A Good Neighborhood for Cells

Bioreactor Demonstration System (BDS–05)

Good neighborhoods help you grow. As with a city, the lives of a cell are governed by its neighborhood connections. Connections that do not work are implicated in a range of diseases. One of those connections — between prostate cancer and bone cells — will be studied on STS–107 using the Bioreactor Demonstration System (BDS–05).

Prostate cancer strikes about 200,000 men a year and is easily cured when diagnosed early, according to the American Cancer Society. Once it spreads to the skeleton it is inevitably fatal and kills more than 30,000 men a year. The public health cost is more than $2 billion a year. To improve the prospects for finding novel therapies, and to identify biomarkers that predict disease progression, scientists need tissue models that behave the same as metastatic or spreading cancer.

Prostate cancer is a key health issue that eventually affects 1 in 6 American males. For African-American males, the disease and mortality rates are up to 50 percent and 200 percent higher, respectively, according to the National Prostate Cancer Coalition.

This is one of several NASA-sponsored lines of cell science research that use the microgravity environment of orbit in an attempt to grow lifelike tissue models for health research.

As cells replicate, they "self associate" to form a complex matrix of collagens, proteins, fibers, and other structures. This highly evolved microenvironment tells each cell who is next door, how it should grow and into what shapes, and how to respond to bacteria, wounds, and other stimuli.

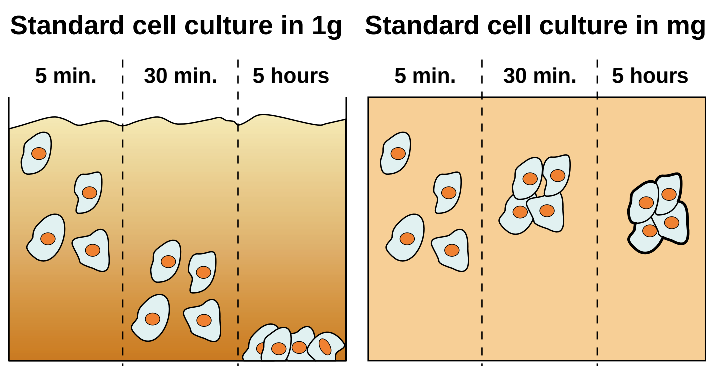
Studying these mechanisms outside the body is difficult because cells do not easily self-associate outside a natural environment. Most cell cultures produce thin, flat specimens that offer limited insight into how cells work together. Ironically, growing cell cultures in the microgravity of space produces cell assemblies that more closely resemble what is found in bodies on Earth.

NASA's Bioreactor comprises a miniature life support system and a rotating vessel containing cell specimens in a nutrient medium. Orbital BDS experiments that cultured colon and prostate cancers have been highly promising. Long-duration experiments are planned for the *International Space Station* where multiple generations of cells can be grown.

Targeted health issues

Therapies: Musculoskeletal tissue disorders (in space and on Earth)
Cancer models: Prostate, breast, ovary, lung, and colon cancers
Diabetes: Pancreatic tissue for transplant
Drug efficacy: Non-animal/nonclinical testing of drug effects and toxicity

On STS–107, the BDS will grow a three-dimensional prostate culture model to support studies of the cellular interaction between the prostate and bone stromal (connective tissue) cells. The model will help scientists assess the effects of gene therapy on the growth of prostate cancer cell aggregates in research, clinical diagnoses, and treatments.



Cell constructs grown in a rotating bioreactor on Earth (left) eventually become too large to stay suspended in the nutrient media. In the microgravity of orbit, the cells stay suspended. Rotation then is needed for gentle stirring to replenish the media around the cells.

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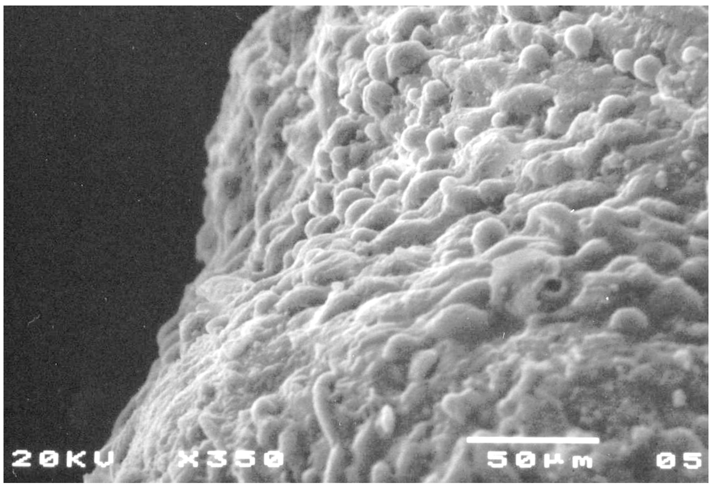
Background Information

Science

A key factor in the growth of prostate cancer is the stimulation of tumor cells by the hormone testosterone. Understanding the factors that control the reproduction and spread of tumor cells will help researchers discover how to slow or stop the growth of a cancer. The BDS–05 experiment will culture human prostate cancer cells in microgravity so investigators can characterize the biochemical, molecular, and behavioral alterations of prostate cancer cells derived from reconstituted prostate organoids (RPCaO) grown under hormone-enriched or -deprived conditions. This will support studies of the "bystander" effects of toxic gene therapy on organoids. The ultimate goal is to develop a model for preclinical studies of drug and gene therapy, preparatory to the establishment of an effective clinical trial protocol.



This prostate cancer construct was grown during NASA-sponsored bioreactor studies on Earth. Cells are attached to a biodegradable plastic lattice that gives them a head start in growth.

Flight Research Equipment

The heart of the BDS is a clear plastic rotating wall vessel, about the size of a soup can, containing the cell culture. A cylindrical filter down the center of the vessel rotates with the vessel and passes oxygen in and carbon dioxide out. Periodically, spent media are pumped into a waste bag and replaced by fresh media. The vessel rotates to provide gentle stirring of media without causing shear forces that would damage or kill the cells.

An Experiment Control Computer controls the Bioreactor, records conditions, and alerts the crew when problems occur. The crew operates the system through a laptop computer. The Biotechnology Specimen Temperature Controller holds cells until their turn in the Bioreactor, and a Biotechnology Refrigerator holds fixed tissue culture bags at 4 °C (39 °F) for return to Earth and analysis. A Gas Supply Module provides oxygen.

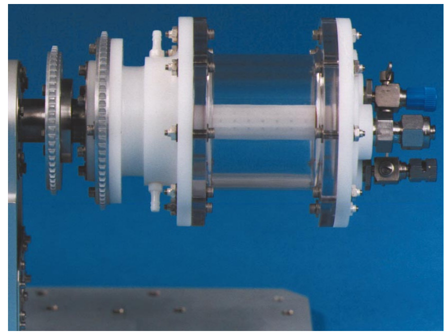
Research partners

National Institutes of Health: Center for Three Dimensional Tissue Culture, studying HIV-1 pathogenesis in tissue models, among other health issues.

Juvenile Diabetes Foundation: Studying the best route for cultivating and transplanting beta cells into Type 1 diabetics.

StelSys: Research in drug development and on a liver-assist device.

On STS–107, the crew will monitor the BDS, inject specimen cells, and periodically withdraw and fix cells and media samples for post-flight analyses. The crew also will exchange media bags as needed. At the end of the mission they will deactivate the system and fix all remaining cultures.



The major component of the Bioreactor Demonstration System is the transparent rotating wall vessel. It resides in a locker containing nutrient media bags and an oxygenator, plus associated plumbing to operate the system.

Previous Results

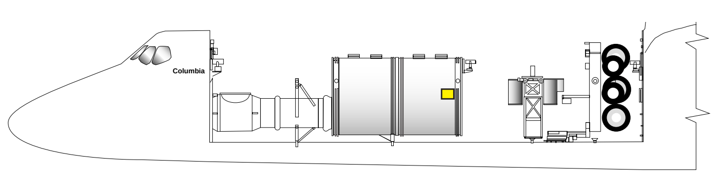
Experience aboard *Mir* has turned microgravity Bioreactor research into a mature science. In its first long-duration experiment, large cultures of bovine cartilage cells grew in the Bioreactor. The last NASA stay aboard *Mir* was crucial as it brought everything together in an effort to culture human tissue in the Bioreactor. Since then, the NASA Bioreactor team has been synthesizing these lessons into an advanced program being developed for the *International Space Station*.

The principal investigator's team has conducted extensive ground-based experiments on prostate tumors in rotating-wall vessels and developed an extensive understanding of many of the chemical pathways and chromosomal changes involved in growing prostate cells. One set of results suggests that bone stromal cells can serve as "suicidal carriers" that deliver and express toxic genes that mediate tumor cell kills *in vivo*.

Commercial applications

In 1990, NASA granted Synthecon Inc. of Houston an exclusive commercial license to NASA patents for the bioreactor system. Since then, Synthecon has sold more than $2 million worth of Rotary Cell Culture Systems™ and sponsored several related research agreements.

In 2000, NASA signed a Space Act Agreement with StelSys, a new venture formed by Fisk Ventures, Inc. and In Vitro Technologies, Inc. StelSys, based in Baltimore, will develop commercial medical products based on Bioreactor technology. They will focus on drug development and a liver-assist device for patients in need of transplant surgery.



Approximate location of this payload aboard STS–107.

Photos. NASA.