

Three Dimensional Human Tissues as Surrogates for Suborbital & Orbital Research into Human Cellular Genomics, Proteomics, and Metabolomic Tissue Responses During Transitional Space Flight"

Next Generation Sub-Orbital Researchers Conference February 2010

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> > 20 February 2010



In Less Than 8 Minutes

In 4-5 Minutes The Human Brain Deprived Of Oxygen Goes Into Irreversible Coma Usually Resulting In A Persistent Vegetative State

In Less Than 8 Minutes A Blood Ph Of At Or Below 7.1 Will Result In Loss Of Consciousness And If Not Corrected Death. (Normal Range 7.35-7.45)

In Less Than 8 Minutes Changes In Na⁺⁺, K⁺, Mg⁺⁺ Below Normal Physiological Ranges May Result In Seizures And Brain And Cardiovascular Damage.

> WHAT ACTUALLY HAPPENS IN THE 8 MINUTE TRANSIT TO SPACE AT THE SYSTEMS BIOLOGY LEVEL ????

Expertise in Growing/Engineering 3D Human Cells/Tissues





Microgravity Research Models



STS-79/Mir 3; Tissue Engineering of Cartilage in Space; Proc. Natl. Acad. Sci. 94 (25) pp. 13885-13890 Dec. 1997. Freed, L.E., Robert Langer, I. Martin, N. Pellis, and G. Vunjak-Novakovic

STS-107 Columbia; Prostate Cancer Experiment: "Three-dimensional co-culture models to study prostate cancer growth, progression, and metastasis to bone". Review: *Seminars in Cancer Biology,* (15) 353-354, 2005. Wang Ruoxiang , Jianchun Xu, Lisa Juliette, Agapito Castilleja , John Love , Shian-Ying Sunga, Haiyen E. Zhaua, Thomas J. Goodwin, Leland W.K. Chung.



Gene Expression in Microgravity



•The response of human cells to microgravity is fundamental to the adaptation of terrestrial life to low gravity environments and is reflected in the genes that are activated in space.

•In May of 1999 Drs. Tim Hammond of Tulane University and Thomas J. Goodwin of NASA/JSC published their first findings from microgravity and bioreactor experiments on the genes that are turned on and off when human embryonic kidney cells are transitioned to space (*Nature Medicine* 5/99)



Genomics (DNA) ~ 47,000 Genes

Expertise in 3D Physiology and Systems Biology

Transcriptomics (RNA) 100,000 mRNAs

Proteomics (Proteins) 1,000,000 Proteins

Metabolomics 5,000-10,000 Metabolites

Genomics **Proteomics Metabolomics Drug Discovery** Vaccine Development **Many Other Opportunities**







- 3D Model: Formation of Tissue Equivalents in NASA Bioreactors



Fibroblast + Epithelial cells

Support Matrix



Culture for 10-20 days







Space Radiation: Mutagenesis Analysis





Mutant Frequency after Exposure to ⁵⁶Fe Particles:

Lacl Target: ~1100 bps

 λ LIZ shuttle vector: 45.5 kbps

Main effects of Mutational Frequency (*10⁶)



Cellular MicroenvironmentDose (Gy)M. Hada et al.
2007Increase in mutational frequency in 3D samplesIncrease in mutational frequency with increasing dose



How To Work With Us

Space Act Agreement With NASA (Sponsored Research Agreement)

NASA Cooperative Agreement

Collaborative Research Proposals For NIH/NSF/Industry Etc.

Working Group Integration With Agency (s) Directed Funds (DoD, DoE, DARPA etc.)



Disease Modeling and Tissue Analogues Collaborations

- Sovaris Aerospace LLC.
 Michael A. Schmidt, PhD
- Research & Clinical Laboratory Systems
 Sandra L Schneider, DrPH, EMBA, Principle/CEO

AM Biotechnologies, Inc



- > Mark W Shumbera, MBA, President & Board Of Managers
- Ross H. Durland, PhD, Director, Product Development
- University Of Colorado Health Science Center Denver
 Randall J. Cohrs, PhD, Research Professor, Department Clinical Neurology
- University Of Texas Health Science Institute of Molecular Medicine
 - > Ferid Murad, MD., Ph.D
 - David G. Gorenstein, PhD Deputy Director, Institute For Molecular Medicine & James T Willerson Distinguished Chair & Professor Medicine



Collaborations (cond.)

 University Of Texas Medical Branch, Galveston
 Thomas B. Albrecht, PhD, Professor, Department Microbiology & Immunology

> Universities Space Research Association

Maureen A. McCarthy, BS, Senior Research Associate



Back Up Slides

Proposed 3D

Systems

 Hematopoietic Stem Cells and Progenitor Cells as Biodosimeters

BLIFE P

- Transgenic Tissue Models as Bioreporters for Radiation Shielding
- Investigation of combinatorial events that effect radiation Damage
- Elucidation of the mechanisms of microgravity induced muscle atrophy and countermeasure development
- Cell-based countermeasures for bone loss
 - Assessment of Pharmacokinetics and Pharmacodynamics (PK&PD) of Cardiovascular Medications for Human Space Exploration: Use of Functional Cardiac and Liver Tissue Constructs in Microgravity Analogue Systems for Testing Drug Metabolism and Drug Efficacy.

- 3D Cell Based Models of Infectious Disease and Hemopoiesis
- Impairment of Immunity, Latent Viruses Reactivation and Autoimmune Disorders Development in Space: Ground-based Program for Risks Assessment and Possible Countermeasures Testing using Microgravity Analogue System (MAS) and Hind Limb Unloading (HU) Animal Model.
- Mechanistic Evaluation of Microbial Response & Host Pathogen Interactions for Spaceflight
- PEMF Therapy Countermeasure to Enhance Wound Healing & Osteoblastogenisis (Cell Model for Countermeasure Dev.)
- Drug Stimulation of Interferon in Human Immune Cells



Advanced Translational Technology

- Advanced & Innovative Regenerative Tissue- Equivalents
 Tissue Engineered Models To Assess Human Eye Oxidative Damage
 - Models To Screen And Test Radiation Effects
 - >Other: Hypoxic/Hyperoxic Ophthalmic Conditions
 - Regenerative Tissue Models For Enhanced Vascularization
 & Bone Repair
 - ▶3D Tissue-like Assemblies (TLAs) Simulate
 - Cellular Differentiations;
 - Cellular Interactions;
 - Modulations In Gene Expression, Proteomics, and Metabolomics



Assembly Of Three– Dimensional Tissue Assemblies In Rotating Wall Vessels: Phase I Of The Synthetic Organ SubSystem (SOS)



Strategic Opportunities

 Provide Documented And Vetted Advanced Translational Technology To Integrate Into Space And Warfighter Applications, And Biosciences Advancement

 Support Applied And Emerging Technology To Address Healthcare To Environmental Hazards, Global Emerging Bio-Agents & Infectious Disease Surveillance

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Overview NASA/JSC Capabilities

- Advanced Translational Technology
- Tissue Bio-Engineering Systems
 - Corneal Model Of Human Eye
 - Major Organ Disease Systems
 - > Neural, Renal, Breast, Prostrate, Bone, Lung, Skin, Etc.
- Predictive & Diagnostic Systems
 - Host Microbe Modelling
 - Tissue Technology Combined With Novel Detection System Proposed To Detect And Identify Early Gene & Protein Regulation For Active Virus Infections For Advanced Medical Monitoring
 - RSV, PIV3, EBV, CMV, VZV, SARS

Technology Development Required to Support

Exploration Initiative





- To Provide Advanced & Emerging Tissue Engineering Technology That Simulates Conditions Of Manned Space Exploration;
- To Understand The Physiological, Radiation, Disease And Other Health Effects Of Space Flight;
- To Meet Critical Health & Medical Needs For Astronauts In Space;
- To Develop Applications Supporting Aerospace And Biosurveillance For the Government