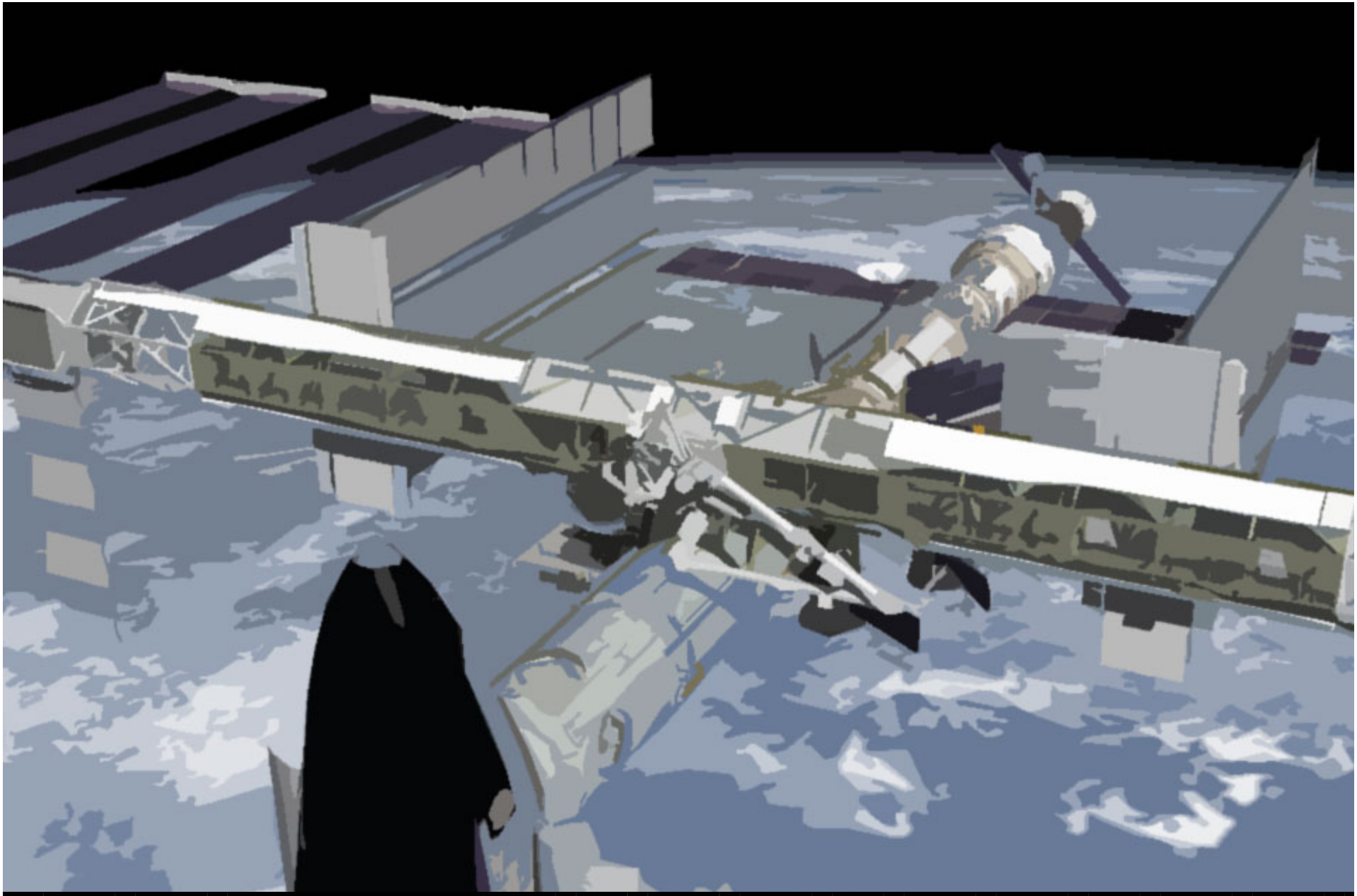


NASA CELL SCIENCE CONFERENCE “BUSINESS MEETING PRESENTATION”

Cellular Biotechnology: The Future

SECTION ONE:

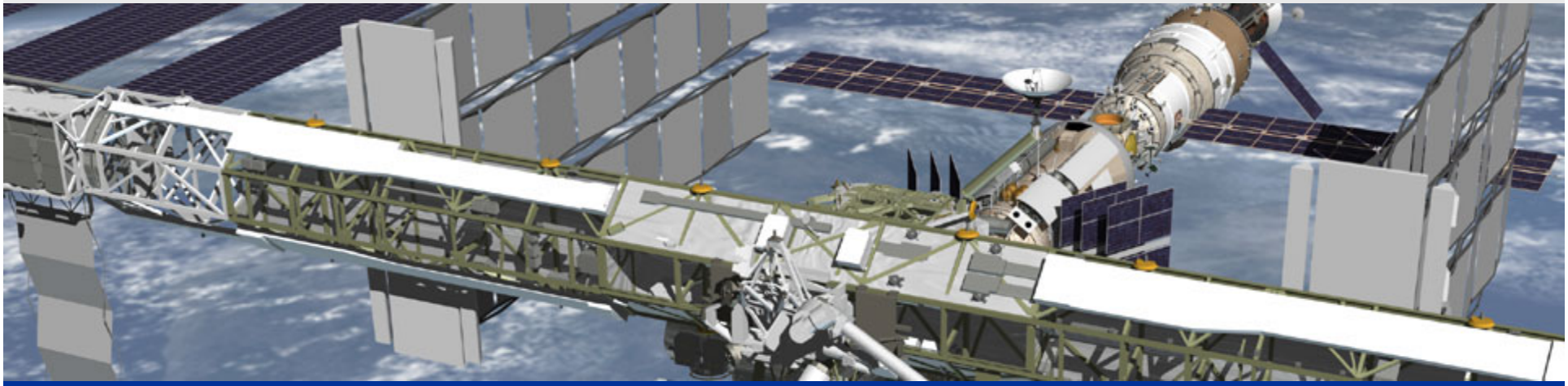
Cellular Biotechnology Accomplishments, a Year in Review

- Research Accomplishments
- Flight Hardware Development Accomplishments

SECTION TWO:

A New Direction – the Human Exploration Initiative

- Strategic Research
- Impacts to ISS Research



SECTION ONE:

Cellular Biotechnology Accomplishments, a Year in Review

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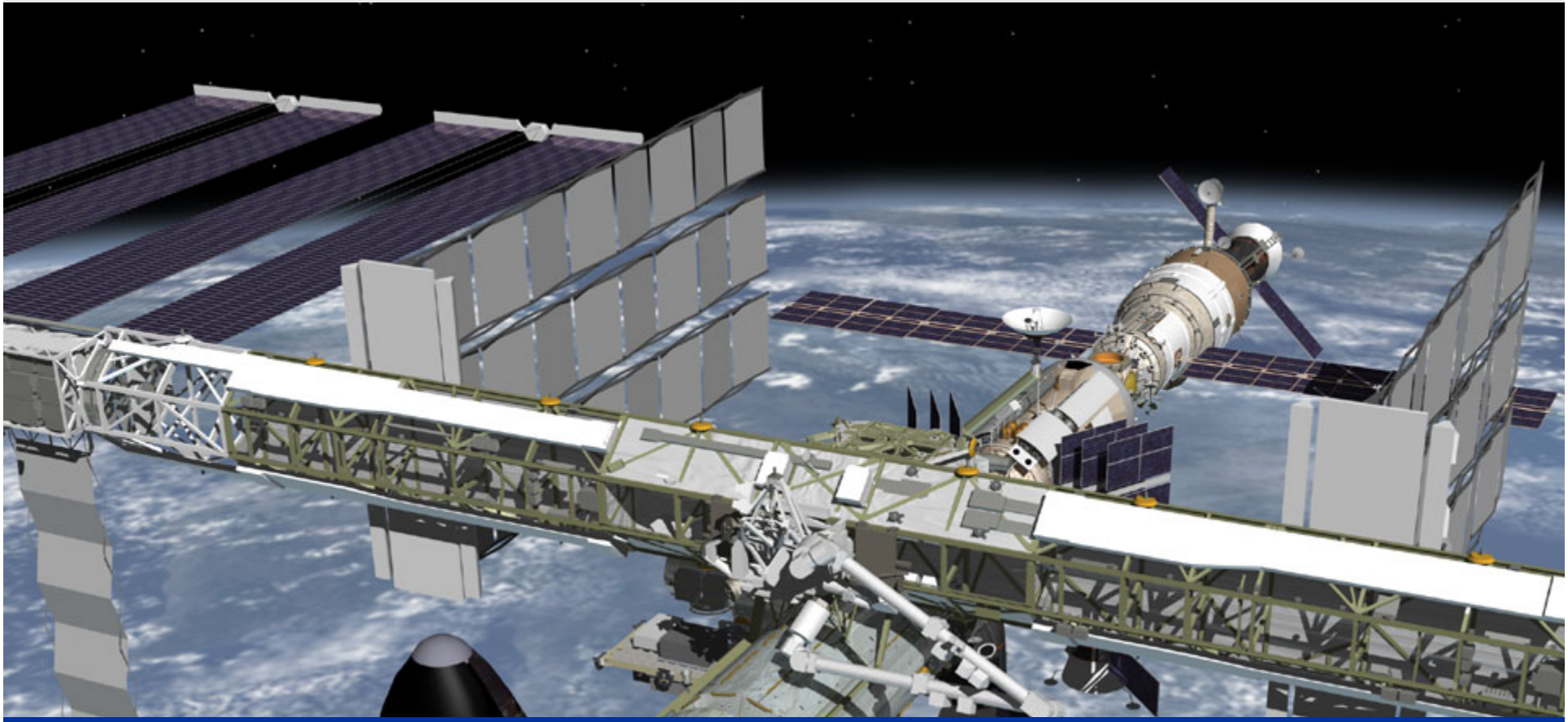
- Flight Hardware Development Accomplishments

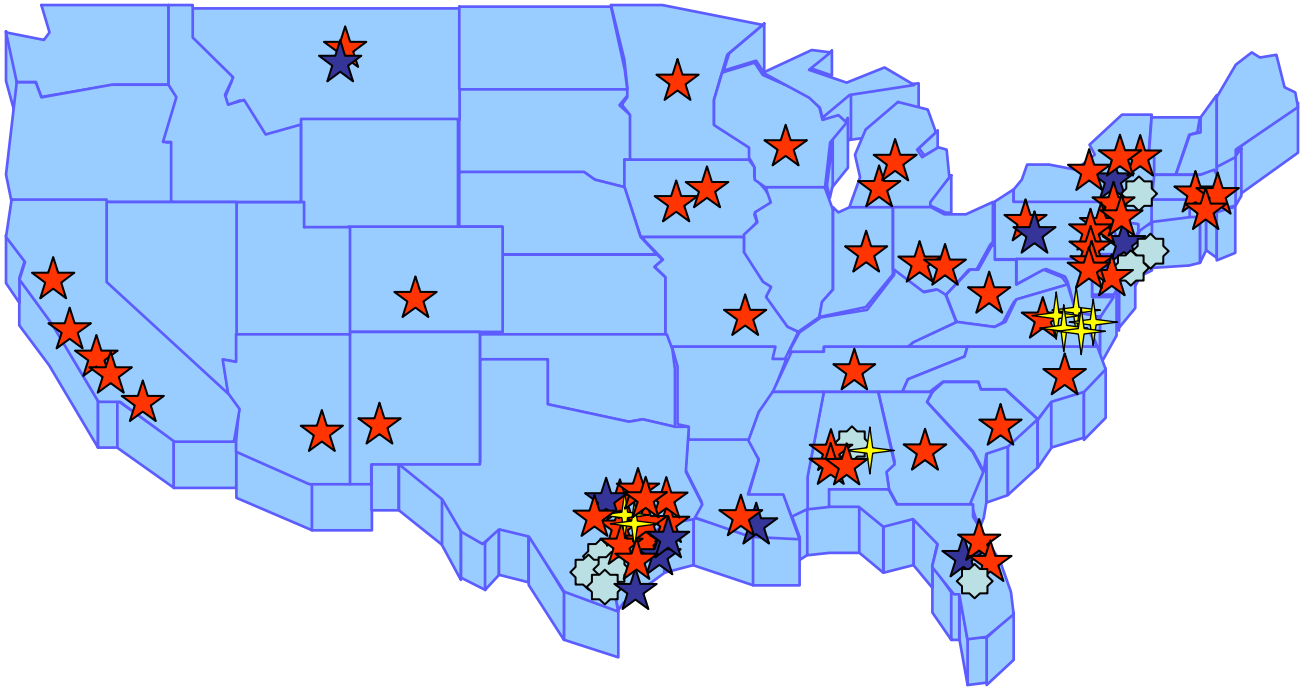


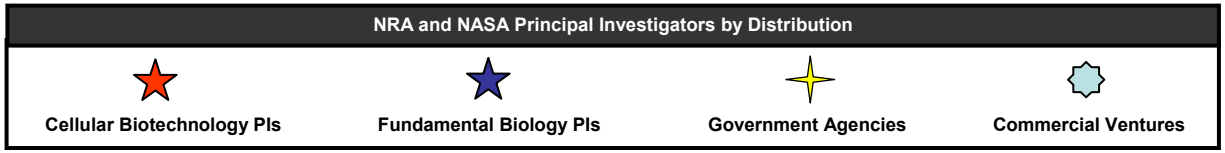
Current Cellular Biotechnology Research Distribution

Cellular Biotechnology PIs

20- (97-HEDS-02)
01- (96-OLMSA-03)
02- (no cost extension)
23- (00-HEDS-03)
08- (01-OBPR-08)
01- NIH Cooperative

55- Total Current PIs



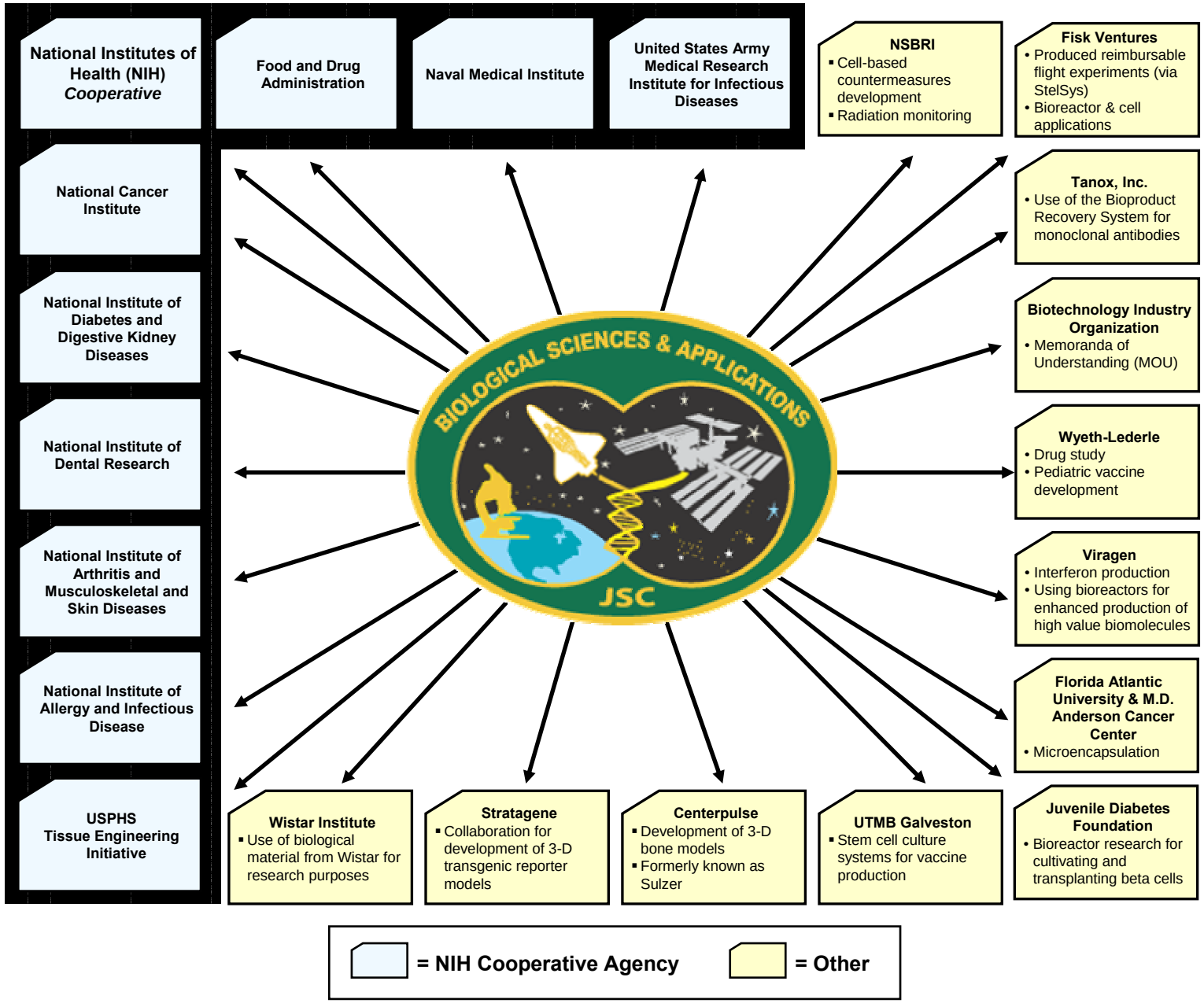


New Research Announcements

NRA 02-OBPR-03, Biotechnology

- Issued 12/02/02
- Submittal start date 04/30/03
- NOI 05/30/03
- Proposals due 07/31/03
- http://research.hq.nasa.gov/code_u/nra/current/NRA-02-OBPR-03/index.htm

NASA Cellular Biotechnology Collaborations



Bioreactor Research – Applications to Human Health on Earth

INFECTIOUS DISEASES

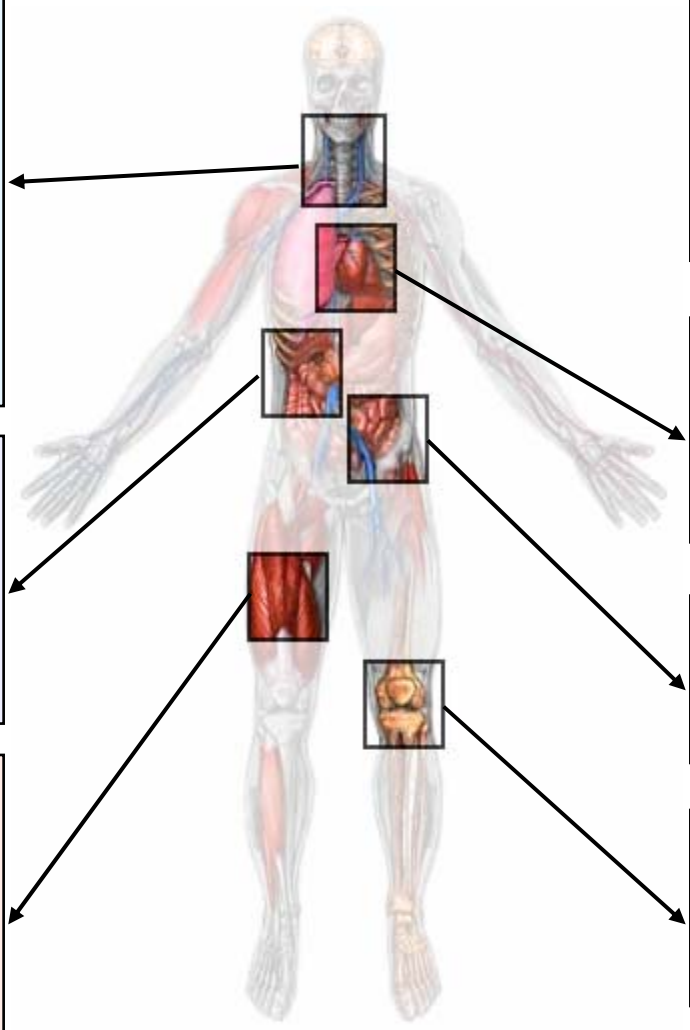
- Established the NASA/NIH Center for Three Dimensional Tissue Culture which provides researchers bioreactors and an opportunity to develop new model systems for diseases whose pathology cannot be reproduced by merely growing the right cells in monolayer culture.
  - Human Immunodeficiency Virus (HIV)
  - Ebola viral transmittal
  - Borrelia, the etiologic agent of Lyme disease
  - Norwalk virus
- Model for Salmonella pathology in engineered colon tissue

DRUG EFFICACY

- Facilitating testing of drugs to determine their safety without using animals and reducing the need to use human volunteers in final testing
- Bio-production of an enzyme that HIV needs to reproduce, analysis of enzyme structure, and designer drugs to inhibit the HIV virus
- Studying human metabolism of drugs

ACUTE INJURY AND RECONSTRUCTIVE SURGERY

- Biodegradable scaffolds to grow cartilage cells needed for reconstructive surgery
- Models and transplantable cartilage tissues that could revolutionize treatment for joint diseases and injuries
- Cytokine synthesis in analog culture to address wound healing



CANCER

(breast, skin, prostate, ovary, bone and colon)

- Co-culture of cancer and somatic cells to understand cancer growth and human immune system response
- 3D tumor disease models for studies in proliferation, signaling, an apoptosis
- Testing three-dimensional tissues for sensitivity to chemotherapy and hormonal therapy

HEART DISEASE

- Engineered heart tissue for research in drug testing, and the eventual growth of transplantable heart tissue
- Studying how heart cells interact to form cardiac structures outside the body

DIABETES

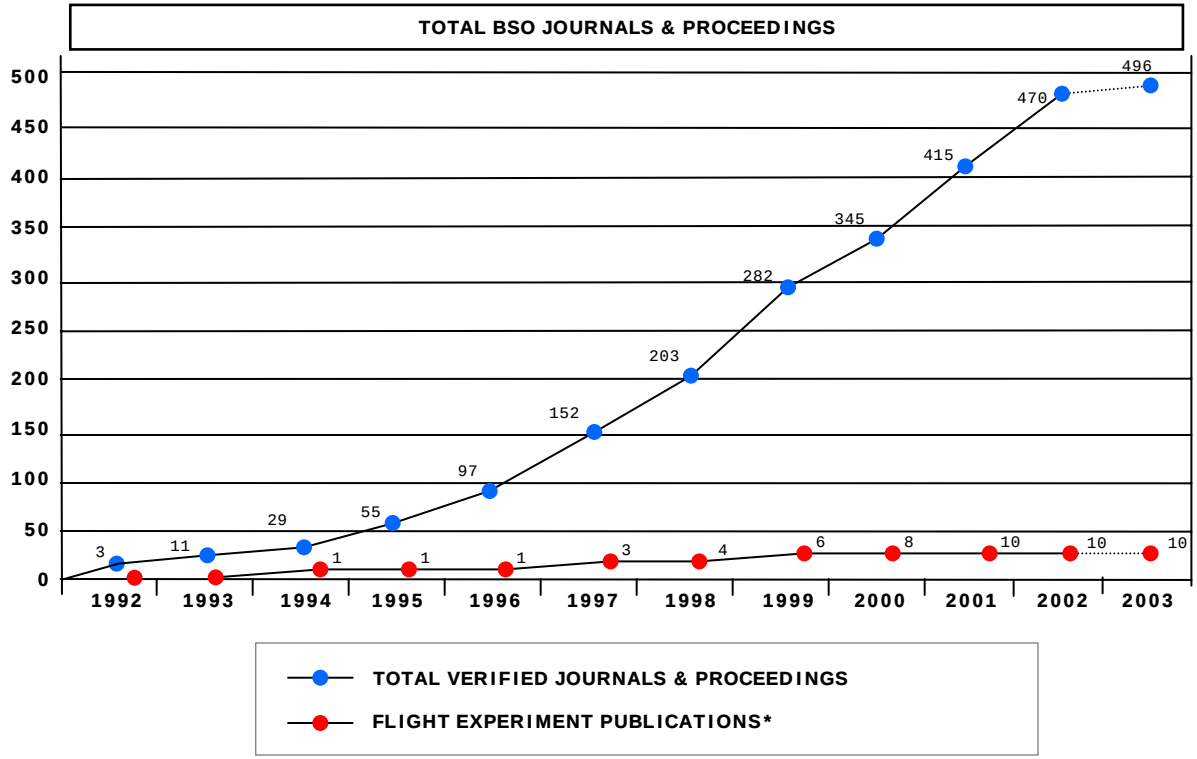
- Working on pancreatic tissue for transplantation
- Cultivating and transplanting beta cells into Type I diabetics

BONE LOSS

- Mechanisms involved in bone loss related to microgravity
- Optimal characteristics of micro-beads for growing bone tissue

Cellular Biotechnology Research Accomplishments – Journals and Proceedings

Cellular Biotechnology Program has generated numerous publications in a variety of peer reviewed journals



Over the past 10 years, produced over 800 publications and presentations

~145 abstracts
~335 articles in journals
~405 presentations

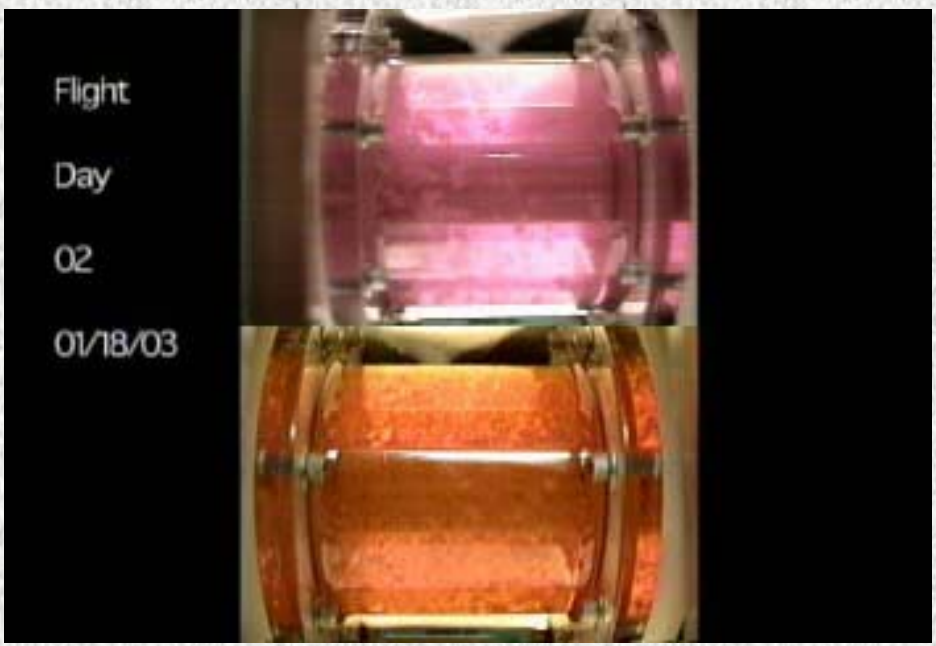
***Average one publication/flight**

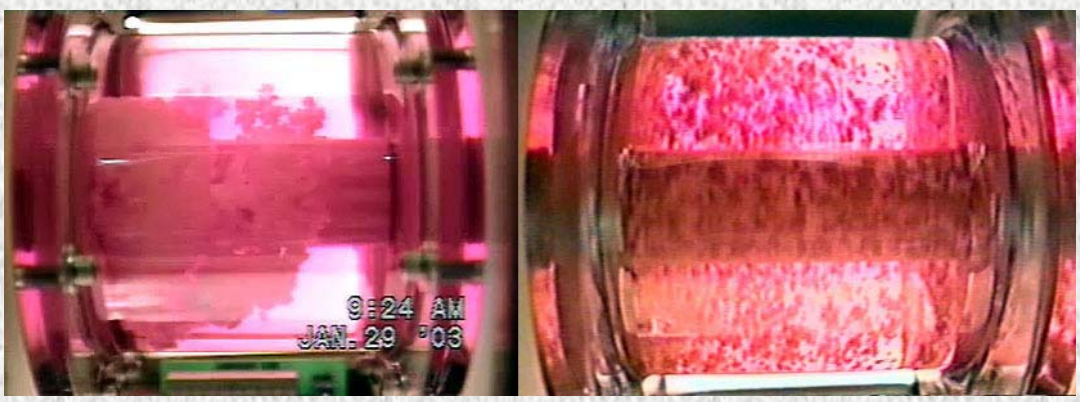
Averaging ~ 50 publications/year in peer reviewed journals

Journal of Applied Physiology • Biomaterials • Analytica Chimica Acta • Nature Medicine • Journal of Membrane Biology • Federation of American Societies for Experimental Biology Journal • Cancer Research • In Vitro Cellular & Developmental Biology – Animal • Journal of Immunology • Journal of Clinical Investigation • Pharmacological Research • Advances in Space Research • Applied Spectroscopy Journal • Gastroenterology • Immunopharmacology • International Reviews of Immunology • Journal of Immunotherapy • Oncogene • Sensors and Actuators B: Chemical • Sensors and Actuators A: Physical • Biotechnology Progress • Hepatology • Biotechnology Bioengineering • Cancer Metastasis Review • Cellular Transplantation • Cells and Materials. • Endocrinology Proceedings • Immunology Newsletter • Journal of Biomolecular Structure and Dynamics • Journal of Respiration • Cellular and Molecular Biology • American Journal of Physiology. Lung Cellular and Molecular Physiology • Environmental and Molecular Mutagenesis • Proceedings of the Indian Academy of Science (Chem. Sci) • Proceedings of the SPIE International Symposium on Biomedical Optics • Tissue Engineering • Transactions of the Orthopedic Research Society • Proceeding of National Academy Sciences

The Year in Review – Flight Research - STS-107 Results

- STS-107 Flight Video
- Chung, Leland, Ph.D. Emory University
- Prostate Tissue Response to Androgen Therapy and Microgravity
- Comparison video footage of bioreactor cell growth in Microgravity (left) and on Earth (right).





The Biotechnology Facility (BTF)

Milestones

- Preliminary Design Review: April 2003
- ASCS, ACWA, & GSM PDRs: summer 2003
- Interim Design Review: October 2003

Description

- Fits inside two EXPRESS racks
- Features complement of hardware and science experiments
- Accommodates experiments from a large research community including government, academia, and commercial
- Includes hardware for researchers, such as:

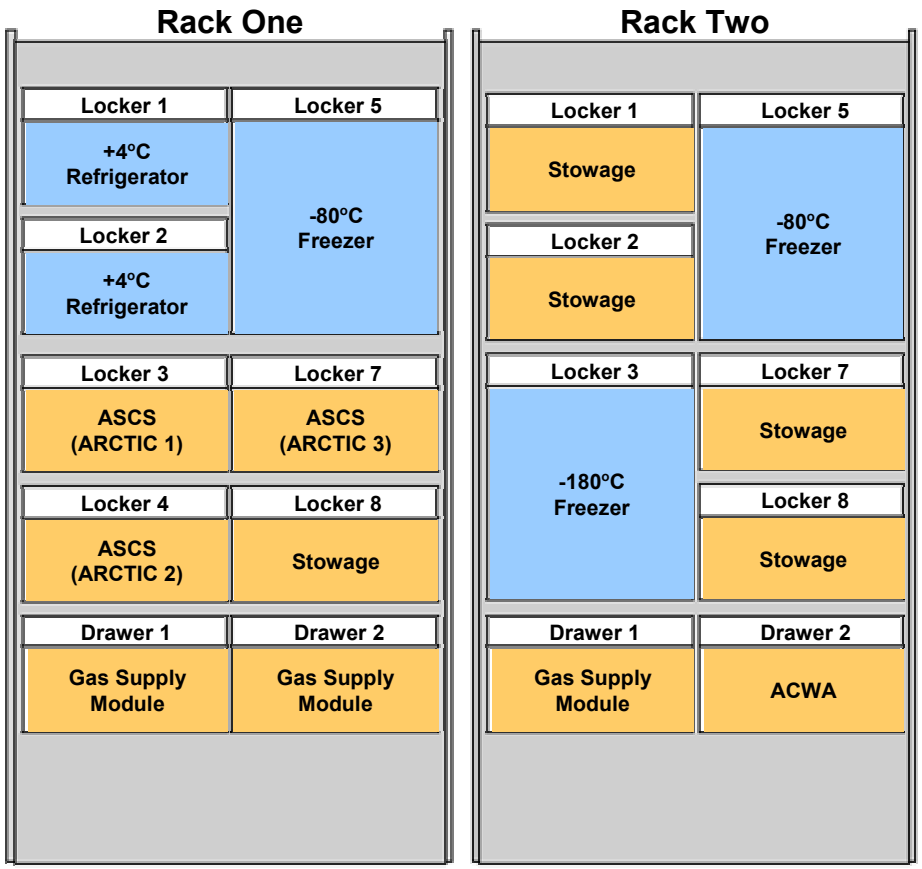
  Incubators, Rotating Bioreactors, freezers and refrigerators, analytical instruments, and gas and water-supply devices

Benefits

- Will support human health research and support human exploration of space

Status

- PDRs successfully completed
- Detailed design in work
- GSM CDR, March 2, 2004
- System CDR – May 2005

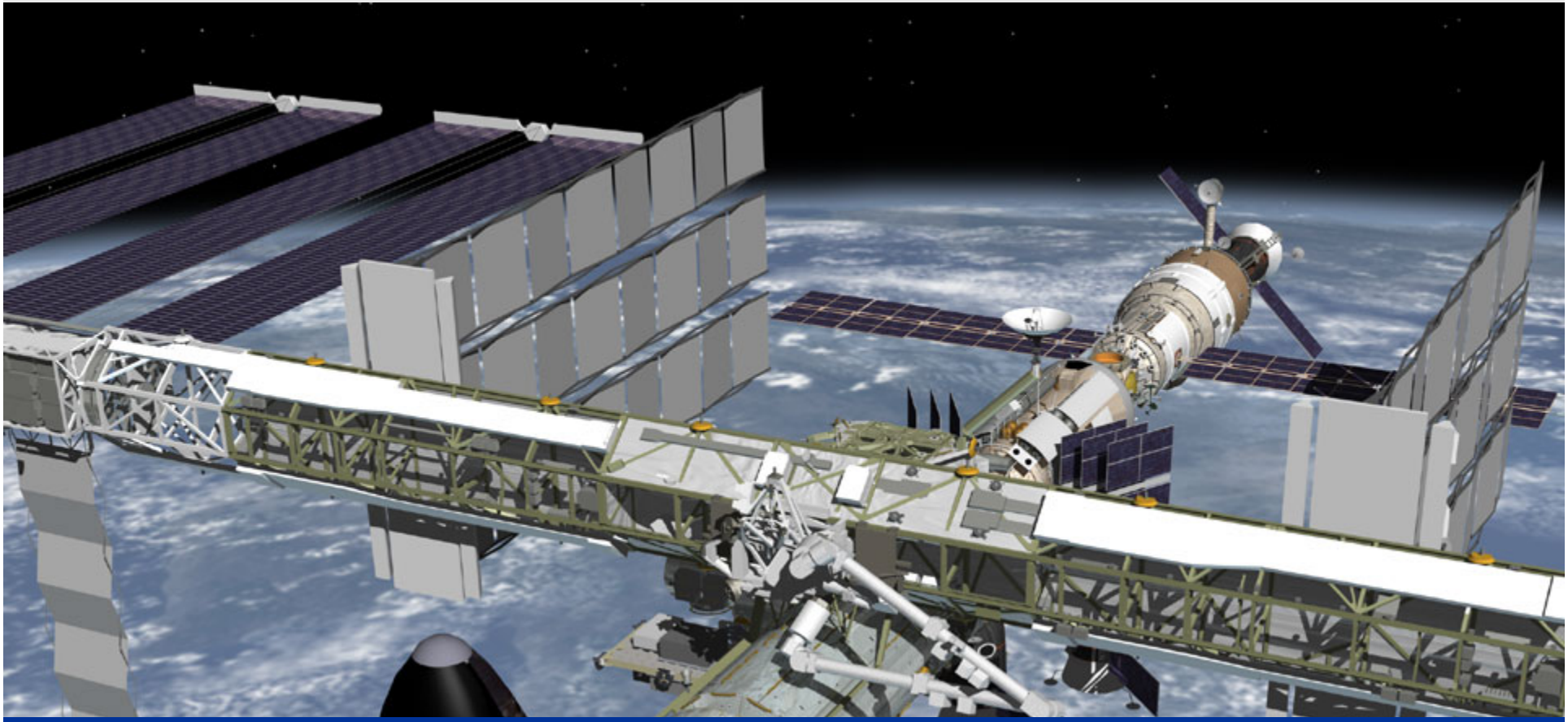


The Biotechnology Facility: 2D Topology Assembly

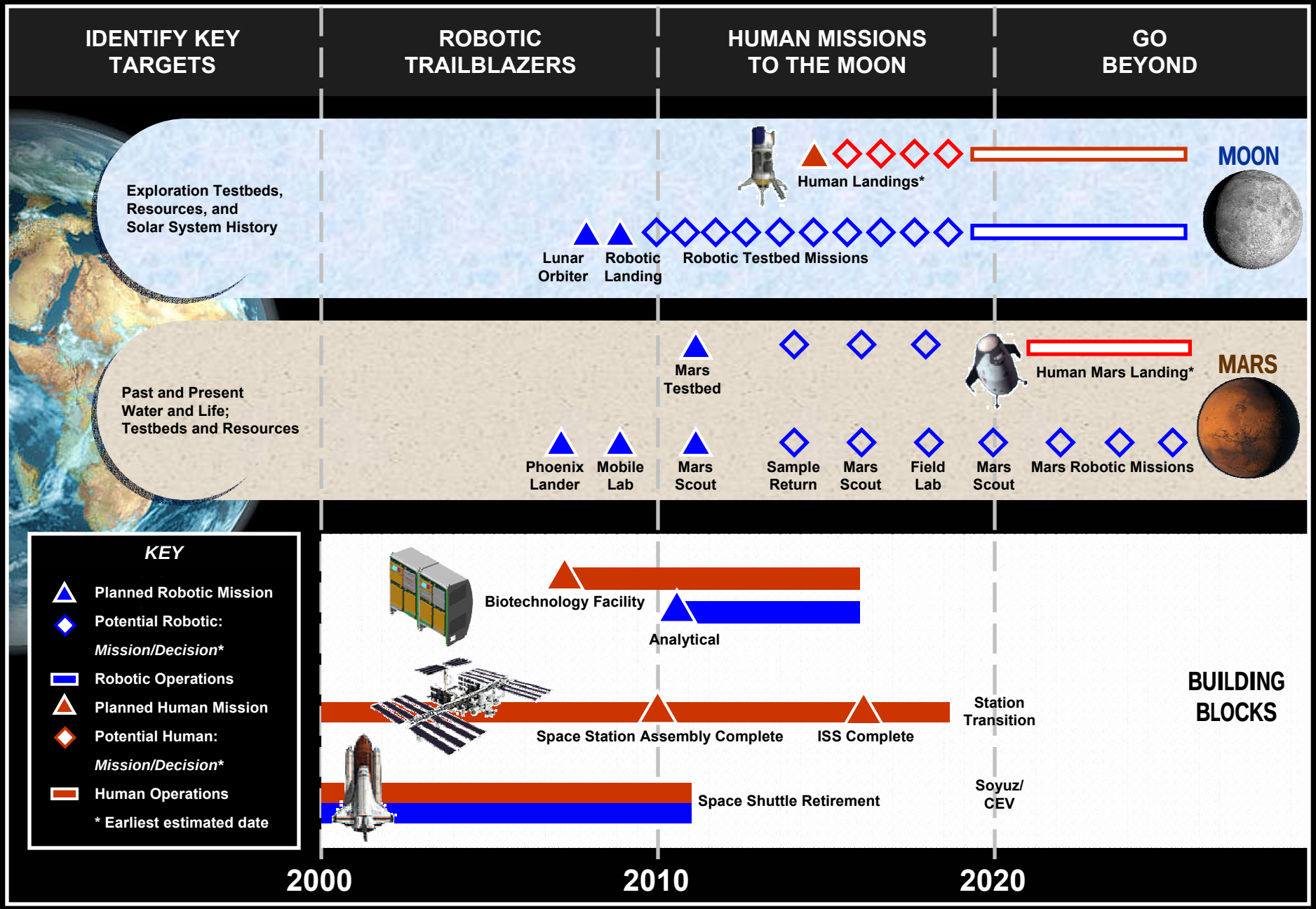
SECTION TWO:

A New Direction – the Human Exploration Initiative

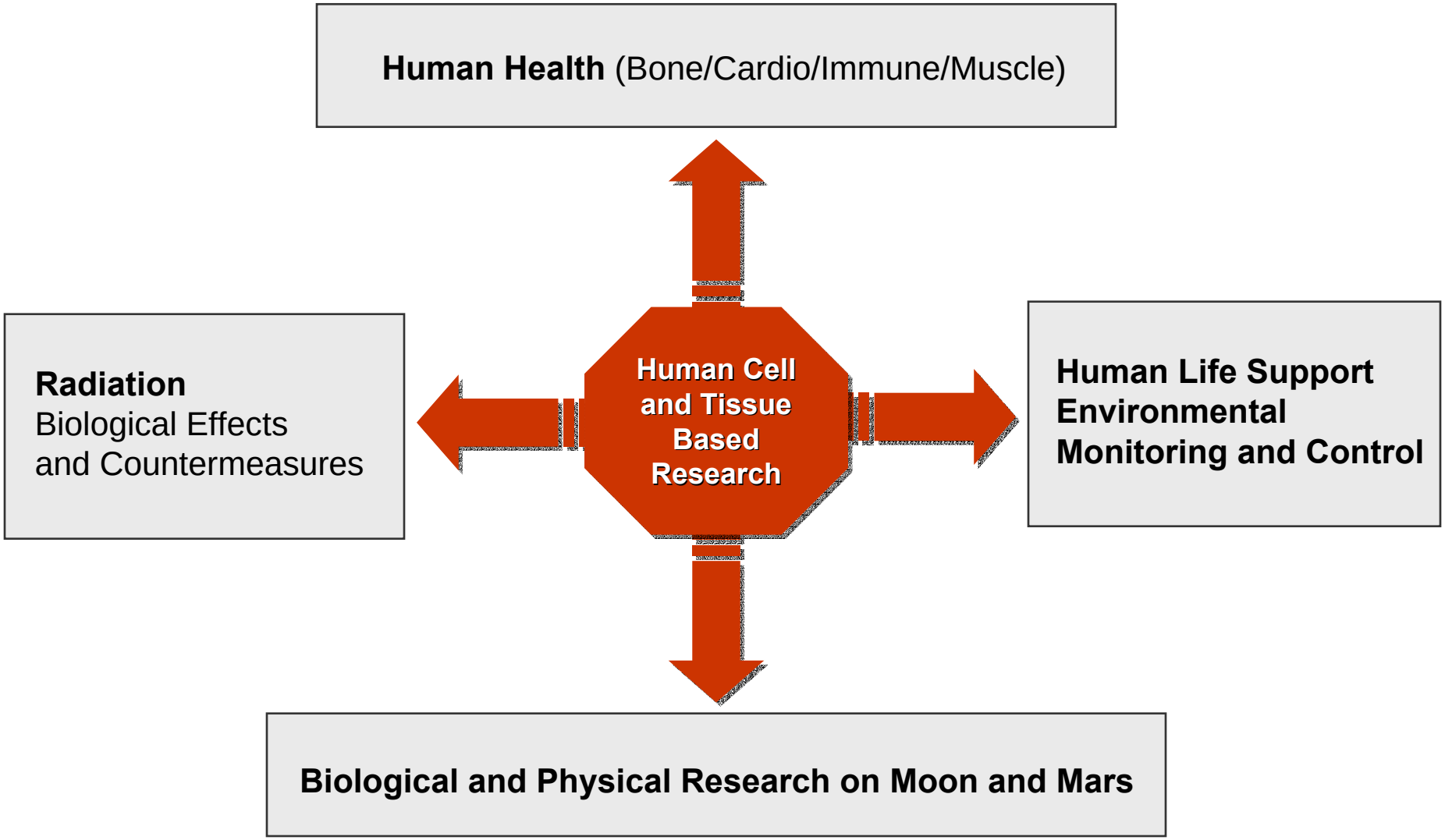
- Strategic Research
- Impacts to ISS Research



EXPLORATION ROADMAP



Human Cell/Tissue Research Applications and Exploration Product Lines



Human Cells Cultured in the Bioreactor

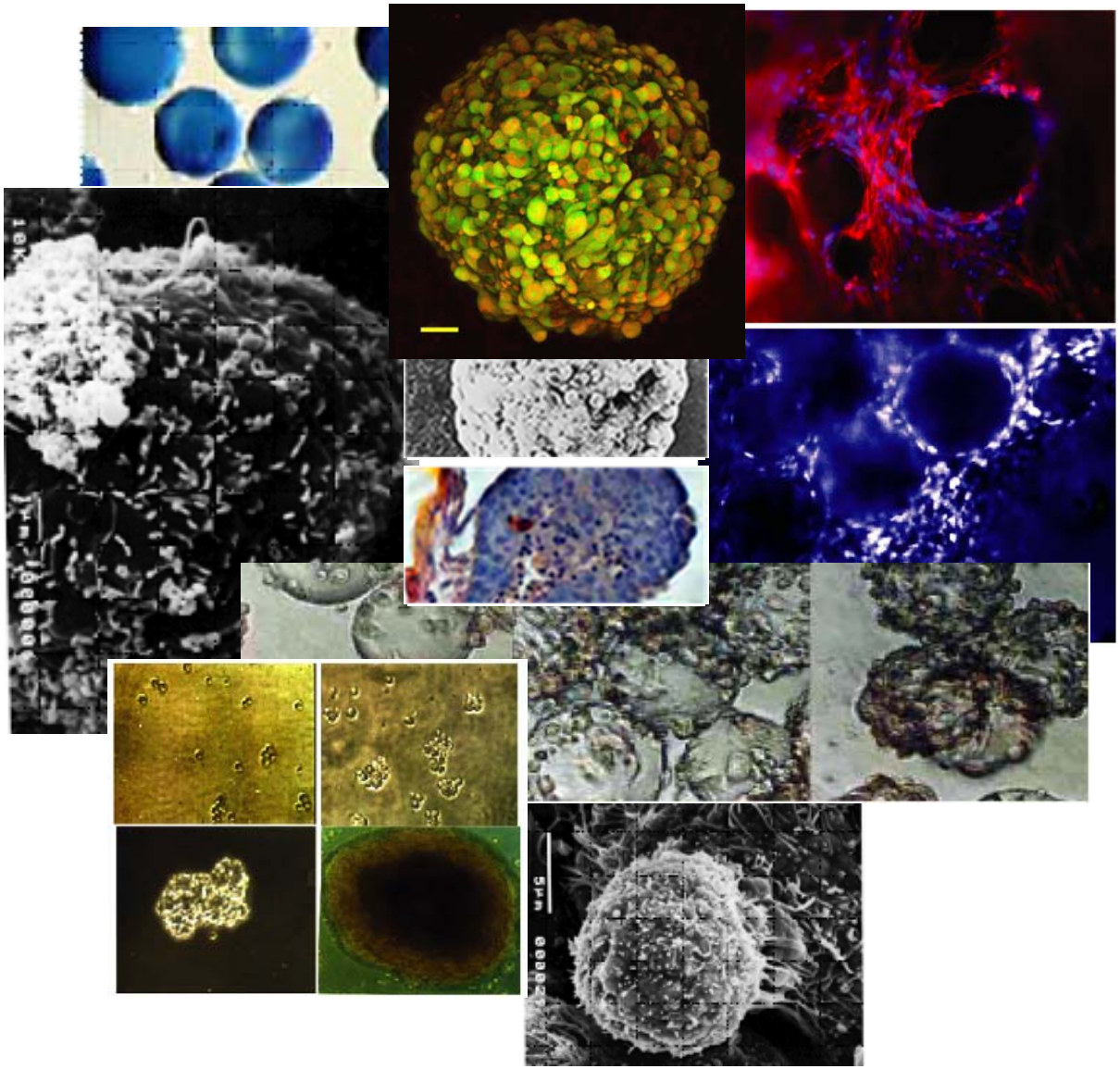
Some Cells Propagated in Bioreactor

Cancer models

- Colon
- Breast
- Ovarian
- Prostate
- Endocrine
- Brain Glioma
- Cervical

Normal Tissue

- Bone (Osteoblast/Osteoclast)
- Skeletal Muscle
- Airway Smooth Muscle (ASM)
- Cornea
- Small Intestine
- Cartilage (chondrocytes)
- Kidney
- Liver
- Lymphoid
- Thyroid
- Skin
- Cardiac
- Adrenal medulla
- Stomach
- Adipose
- Pancreatic islet cells
- Intestinal epithelial
- Renal proximal tubule
- Peripheral Blood Lymphocytes
- Embryonic Stem Cells



Bioastronautics Challenge – small n!

2005		2006		2007		2008		2009	
Increments		Increments		Increments		Increments		Increments	
1	2	1	2	1	2	1	2	1	2
3 crew	3 crew	3 crew	3 crew	3 crew	3 crew	3 crew	3 crew	3 crew	3 crew

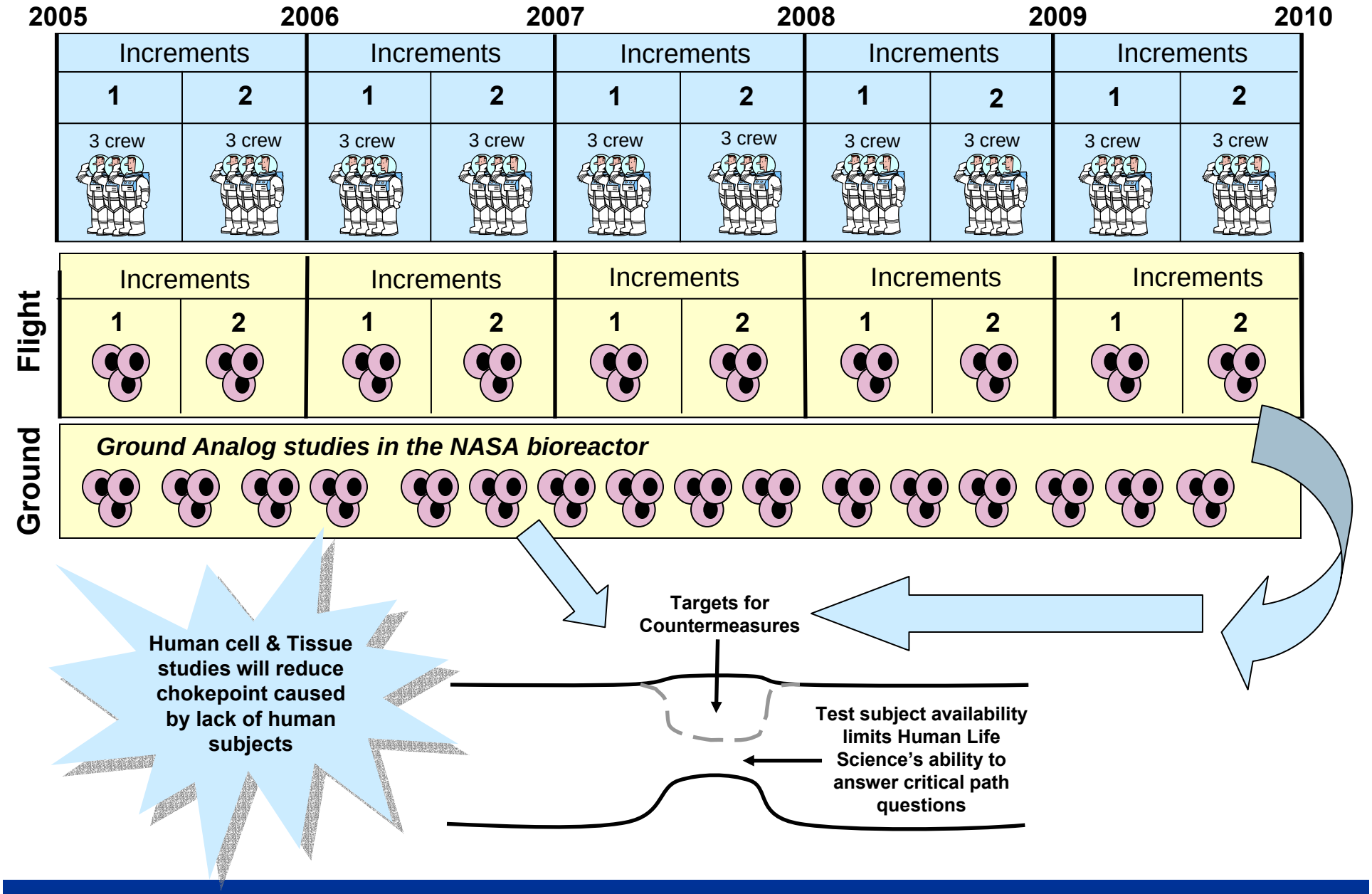
- **6 crew/year x 5 years = 30 crew**
- **Only half of crew is US ≈ 15 astronauts**
- **3 experiments/astronaut x 15 astronauts = 45 experiments**
- **45 experiments ÷ 6 necessary subjects ≈ 8 investigations over 5 years**

8 total PIs over 5 years for 339 Critical Questions!

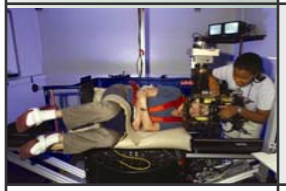
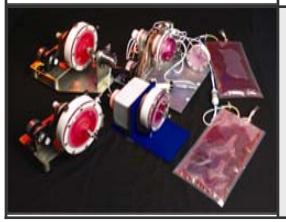
Test subject availability limits Human Life Science's ability to answer critical path questions

Need to augment human tests with cell/tissue studies and ground analogs

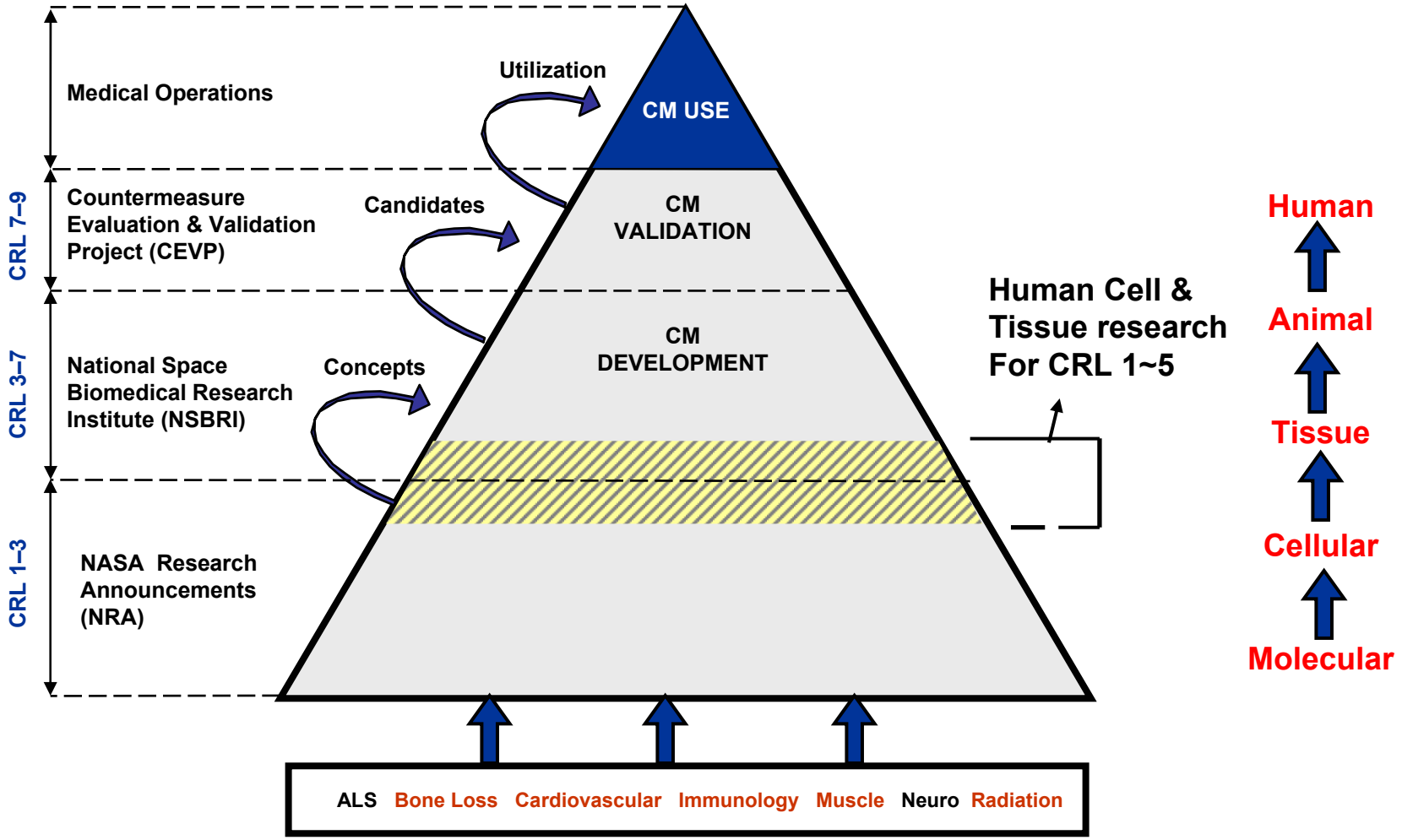
Cell/Tissue Studies can Augment Human Studies



Microgravity Analog Facilities

Spaceflight Analog		Utility for CPR	Cost/Study
	Drop Tower	Limited – time too short for biological relevance	$20K
	KC-135	Limited – time too short for biological relevance	$10K
	Centrifuge	Neurovestibular	$50K?
	Bed Rest	Bone/Muscle/Nutrition/Human Behavior & Performance/Cardio	$1.5M
	Bioreactor	Bone/Cardio/Environmental Health /Immune/Muscle/Radiation	$150K

Countermeasure Life Cycle



Research Requirements – Bioastronautics Critical Path Roadmap

Human Cell/Tissue Biology: Relevance to CPR Risks

Risks Addressed

Bone

#10 Fracture & Impaired Fracture Healing

#11 Renal Stone Formation

Cardio

#15 Diminished Cardiac Function

Environmental Health

#51 Inability to Maintain Acceptable Atmosphere in Habitable Areas due to Environmental Health Contaminants

#52 Inability to Provide and Recover Potable Water due to Environmental Health Contaminants

Immune

#22 Immunodeficiency/Infections

#23 Carcinogenisis Caused by Immune System Changes

#26 Altered Host-Microbial Interactions

#27 Allergies and Hypersensitivity Reactions

Muscle

#28 Loss of Skeletal Muscle Mass, Strength, and/or Endurance

Radiation

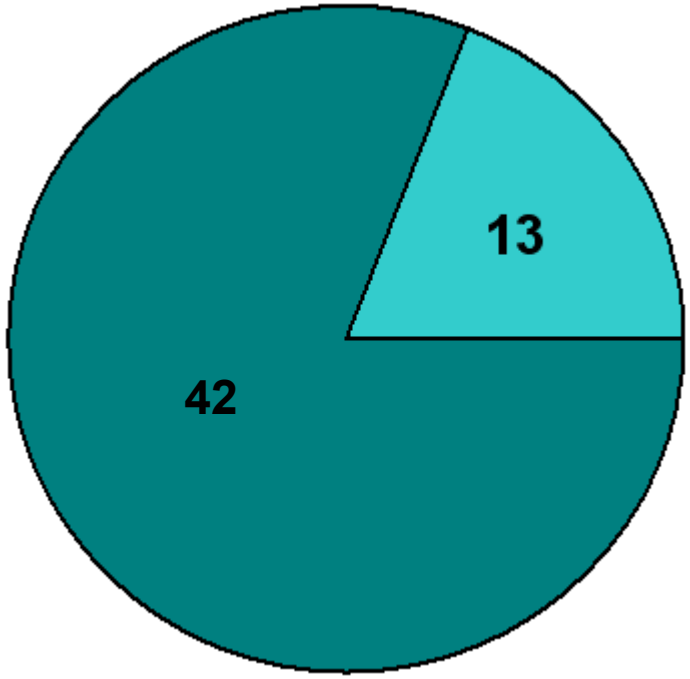
#38 Cacinogenisis Caused by Radiation

#40 Synergistic Effects from Exposure to Radiation, Microgravity, and Other Spacecraft Environmental Factors

#41 Early or Acute Effects from Radiation Exposure

24% of CPR risks can be addressed by studies at the cell/tissue level:

Bone/Cardiovascular/Environmental Health/Immune/Radiation



55 Total Critical Path Risk Areas

Critical Path Roadmap: Human Cell/Tissue Research

BONE/MUSCLE LOSS	• Is there an additive or synergistic effect of estrogen deficiency (as in post menopausal or amenorrheic women) and prolonged exposure to microgravity? • Does hypogravity exposure change the nutritional requirements for optimal bone health (eg., does calcium absorption decrease)? • What are the signal transduction pathways allowing bone cells to sense gravity and loading on bone? • Does hypogravity affect the size, viability or differentiation of precursor bone cell populations? • Are there important other mechanisms for bone loss with hypogravity that are critical to developing effective countermeasures (eg, fluid shifts, changes in blood flow, immune system alterations • What pharmacological agents will most effectively minimize the decrease in bone mass with hypogravity? Are anabolic as well as anti-resorptive agents req'd? • How do muscle cells sense the mechanical stress of gravity?
CARDIOVASCULAR	• Does long duration spaceflight lead to diminished cardiac function and what are the mechanisms?
ENVIRONMENTAL HEALTH	• What are the effects of the space environment on microbial interactions with space systems and humans?
IMMUNE	• Does the spacecraft environment exert a selective pressure on environmental microorganisms which presents the crew with increased health risks? • Do conditions of mechanical forces of space travel disrupt cytokine: cytokine receptor signal transduction in immune cells? • Are there surrogate marker assays that can be adapted to space travel that will quantitate the degree of immunodeficiency for Ab, Tcell, phagocyte, and complement function? • Which oncogenic mechanisms may be activated by in-flight radiation exposure? • Does spaceflight alter microbial growth rates, mutation rates, or pathogenicity? • Does spaceflight alter the exchange of genetic material between microorganisms? • Does spaceflight alter host-microbe balance? • What diagnostic and environmental monitoring laboratory technologies need to be developed for the detection and diagnosis of infections in microgravity?
RADIATION	• How can animal and cell experiments be done and data best used to extrapolate to the human risk from space radiation? • Are the biological effects for protons above 10 MeV sufficiently similar to photons that photon data can be used for their consequences? • Are there chemopreventative or biological agents which would mitigate acute or late effects? • Are there adverse synergisms between radiation and other space environmental and biological factors?