ISS National Laboratory Research Potential

There are many areas of opportunity for basic and applied research on the ISS National Laboratory, in fields that are high priorities for Federal agencies and commercial enterprises. NASA-sponsored research and private sector-sponsored space projects prior to the implementation of the Vision for Space Exploration have made substantial investments that will help guide future activities. Some promising areas include:

Research on the culture of human tissues, to provide tools for biomedical researchers to develop treatments and test therapies in effective model systems. Human tissue culture research by NASA has contributed significantly to understanding the role of mechanical stress and fluid transport in cell and tissue culture. NASA has developed a number of bioreactor technologies for very low-stress culture of human tissues in liquid suspension. This technology has been demonstrated to yield extremely desirable results in a number of challenging problems in the culture of mature, differentiated, three-dimensional tissues. Space provides an extremely low-stress environment for tissue culture, much lower than is possible on Earth, and promises to extend the results of the NASA bioreactor to a new range of problems. Dr. J.M. Jessup, now at the National Cancer Institute, uses a NASA-developed bioreactor to learn how colon cancer tumors metastasize. Extending projects such as his to flight could be a priority area for interagency work under the National Laboratory. In the following abstract of a paper presented by Dr. Jessup and his colleagues at the American Association for Cancer Research 2006 Annual Meeting, results of his NASA-sponsored project are presented.

Laguinge, L.M.; Samara, R.; Jessup, J.M. "TRAIL DR5 receptor mediates anoikis in human colorectal carcinoma cell lines through the extrinsic apoptotic pathway"Paper #756, Annual Meeting of the American Association for Cancer Research, April 2006.

Abstract

Human colorectal cancer (CRC) cells must detach from a substratum to metastasize to distant sites. During this process CRC are susceptible to detachment-induced cell death or anoikis - a form of programmed cell death (apoptosis) that occurs when anchorage-dependent cells go into suspension. Our purpose was to identify the mechanism that mediates anoikis in human CRC. Since we have previously shown that metastatic potential of CRC is inversely associated to anoikis, we used weakly metastatic (MIP-101 and Clone A), and highly metastatic (CX-1 and MIP-101.8) CRC cell lines. CRC were cultured on PolyHEMA-coated surfaces for 1 - 4 days to induce apoptosis which was measured by TUNEL or Annexin V/Propidium Iodide flow cytometry. CRC cultured for at least 24 hr had death rates >5% compared to <1% for CRC in attached monolayers. We then assessed whether caspases of the extrinsic (Caspase 8) or intrinsic (Caspase 9) death pathway were active and found that Caspase 8 and Caspase 3 were cleaved during exposure to suspension culture in four CRC lines and cell death was inhibited by caspase 3 and 8 inhibitors but not by a caspase 9 inhibitor. Gene expression analysis of death receptors in CRC 24 hr in suspension was confirmed at the protein and gene transcript level and revealed increased expression of DR5 and osteoprotegerin but not DR4, Fas,

CD27, CD30 or CD40. Treatment with 5 µg/ml of antagonistic antibody to DR5 inhibited anoikis in 3 of 4 human CRC lines but treatment with a similar DR-4 antibody reduced anoikis only in CX-1 and MIP-101. Anti-DR5 antibody decreased caspase 8 activation in MIP-101 cells in suspension. siRNA to DR5 specifically reduced expression of DR5 and inhibited anoikis to levels significantly below transfection controls that included siRNA to DR4 for up to 4 days. In summary, DR5 receptor mediates death signals for anoikis in human CRC cells through the extrinsic apoptotic pathway.

Research on liquid crystal physics for advanced displays and other novel applications. In space. states of matter that are particularly sensitive to disturbances arising from their own density can be studied, with unique insights obtained. In this example, Professor Noel Clark of the University of Colorado and his colleagues are preparing to examine the physics of two-dimensional films of liquid crystals in experiments on the ISS. Professor Clark is also the Principal Investigator for a National Science Foundation-sponsored Materials Research Science and Engineering Center for liquid crystal materials. His center is one of the principal centers of liquid crystal study and expertise in the US, with a broad range of basic and applications-oriented research. There is a clear opportunity for interagency cooperation through the National Laboratory in the physics of liquid crystals. The publication abstract below from Professor Clark describes ground-based progress on some of the phenomena of interest to physicists:

Pattanaporkratana A., Park C.S., Maclennan J, and N. A. Clark
Direct Measurement of Interaction Forces between Islands on Freely Suspended Smectic C Films Using Multiple Optical Tweezers, Electronic-Liquid Crystal Communications, http://www.e-lc.org, December 2006

Abstract
Smectic liquid crystals can be made to form freely suspended films, two-dimensional systems locally quantized in thickness by an integral number of smectic layers, on which islands, circular regions of greater thickness than the surrounding film area, can be generated. In smectic C films, each such island is accompanied by a topological defect pair, an s = +1 topological defect inside and an s = -1 defect nearby on the background film. The distortions of the in-plane orientational order of the smectic C director field result in elastic interactions between the islands, with a short-range repulsion and a long-range dipolar attraction governing their stability and leading to their organization in chain-like structures with an equilibrium island separation. We demonstrated previously that such islands can be manipulated using optical tweezers. Using an acousto-optically scanned infrared laser system to generate dynamically controllable, multiple optical traps, we have now directly measured the repulsive and attractive elastic interaction forces between smectic C* islands and have compared the results quantitatively with theory. We find that the interactions between islands are much smaller in the racemic smectic C case than in the chiral smectic C*, an effect we attribute to long-range coulombic forces arising from polarization charges.

Research on the physics of macromolecular crystallization, aiding in the advance of molecular biology for biomedical applications. Difficulties in the growth of high quality crystals of biological macromolecules, such as proteins and complexes of proteins and nucleic acids, is a major factor limiting the advance of knowledge in molecular biology. Space research has stimulated much new thinking about the detailed mechanisms of macromolecular crystal growth, and the origin of defects in macromolecular crystals. Much remains unknown, and crystal growth retains many aspects of trial and error. Space-based crystal growth has shown promising results in a number of challenging cases. Potential National Laboratory participants in this area could include biomedically oriented researchers sponsored by Federal agencies, commercial organizations, or scientists interested in advancing the tools available for biological science.

An example of the use of space-grown protein crystals to obtain high-resolution structural information is in the following publication abstract:

A. Vahedi-Faridi, J. Porta, and G. E. O. Borgstahl Improved three-dimensional growth of manganese superoxide dismutase crystals on the International Space Station
Acta Crystallographica (2003). D59, 385

Abstract
Manganese superoxide dismutase was crystallized in microgravity with 35 PCAM experiments (Protein Crystallization Apparatus for Microgravity) on the ISS (International Space Station) from 5 December 2001 to 19 April 2002. Crystals were very large in size and could easily be seen by eye. Crystals with 0.45 × 0.45 mm cross-sections and of up to 3 mm in length were obtained in several drops: an 80-fold increase in crystal volume compared with the largest earth-grown crystal. A smaller crystal (0.15 × 0.30 mm in cross-section and 1.6 mm in length) was soaked in cryoprotectant and placed in a cryoloop. Diffraction data were collected at 100 K at the BioCARS bending-magnet beamline. The space group was C2221, with unit-cell parameters a = 100.64, b = 107.78, c = 179.82 Å. Diffraction spots to 1.26 Å resolution were observed. Unfortunately, the high-resolution diffraction degraded owing to radiation damage and the resolution limit for the complete data set was 1.35 Å. It is anticipated that increasing the crystal volume and diffraction limit through microgravity crystal growth will enable several types of technically challenging structure determinations.

Research using the space environment as a probe to develop therapeutic insights in areas such as osteoporosis and bone disorders, neurovestibular diseases, muscle wasting conditions. The space environment produces effects on the human body effects that can resemble in many ways diseases and disorders encountered in Earth-based medical practice. Research in space physiology provides a unique window into the origins and treatment of diseases that impact millions of Americans. NASA currently partners with a consortium of leading national research institutions, the National Space

Biomedical Research Institute, to conduct research in this area. The potential for further collaboration with Federal and private organizations appears high.

The FOOT experiment, which has recently been completed on the ISS, is an example of research on bone loss in space. The abstract of a recent publication from the project describes some preliminary results:

Pierre MC, Genc KO, Litow M, Humphreys B, Rice A, Maender CC, Cavanagh PR. Comparison of Knee Motion on Earth and in Space: An Observational Study. Journal of Neuroengineering and Rehabilitation. 2006; 3:8.

Abstract

Background: Spaceflight has been shown to case atrophy, reduced functional capability, and increased fatigue in lower-limb skeletal muscles. The mechanisms of these losses are not fully understood, but are thought to result, in part, from alteration in muscle usage.

Methods: Knee-joint angles and lower extremity muscle activity were measured continually, via electrogoniometry and surface electromyography respectively, from two subjects during entire working days of activity on Earth and onboard the International Space Station (ISS).

Results: On Earth the distribution of angular positions of the knee was typically bimodal, with peaks of >75 degrees of flexion and almost full extension (<15 degrees of flexion). However, on the ISS, a single peak in the mid-range of the available range of motion was seen. The knee joint was also moved through fewer excursions and the excursions were smaller in amplitude, resulting in a reduced span of angles traversed. The velocities of the excursions in space were lower than those used on Earth.

Conclusion: These results demonstrate that, in space, overall knee-joint motion is reduced, and there is a transformation in the type of muscle action compared to that seen on Earth, with more isometric action at the expense of concentric and particularly eccentric action.