types of cancer: a drug sensitive and a drug resistant colon cancer. *(Ref 14)*

Champions Oncology provides diagnostic support to physicians using a mouse model to select chemo-therapies. They grow an individual patient's tumor in a mouse, then test a variety of different therapeutic agents to see which drugs work on that specific patient's type of cancer. The problem is that it takes 20-30 weeks to grow the tumors in the mouse and they were seeing too much variability in the results. *(Ref 15)*

Chemotherapeutic agents are poisons that significantly weaken the patient. *(Ref 16)*

They are used because cancer cells are often weaker than healthy cells to certain chemicals and the goal is to eradicate the cancer before killing the patient.

Treating a patient with the wrong chemotherapeutic agent not only will not work, it will further weaken an already seriously ill person.

However, colon cancer is a very aggressive cancer. Thirty weeks can be too long to wait before starting cancer therapy.

CHAMPIONS ONCOLOGY — FINDING THE RIGHT PATIENTS AND THE RIGHT DRUGS

In a blind study using VBI's technology, patient tumors were grown in HuBiogel™ and treated with known drugs along with control samples.

Neither Vivo Biosciences nor Champions Oncology identified which samples were which. Vivo Biosciences submitted the HuBiogel™ test results to Champions Oncology for data analysis.

In the very first study performed, *HuBiogel™ tests were correct in 70-80% of the cases, but it only took 2-3 weeks to get the results and not 30 weeks.* *(Ref 17)*

This speed can make a critical difference for a patient suffering from colon cancer and other aggressive cancers.

The goal now is to predict and achieve >90% accuracy in 2 week analyses. Achieving this accuracy is where VBI believes that space research could make the difference.

Image 7

Scope of Case Study

ESO funds were limited to the first step of development of a commercial biotech flight investigation by a small company (Vivo Biosciences) that had never conducted space research.

The company was chosen through an unsolicited proposal that was technically reviewed for merit. It was determined that the company was credible, at the cutting edge of medically important research and, if the space investigations were successful, the results would provide significant public benefits.

It was also determined that there were almost no funding opportunities for this type of research.

One reason for ESO's interest is that Vivo Biosciences represents the kind of new high tech small business community who might be both early adopters and early successes in the ISS National Laboratory and other commercial space platforms, like a SpaceX Dragon Lab or a Bigelow Space Laboratory.

The specific technical objective was to determine whether existing commercial off-the-shelf hardware would work sufficiently well to meet the VBI's stringent culture requirements on the ground before committing to a space flight project.

The hope is that space would offer medically superior results. If the cultures could not be grown adequately in the flight hardware on the ground, there would be no point in pursuing a flight investigation.

After the initial phase of the study was complete, the intent was to provide this information to CASIS, to NASA's Space Life and Physical Sciences Research and Applications Division, and other interested parties for their consideration, however, ESO did not intend to provide flight funding.

Specifically, ESO provided $50K to Vivo Biosciences to document their experience as they worked with the flight equipment and support of a well-established ISS commercial flight research services provider (BioServe Space Technologies).

The technical goal was to evaluate BioServe's tissue culture hardware (BioCell) to determine if it would support VBI's unique needs for developing a better cancer research tool (focused on colon cancer and breast cancer, initially).

Technical success would be characterized by the ability to grow, on the ground, well-understood test tumors in existing commercial space flight hardware (Bioserve's Biocell).

The goal was to produce, in the flight hardware, tumors of the size and characteristics necessary for scientifically valid results. This is the necessary technical prerequisite for deciding to proceed to flight.

VBI HuBiogel™ plus human tumor cells in BioServe Space Technologies' BioCell initiating flight test.

Image 8

VIVO BIOSCIENCES

ADVANCING DRUG DEVELOPMENT

Science of 3-D Tissue Cultures

From microbe to human, all life that we know begins with a single cell. Cells are the fundamental unit of life. When cells multiply and assemble themselves into an organized structure, it is called a tissue. Tissues assemble into organs. Organs assemble into systems. Systems assemble into all of the unique multicellular creatures of Earth, including humans. The process by which the type of cells in a tissue or organ change is known as *differentiation,* and is an outcome sought from 3-D cultures, whether grown on Earth and in space. *(Ref 18)*

Cell culture is the complex process by which cells are grown under controlled conditions, generally outside of their natural environment (*in vitro*).

Tissue culture is the complex process by which cells taken from a body (*in vivo* cells) and placed in an artificial environment (*in vitro* culture) are managed in such a way as to cause the cells to associate, organize and change (*differentiate*) to form tissues. *(See Image 9)*

Because they reduce misleading variables generated by research in an entire human being or animal model, good tissue and tumor cultures can significantly reduce the time it takes to determine the cause of a disease, to characterize how it progresses, as well as to reduce the time it takes to develop and test effective pharmacological solutions. Good cultures can accelerate research progress by years, saving lives and millions of dollars in the process. *(Ref 19)*

The quality of a tissue or tumor culture depends entirely on how well that culture mimics the dynamics of cells and tissues resident in three-dimensional structures (organs, tissues, tumors) inside the body. *(Ref 20)*

Cells and tissues react based on the physical, chemical and biological signals in their environment. *(Ref 21)*

Cells are not smart, but they are highly adaptable. If they are given the same environmental cues outside the body (*in vitro*) that they receive inside the body (*in vivo*), the cells will behave as if in they are still part of the patient. If they are given different environmental cues, they will react in ways that are not medically useful and may, in fact, be misleading.

Cells and tissues (including tumors) receive information from their entire surface – top, sides, and bottom. Cells and tissues also communicate with each other in complex and subtle, but important, ways.

The goal in tissue cultures is to provide the right environmental cues and manage the development process *in vitro* over days and weeks so that cells and tissues *differentiate* correctly.

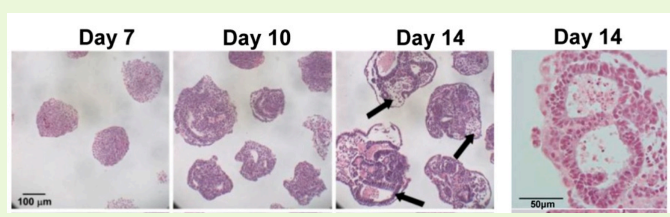


Image: 9. Cell aggregates in culture differentiating into tissues

Genes direct the assembly of particular proteins. We develop from an egg to a human by the production of specific proteins, our health is determined by the production of specific proteins, and we die because of the presence or absence of specific proteins.

The genome is a the complete set of genes in an organism, and each cell contains a full copy of its genome.

Differentiation is caused by the particular combination of genes that are turned on (expressed) or turned off (repressed) in each cell. *(Ref 22)*

The specific pattern of genes expressed or repressed dictates each cell's shape and function, as shown in image 9.

Science of 3-D Tissue Cultures

continued

This process of gene expression is regulated by factors from both within the cell (intrinsic) and outside cells (extrinsic), and the interplay between these cues and the genome affects essentially all processes that occur during embryonic development and adult life. *(Ref 23)*

Cell-extrinsic factors that regulate expression include environmental cues, such as small molecules, nutrients, toxins, temperature, oxygen, … and gravity. These cues can originate from other cells within the organism, or they can come from the organism's environment. *(Ref 24)*

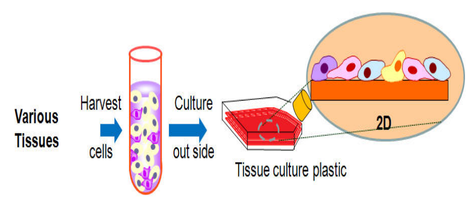
Within the organism, cells communicate with each other by sending and receiving proteins, also known as growth factors, morphogens, cytokines, or signaling molecules. Receipt of these signaling molecules triggers signaling cascades within the cells that ultimately cause semi-permanent changes in the expression of genes. *(Ref 25)*

Such changes in gene expression can include turning genes completely on or off, or just slightly tweaking the level of transcript produced. This process regulates a vast number of cell behaviors.

To produce tissue cultures that mimic what happens in the body, scientists must provide an environment that accurately simulates the environmental cues the tissues received *in vivo*. The better this is done, the more useful the cultures are for medical research.

The problem is that organs and tissues in the body support each other in three dimensions. When they are removed from the body and put in artificial culture systems, gravity prevents the normal development of tissues in ways that often yield misleading results.

Gravity causes cells and tissues that have been removed from the body and placed into petri dishes filled with a nutrient solution to settle to the bottom. The layer of cells in direct contact with the bottom of petri dish change inappropriately in response to contact with the flat surface. This error propagates to the cells above them, and the errors multiply with each new generation of cells.



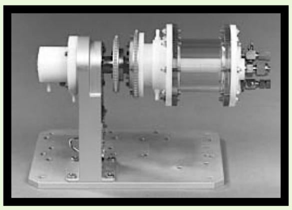
Scientists know this, so in an attempt to overcome the extreme limitations of 2-D tissue cultures, they began suspending the cells in a nutrient solution, using a stirrer and small mixing motor to keep the cells from settling to the bottom. Unfortunately, as the 3-D tissue aggregates get larger, more mechanical energy is required to maintain the tissues in suspension. About the time the tissues become useful to medical research, so much mechanical energy is required to keep them suspended that the sheer and turbulence forces generated by the motor causes the tissues to break apart.

The major advance in this area came from NASA JSC's invention of the Rotating Wall Vessel, a spinoff now being sold by Synthecon and marketed worldwide and is the industry standard in certain types of research, including Vivo Biosciences'. *(Ref 26)*

Science of 3-D Tissue Cultures

continued

Image 10



The basic design of a Rotary Cell Culture system (shown left) is a cylindrical vessel called a bioreactor that is turned on its side and rotated using an electric motor (initially an electric drill). As long as the cylinder is completely filled with nutrient fluid, the cells remain suspended and the low shear and turbulence environment produced higher quality tissues – until the cell aggregates become too large. *(Ref 27)*

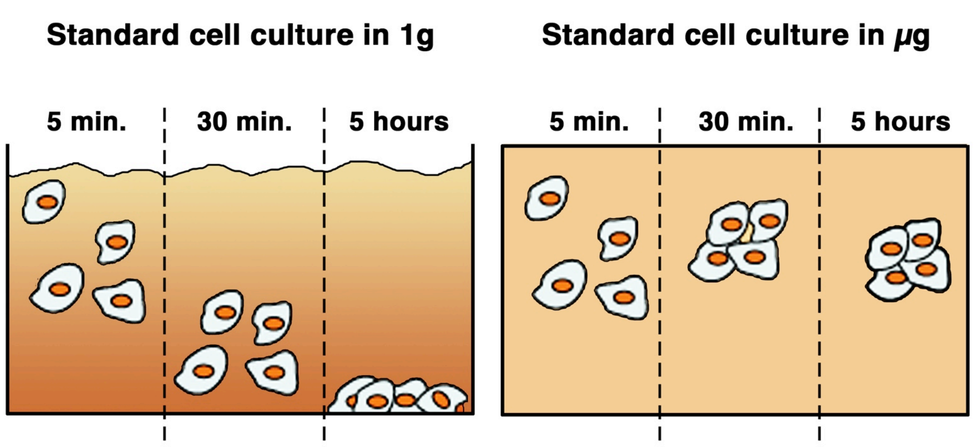
The tissues and tumors produced in the Rotating Wall Vessel are larger than those produced by any other method, but even so, gravity limits the size of the tissues to about 1-2 mm, which is still too small to investigate many of the issues related to cancer, infectious diseases, and organ diseases. *(Ref 28)*

Microgravity does three things.

First, in suspension culture, shear is directly proportional to gravity. Reduction of gravity allows suspension cultures to be managed in a range of shear stresses only available in space (or magnetic levitation but then the flux complicates things). Under these conditions cells of different densities and sizes can be collocated.

Second, convection is reduced in space, which is especially important for gas and other nutrient exchange, and allows study of redox states not available in any other model.

Third, there may be direct effects of microgravity on the cell via microtubules or some other gravity sensor. This is a possibility that is still debated and controversial.



(Left) Cell constructs grown in a rotating bioreactor on Earth eventually become too large to stay suspended in the nutrient solution.

(Right) In the microgravity of orbit, the cells stay suspended. Gentle stirring or rotation is still needed to replenish the nutrients around the cells.

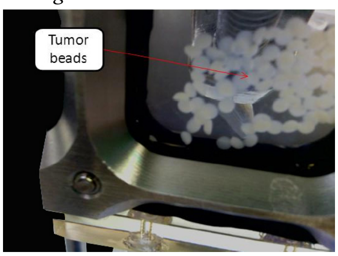
So, in space, the gravitational limitations to the size of tissue cultures are removed.

Then the challenge is to manage the rest of the environmental parameters well enough in space to take advantage of the unconstrained opportunities for tissue and tumor growth. The goal is to produce higher quality, not just larger, tissues and tumors.

This will take a great deal of practice in space. *(Ref 29)*

Results and Findings

Image 11



Research Outcome Sought: **Vivo Biosciences wants to know as soon as possible whether using their product in space will yield knowledge products that result in increased accuracy, prediction and insight in any of the types of cancer research that they support.**

Summary of Research Strategy:

Vivo Biosciences selected representative samples for study (Colon tumor: HT29 and Breast tumor: MDA231) and test protocols were established. *(Ref 28)*

The test would require successfully managing the culture conditions and fixation strategies for 4-6 weeks in the flight hardware under anticipated space flight conditions.

From this, Vivo Biosciences would determine the adequacy of tumor growth and function in the BioCell using imaging and biochemical analyses.

The results would determine whether a flight investigation had a high probability of yielding new important insights for project improvement.

After six months, Vivo Biosciences concluded that some but not all their technical goals could be met because the BioCell chamber was too small.

The most critical technical goal was to produce larger 3-D tumors in HuBiogel™ than could be grown on the ground and with medically important features that could not be achieved in smaller tissues. The BioCell Chamber was too small to achieve this.

However, they did determine that there were no fundamental biocompatibility issues with the BioCell materials; that they could manage the tissue growth environment for the necessary 4-6 weeks; and that the necessary protocols could be automated and would effectively fix samples to produce scientifically valid samples for postflight analyses.

Once hardware modifications are made and flight-tested (BioServe has a manifested flight test on Dragon during fall 2013), the Vivo Biosciences biocompatibility study would need to be repeated in order to confirm that the redesigned hardware will meet the company's technical requirements.

For these reasons, this investigation still remains in the first step of development and provides the first insight of the study:

Commercial biotech research will seek specific research outcomes that are likely to require changes in flight hardware.

Even the initial test and iteration of a flight experiment costs so much time and money that most small companies will be unable to fund flight research without help from the government or other angel investor.

However, these small companies are often the pathfinders for new capabilities in high tech industries.

This is the kind of community that can pioneer important new uses for the ISS National Laboratory, serving both the nation and NASA's interest well.

ESO Commercial Microgravity Case Study 1 – Novice Users – A Small Business Perspective

Results and Findings

continued

From the Emerging Space Office's (ESO) perspective, success in this study was characterized by insights obtained from the experience of a small company, unfamiliar with spaceflight, as they attempted to develop a successful space flight investigation, especially those that can be applied to other similar commercial ventures. This goal was met.

Of the $50K ESO funding *(Ref 29)*:

- $28K supported the Vivo Biosciences PI and a part time temporary research assistant for preparation and analyses;
- $11K went to BioServe Space Technologies for leasing the flight test unit and design services; and
- $11K went for tissue culture supplies and reagents used to grow the tissues.

The result is that the investigation is still not ready to fly because the flight hardware is not configured for the specific research outcome sought by the customer.

Flight accommodations as currently configured are not customer-friendly for novices, although BioServe Space Technologies provided excellent support to Vivo Biosciences throughout the study.

It is because of the quality of BioServe's support and because Vivo Biosciences currently does not have better options than space for product improvement that VBI is willing to continue working towards a flight investigation after this study.

Image 12

If either BioServe's support is unavailable or another option for improved tumor quality arises, it is highly unlikely that Vivo Biosciences would still pursue flight research.

The Case Study illuminated a number of important existing capabilities and exemplars useful to a community of potential commercial customers, such as :

- The existence of a continually operating crewed platform like the ISS,
- The immediate availability of flight hardware,
- Regular flights for payload delivery
- Sample return on SpaceX's Dragon,
- The services of guides like BioServe;

The Case Study also revealed issues that may be common in 3-D tissue research in space in general, and, in particular, with small companies attempting medically oriented commercial research in space. For example:

- Unfamiliar environments,
- Long lead times, high costs of and long delays between iterations,
- Lack of seed funding.

If uncorrected, some of these issues are serious enough to preclude or at least significantly inhibit the participation of paying customers on the ISS or other commercial carriers.

Results and Findings

continued

In biotech, no one does research on the ground the way it has to be done in space.

The Case Study made clear that space research for a commercial company is a very high-risk strategy, even if the potential payoff is high.

Funding opportunities both inside and outside of NASA for this type of research are few.

When the VBI Case Study started, it was not known whether tumors could grow well enough in existing space flight hardware to make a space investigation worth the money, time, and company resources that the attempt would require.

It is still not known, but initial results are promising.

But even if the ground-based biocompatibility study were successful, it would still not be known whether this investigation would be successful in space without doing the experiment in microgravity.

However, because there were no critical flaws and because the hardware issues are being corrected, all participants are still interested in re-doing the biocompatibility test, at a minimum.

It is recommended that NASA support the next iteration and track the next stage of the company's experience because whether VBI's research objectives are met or not, VBI's experience will offer valuable insights NASA and the commercial space community.

Image 13

Terrestrial labs do not have to manage launch stresses, unwanted and non-intuitive effects of microgravity, crew time priorities, re-entry stresses, and post-flight recovery delays.

Space laboratory research is a skill that takes years and multiple hands-on flight experiences to develop. Novice flight investigators need guides.

Laboratory research in microgravity is so different from anything a typical laboratory scientist would experience on Earth that it is akin to pursuing a graduate degree in a new technical subject.

ESO Commercial Microgravity Case Study 1 – Novice Users – A Small Business Perspective

Results and Findings

continued

The role of a mentor or guide who provides a bridge between the needs of a novice flight investigator and the accommodations and constraints of space flight is the single most essential element in crafting a successful research experience for new entrants into space laboratories.

BioServe was a proactive and supportive technical and scientific partner in the development of the research. They provided a significant amount of useful guidance to Vivo Biosciences that shorted their learning cycle.

This is the result of BioServe's long and successful experience in flying pioneer biotech investigations in space and their experience in selecting materials that minimize biocompatibility issues. They are accustomed to working with novice commercial investigators.

The hardware modifications needed for the VBI flight study are relatively minor. This makes the experiment still worth pursuing.

The feedback from Vivo Biosciences and other potential customers helped BioServe decide to modify their flight hardware to enable larger 3-D tissue and organ growth.

The modified flight hardware will be flown on Dragon to ISS in the fall 2013 for testing.

The Case Study became a catalyst for developing improved capabilities based on customer needs, which is another feature of a commercial venture: *timely product improvement based on customer feedback.*

That the International Space Station (ISS) is available for research and that SpaceX Dragon can provide the critical return of samples to earth as well as payload transportation to the ISS were all essential to Vivo Biosciences research goals.

Commercial companies who contemplate using space to improve their product lines are agnostic about which vehicle to use.

They are only interested in selecting the strategy that delivers the highest value at the lowest cost.

For these reasons, multiple flight research platforms are mutually synergistic.   As an example, for VBI's research, sample return is a deal-maker.

Image 14

Results and Findings

continued

Laboratory research is iterative and the first steps often involve calibrating equipment and reagents before the actual research begins. This is especially true for spaceflight. While calibration is a minor step for a terrestrial lab, it is much more difficult and takes much longer both in space and in preparing for space.

For example, after BioServe flies its modified hardware and confirms performance (approximately 6 months after this study was completed), Vivo Biosciences will again need to test their tumor system on the ground in the modified hardware.

The cost and time to do the next iteration for biocompatibility testing for space flight are expected to be roughly the same as in the first study.

Only if the ground tests are successful the second time can the flight phase commence, no earlier than 6 months later. Then another set of anomalies is likely to be encountered in space that requires adjustments to be made and the experiment flown again.

It I almost certain that this process will need to be repeated multiple times in space before a breakthrough or even an insight is achieved.

One thing is clear. Vivo Biosciences, as a small business, is highly unlikely to be able to afford to pay for all of the R&D it needs to achieve a successful outcome from flight research without outside support.

Yet this kind of research could reveal important new insights into what is still one of humanity's most intractable diseases.

Unfortunately, exploratory research, which describes the Vivo Biosciences flight investigation, has far fewer places to go for funding than more mature research ventures.

In some ways, this is what makes commercial space laboratory research and commercial space services such natural partners: both benefit from flight frequency to realize profits.

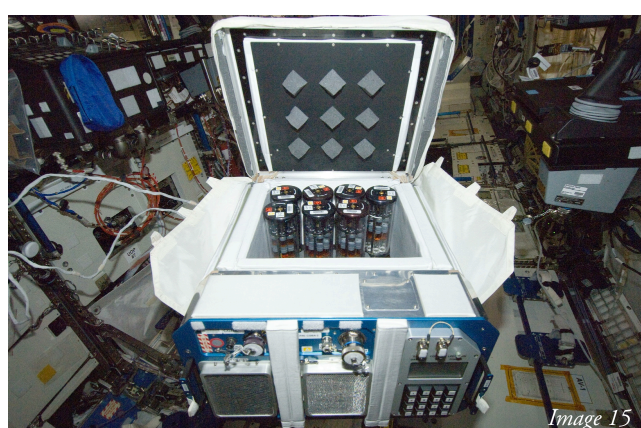


Image 15

Results and Findings

continued

Government support of this type of investigation is not just important, but enabling.

For any company, time is money.

During the six months that Vivo Biosciences conducted this study, it completed two landmark studies for paying customers, which illustrates another point.

The priority of companies, especially small companies, must be to support their paying customers while the space flight investigations are being developed. Often they won't have the resources to do both with internal funds.

It will be another six months before the modified hardware completes its flight test. The next biocompatibility test will take another 2-4 months at best.

If all of that works, then Vivo Biosciences could be manifested for flight 6 months later, assuming that they are selected for funding.

The amount of time it takes to do a flight investigation (months to years) is significantly out of scale with a commercial laboratory investigation on Earth, which measures projects in days to weeks.

Vivo Biosciences believes that removing gravity to obtain larger, better-quality tumors is one of the few, and perhaps the best, option it has for improving research outcomes with their product.

It is clear that given the size of their company and the demands on their resources to support their paying customers, a small company like Vivo Biosciences cannot self-fund research ventures in space.

It is simply too expensive, takes too long, and requires too much specialized knowledge.

Whether Vivo Biosciences can implement its investigation series soon enough, cheaply enough, and well enough to meet their needs, still remains to be seen.

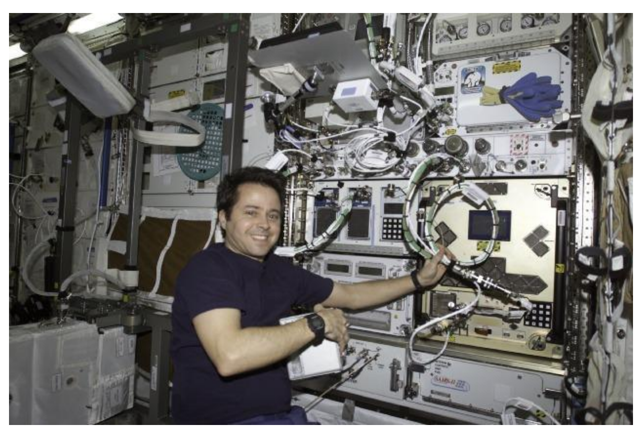


Image 16: When Vivo Biosciences investigation is ready to fly, the experiment will be conducted in BioServe's Commercial Generic Bioprocessing Apparatus (CGBA) shown here on the ISS.

ESO Commercial Microgravity Case Study 1 – Novice Users – A Small Business Perspective

Results and Findings

continued

Nationally, there are insufficient funds for this type of early stage exploratory applications research that investigates promising but unproven microgravity techniques and addresses a terrestrial versus space need.

Once a company has determined that their product development is limited by gravity, the next step is to determine whether any funding opportunities exist to support its development.

In this economy, even large corporations are limiting their high risk high payoff IRAD investments. Small companies usually can't afford them at all.

Successful mature research that has demonstrated desirable results for high priority medical problems and has a clear hypothesis to be tested has many opportunities to compete for funding.

Pharmaceutical companies, philanthropic organizations, sometimes venture capitalists as well as government, are willing to help an obviously promising and medically important technology to market. And they should. This is a good investment.

However, exploratory applications R&D, like that proposed by Vivo Biosciences, is at the earliest stages of credible research, often too immature for even basic research funding.

NIH funds almost no research for space applications.

NASA's Space Life and Physical Sciences Research Program funds basic research but not applied research for commercial terrestrial market.

NASA's Biomedical Research Program is focused on astronaut health.

The Center for the Advancement of Science in Space (CASIS) is the most appropriate funding source for this kind of work, but they have a very low research budget for the scope of flight activities in their portfolio. However, even CASIS prefers more mature investigations to support with their limited research dollars.

Exploratory research that is high risk (it probably won't work right way) and high payoff (but it is a breakthrough if it does) needs more support.

Funding for this type of research is usually in the purview of the government and angel investors. Even corporate IRAD usually won't support it.

And a small business like Vivo Biosciences can't afford to self-fund a lengthy and expensive flight investigation even if they were confident that it would work.

Yet exploratory research is where revolutionary breakthroughs often begin.

"A reinvented business model won't change what is fundamental: Higher pipeline productivity in the form of new patented products is still the best source of future profits." [30]

PharmaExec. Com Jan. 1. 2012

Conclusion

"Congress declares that the general welfare of the United States requires that the Administration seek and encourage, to the maximum extent possible, the fullest commercial use of space."

Space offers potentially important new opportunities for commercial R&D that could result in significant public benefits. But …

It will take the companies a significant amount of practice in space to achieve the necessary research outcomes reliably and predictably.

Because of the uncertainties inherent in flight investigations, the expectation that the ISS National Lab will attract a large number of paying customers under the current conditions (high start-up costs, unfamiliar procedures, lengthy development times, high risk of insufficient outcome and long delays between iterations) is unrealistic.

It will take more seed funding by the government, CASIS, or other angel investors, because few, if any, small biotech companies like Vivo Biosciences can afford to pay for flight development, no matter how great the potential space offers and no matter how few other options are available to them on Earth to meet their needs.

And while larger companies may have more flexibility to fund research, space remains a virtual unknown to them and a very difficult place to conduct work compared with their other options.

Unless they have no choice or are supported by external funds, most companies will stay with ground-based research.

The government in general and NASA in particular can play a key role in the development of this emerging field.

In fact, if the government does not help this new field of laboratory sciences to grow, it is unlikely to develop the critical mass of talent and ideas necessary to achieve breakthroughs that can yield a better return on the taxpayers' investments. The ISS and commercial space synergy is capable of delivering more value.

However, it will take more resources than are currently being allocated to exploratory research -- and not by reallocating funds from other ISS research efforts. The current research efforts are synergistic with and inspire new exploratory research applications. The investment pool needs to grow, not be redistributed.

Breakthroughs will also take more opportunities to learn and refine strategies in space.

The necessity of faster iteration will require a more user-friendly set of policies and protocols (for both the customer and for the NASA or commercial flight services providers) that accommodates the needs and pressures of America's innovative high tech businesses and the requirements and challenges of safely managing investigations in space.

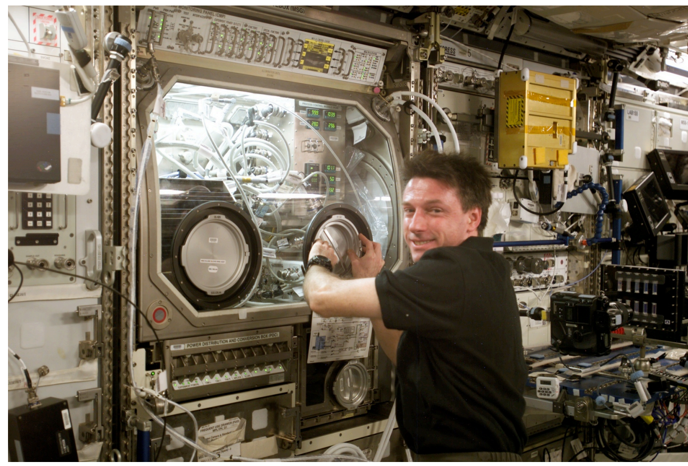
These are not easy challenges, but the potential payoff is worth the effort and the investment.

ESO Commercial Microgravity Case Study 1 – Novice Users – A Small Business Perspective

Recommendations

"Congress declares that the general welfare of the United States requires that the Administration seek and encourage, to the maximum extent possible, the fullest commercial use of space."

Image 17



Dr. Jeanne Becker fairly pointed out both the possibility and the uncertainty inherent in cancer research in space in her landmark review article in Nature [31]:

"Experiments conducted in the microgravity environment of space are not typically at the forefront of the mind of a cancer biologist.

However, space provides physical conditions that are not achievable on Earth, as well as conditions that can be exploited to study mechanisms and pathways that control cell growth and function.

Over the past four decades, studies have shown how exposure to microgravity alters biological processes that may be relevant to cancer …

Combination of the resources available in the unique environment of microgravity with the tools and advanced technologies that exist in the laboratories across Earth may inform new research approaches to expand the knowledge necessary for improving treatment options, and enhancing the quality of life for those affected by this illness."

One thing is clear.

There is no way to develop, or even determine, the value of removing gravity for advancing this type of potentially life saving research without doing the experiments in space.

Recommendations:

Therefore, it is strongly recommended that, at a minimum, NASA and/or CASIS continue to support VBI's investigation through flight and that ESO monitor its progress because of its potential benefit to public health; its utility as a Case Study for this class of commercial biotech research in space for a terrestrial (rather than space) market; and its value in understanding and better developing the commercial research and applications potential of the ISS and the emerging commercial space transportation and service providers.

Further it is strongly recommended that NASA establish funded solicitation mechanisms to encourage worthy applications R&D in space, at least through the initial flight test, when such studies have the potential to yield important public benefits, even if they don't provide a NASA application or fit within standard programmatic boundaries.

ESO Commercial Microgravity Case Study 1 – Novice Users – A Small Business Perspective

Recommendations

"Congress declares that the general welfare of the United States requires that the Administration seek and encourage, to the maximum extent possible, the fullest commercial use of space."

Mentors, advisors, guides and integrators (MAGIs) who can help a novice craft a successful flight experiment -- like those at Bioserve Space Technologies, Dr. Lawrence DeLucas at University of Alabama, Nanoracks, and investigator flight support groups at NASA Centers -- are essential to the development of the ISS National Laboratory and the commercial microgravity laboratory market of emerging space companies.

Because they play such essential roles in delivering value back to the public from spaceflight, it is recommended that the MAGIs be supported to maintain critical staff expertise during the intervals between funded flight developments.

Novel research of the kind that can lead to breakthroughs will almost always require hardware modification.

Some mods will be relatively easy and cheap, like those required by Vivo Biosciences. But some that are important for opening new markets – like onboard analyses and the ability to handle sensitive biological samples on the launchpad, through the launch interval, and during return to Earth – may need funding in the $5M-$10M+ category.

However, given the magnitude of taxpayer investments required to build the ISS and the billions of dollars per year spent in operating it, increasing funding to support more space research for public benefit and increasing the investment in infrastructure that opens new fields and makes breakthroughs possible is a sound and worthy strategy, even with the challenges of sequestration.

Finally, it is strongly recommended that NASA and CASIS continue their wise practice of encouraging and supporting exceptions to standard plans and procurement strategies for flight studies when "out of the box" and "out of the blue" proposals offer the potential for exceptional outcomes that could serve the public in important ways.

Without ESO's support of the first stage of the VBI's flight concept, this important story of the ISS, potential public health benefits, and new commercial interests for using space would not have been told.

The findings are relevant and timely, not only to NASA and CASIS who are working to amplify the value of the ISS system for public benefit, but also to emerging space companies seeking to understand the needs of potential new customers for the economic development of space.

Experiments like the one proposed by Vivo Biosciences don't fit easily within traditional programmatic constraints. But as often observed, new discoveries, disruptive technologies, and innovation rarely do.

Image 18

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Image 1 Image of SpaceX Dragon Capsule attached to the International Space Station. Space.Com. http://www.space.com/15476-gallery-spacex-capsule-space-station-guide.html

Image 2 Vivo Biosciences Clients and Collaborators. New High Throughput Human Micro Tumor Assay Platform for Pre-clinical Drug Development. Raj Singh. Molecular Medicine Tri-Conference TRICON-2013. https://dl.dropboxusercontent.com/u/51989053/Vivo%20Biosciences%20Final%20Report/TRICONSpkr%20RSingh-Fnl%2021413.pdf

Image 3 Vivo Biosciences Hu-Biogel™ from the Vivo Biosciences website. http://www.vivobiotech.com/

Image 4 Describes how Vivo Biosciences' MicroTumor Models translate into clinical results for patient drug treatment. New High Throughput Human Micro Tumor Assay Platform for Pre-clinical Drug Development. Raj Singh. Molecular Medicine Tri-Conference TRICON-2013. https://dl.dropboxusercontent.com/u/51989053/Vivo%20Biosciences%20Final%20Report/TRICONSpkr%20RSingh-Fnl%2021413.pdf

Image 5 Describes MicroTumor Validation Projects with Novartis Oncology. New High Throughput Human Micro Tumor Assay Platform for Pre-clinical Drug Development. Raj Singh. Molecular Medicine Tri-Conference TRICON-2013. https://dl.dropboxusercontent.com/u/51989053/Vivo%20Biosciences%20Final%20Report/TRICONSpkr%20RSingh-Fnl%2021413.pdf

Image 6 Describes Vivo Biosciences Desired Outcomes. From the Vivo Biosciences website. http://www.vivobiotech.com/

Image 7 Describes Vivo Biosciences Desired Outcomes. From the Vivo Biosciences website. http://www.vivobiotech.com/

Image 8 Image of VBI HuBiogel™ plus human tumor cells in BioServe Space Technologies' BioCell initiating flight test. Appendix III Vivo Biosciences Final Report. https://dl.dropboxusercontent.com/u/51989053/Vivo%20Biosciences%20Final%20Report/NASA-Ames%20Vivo%20Report%205-13.pdf

Image 9 Image showing how cells aggregate in culture and differentiate into tissues. Histone H1 Depletion Impairs Embryonic Stem Cell Differentiation. Zhang Y, Cooke M, Panjwani S, Cao K, Krauth B, et al. (2012) PLoS Genet 8(5): e1002691. doi:10.1371/journal.pgen.1002691

Image Captions and Credits

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Image 10 Early design of NASA's Rotating Wall Vessel. NASA Educational Brief. NASA's Bioreactor: Growing Cells in a Microgravity Environment. EB-2002-12-187-MSFC. pdf

Image 11 Vivo Biosciences HuBiogel™ and tumor beads close-up in BioServe BioCell. Appendix III Vivo Biosciences Final Report. https://dl.dropboxusercontent.com/u/51989053/Vivo%20Biosciences%20Final%20Report/NASA-Ames%20Vivo%20Report%205-13.pdf

Image 12 BioServe Space Technologies Logo. http://www.colorado.edu/engineering/BioServe/

Image 13 ISS026-E-018760 (18 Jan. 2011) --- NASA astronaut Catherine (Cady) Coleman, Expedition 26 flight engineer, performs a Capillary Flow Experiment (CFE) Interior Corner Flow 2 (ICF-2) test. The CFE is positioned on a Maintenance Work Area in the Destiny laboratory of the International Space Station. CFE observes the flow of fluid, in particular capillary phenomena, in microgravity.

Image 14 Artist Compsite drawing showing possible future synergies for space biotech work. L. Harper. NASA ARC.

Image 15 Photograph of BioServe's CGBA during Increment 33 showing open containment volume and sample canisters. Image courtesy of NASA. http://www.nasa.gov/mission_pages/station/research/experiments/CGBA.html

Image 16 NASA Image: ISS004E11048 - Commercial Generic Bioprocessing Apparatus (CGBA) Isothermal Containment Module (ICM) v.3, installed in EXpedite the PRocessing of Experiments to Space Station (EXPRESS) rack 4 just above Expedition 4 flight engineer Dan Bursch's extended left arm.

Image 17 Expedition 8 Commander and Science Officer Michael Foale conducts an inspection of the Microgravity Science Glovebox. http://spaceflight.nasa.gov/gallery/images/station/crew-8/hires/iss008e20622.jpg

Image 18 Artists concept of the International Space Station against the backdrop of the Earth's horizon. http://wallpaperswa.com/thumbnails/detail/20120811/outer%20space%20satellite%20orbit%20international%20space%20station%20space%20station%20artwork%201920x1080%20wallpaper_wallpaperswa.com_65.jpg

Appendix Links

Appendix I: Vivo Biosciences Proposal	https://sites.google.com/site/esocasestudyvivobiosciences/eso-appendices
Appendix II: Vivo Biosciences Technical Reviews	https://sites.google.com/site/esocasestudyvivobiosciences/eso-appendix-ii-vivo-biosciences-technical-reviews
Appendix III: Vivo Biosciences Final Report	https://sites.google.com/site/esocasestudyvivobiosciences/eso-case-study-appendix-iii
Appendix IV: Vivo Biosciences Presentation to Tricon on results of blind studies for cancer research with Champion Oncology and Novartis Genomic Institute	https://sites.google.com/site/esocasestudyvivobiosciences/eso-appendix-iii-vivo-biosciences-final-report