Life Science Research on the International Space Station

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Texas Southern University, March 28, 2017

Micro-7 experiment flight schedule

4/18/14 – Cells were launched to ISS on board SpaceX-3.

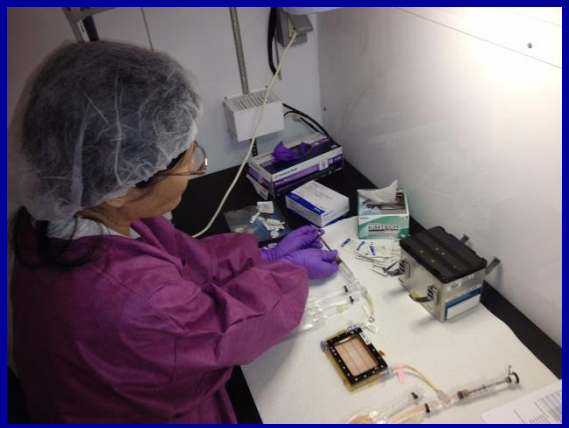
4/22/14 – Cells were transferred to a 37 C incubator.

4/25/14 – Cells were fixed with RNAlater II and PFA (Day 3).

4/25/14 – Cells were treated with bleomycin (1 μg/ml) (Day 3).

5/6/14 – Cells were fixed with RNAlater II and PFA (Day 14).

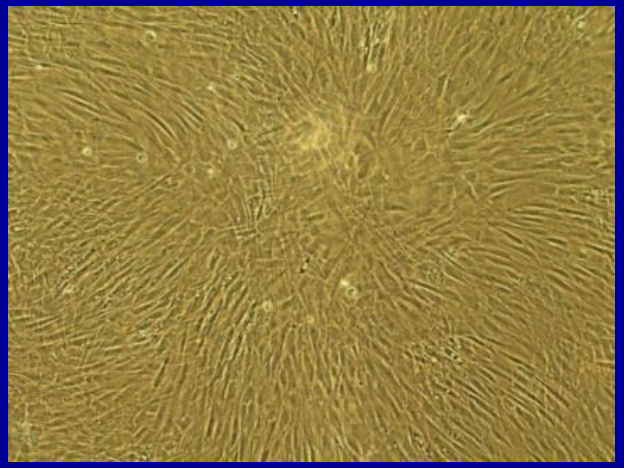
5/20/14 – The fixed samples returned to JSC.



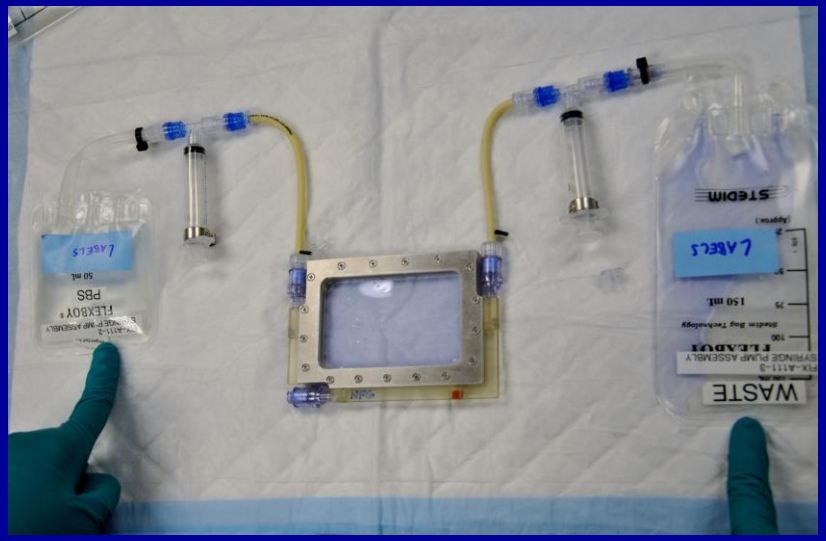
Cell culture and flight hardware

Confluent human fibroblast cells were cultured in BioCells. The cells were kept in CGBA on ISS at 37 C.

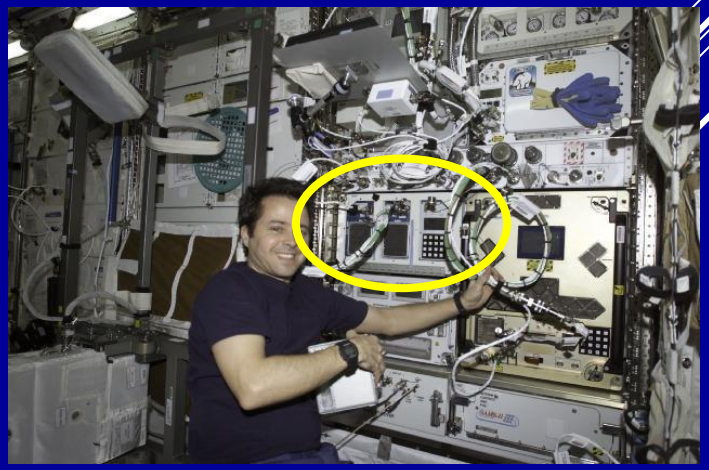
Human fibroblast cells



BioCell from BioServe



BioServe's CGBA incubator



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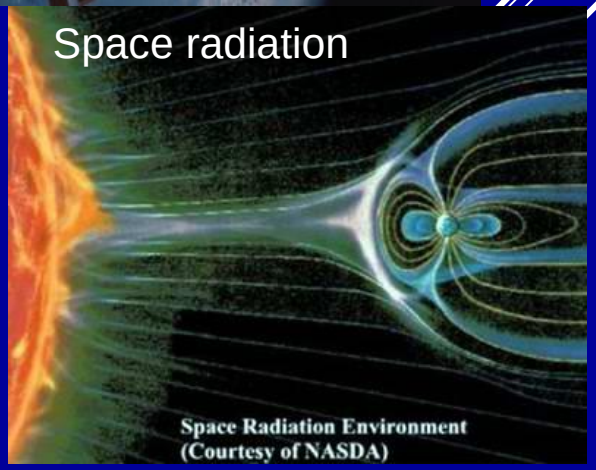
Xiaoyu Wang

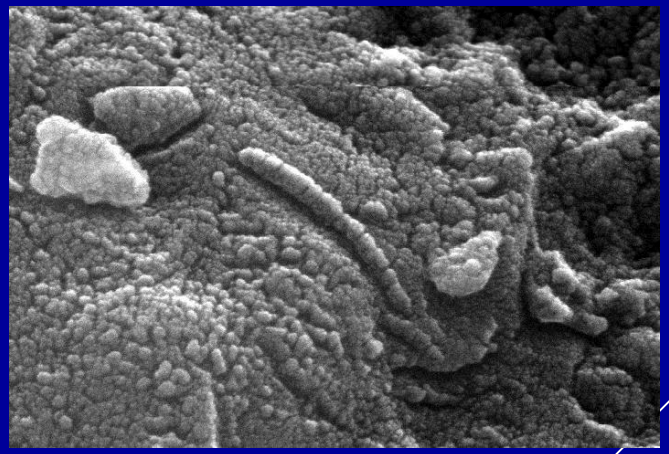
Life sciences research at NASA

- Crew health
  - Bone loss
  - Muscle atrophy
  - Psychological stress
  - Radiation risks
  - Immune dysfunction
  - Others



Life sciences research at NASA

- Fundamental space biology
  - Adaptation of living organisms in space
  - Plants
  - Microorganisms
  - Reproduction
  - Others
- Astrobiology
  - Life in the universe
  - Life in extreme environment
  - Others



The International Space Station (ISS)

Glove box

Commercial Generic Bioprocessing Apparatus (CGBA – BioServe))

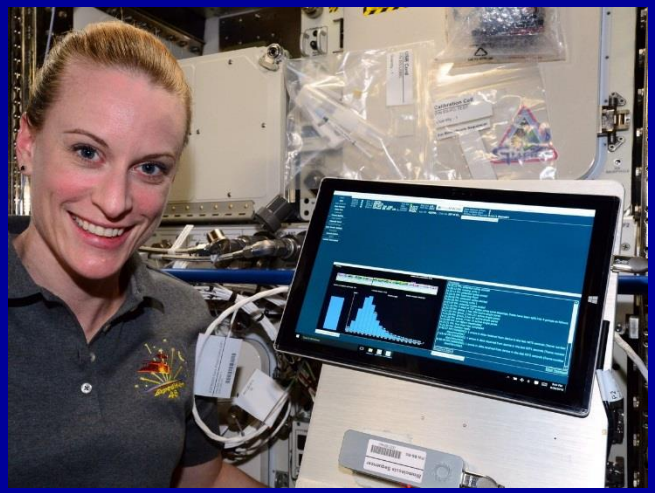
Minus Eighty-Degree Laboratory Freezer for ISS (MELFI)

Rodent habitat

The ISS U.S. National laboratory is a is a functioning research laboratory with the tools and facilities to conduct experiments in space.

ISS onboard analysis capability

Sequencer



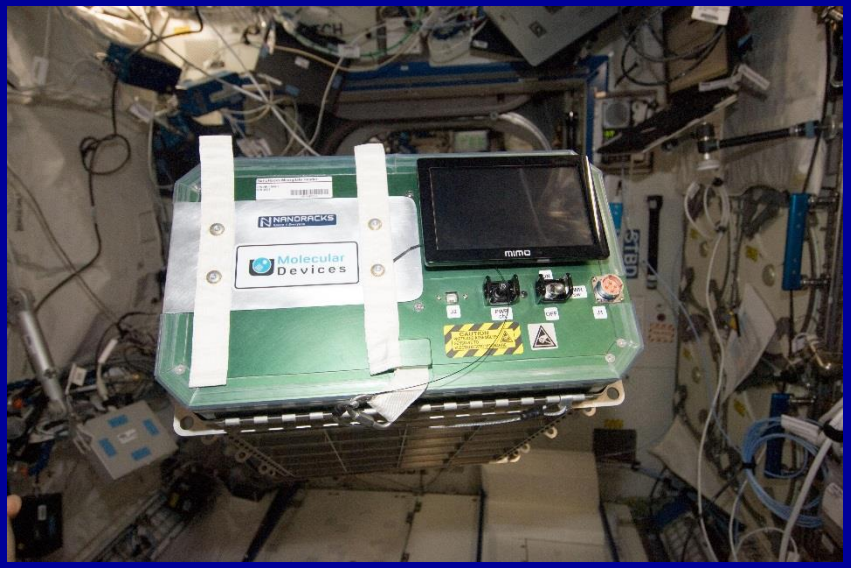


Plate reader (NanoRacks)

Flowcytometer

Ground based spaceflight analog (Bed rest)

Ground based spaceflight analog (Confined space)

NASA Extreme Environment Mission Operations (NEEMO)

Human Exploration Research Analog (HERA)

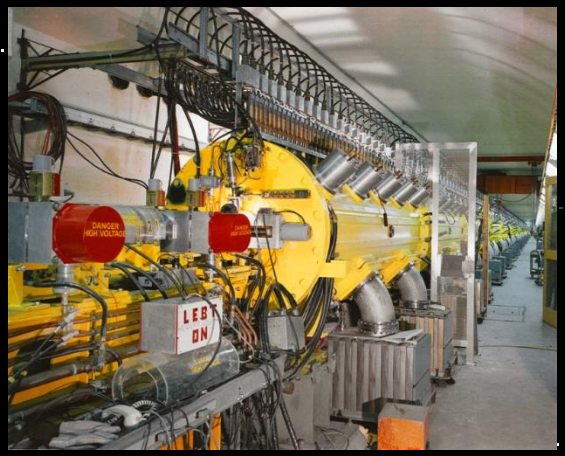
Ground based spaceflight analog (Microgravity)

Parabolic flight

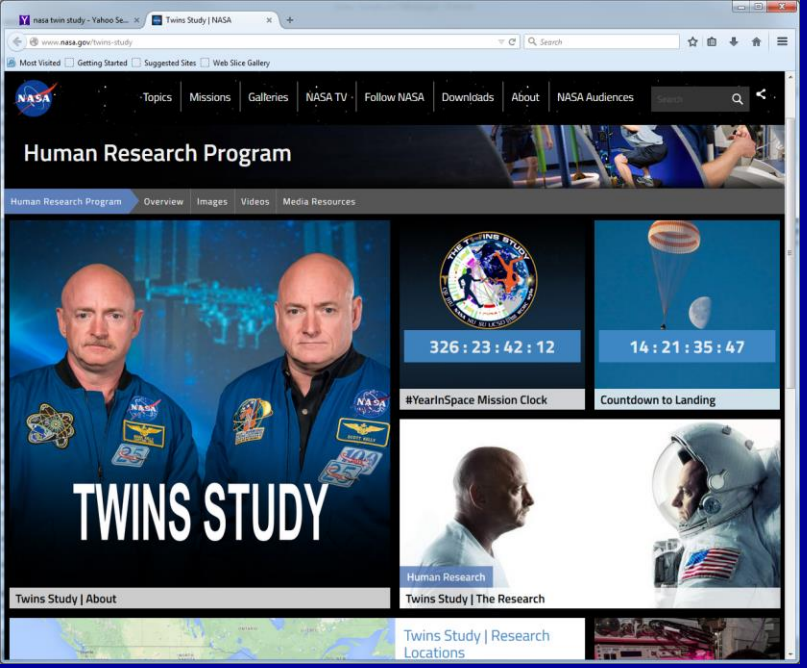
Mouse hind limb suspension

Rotating wall vessel bioreactor

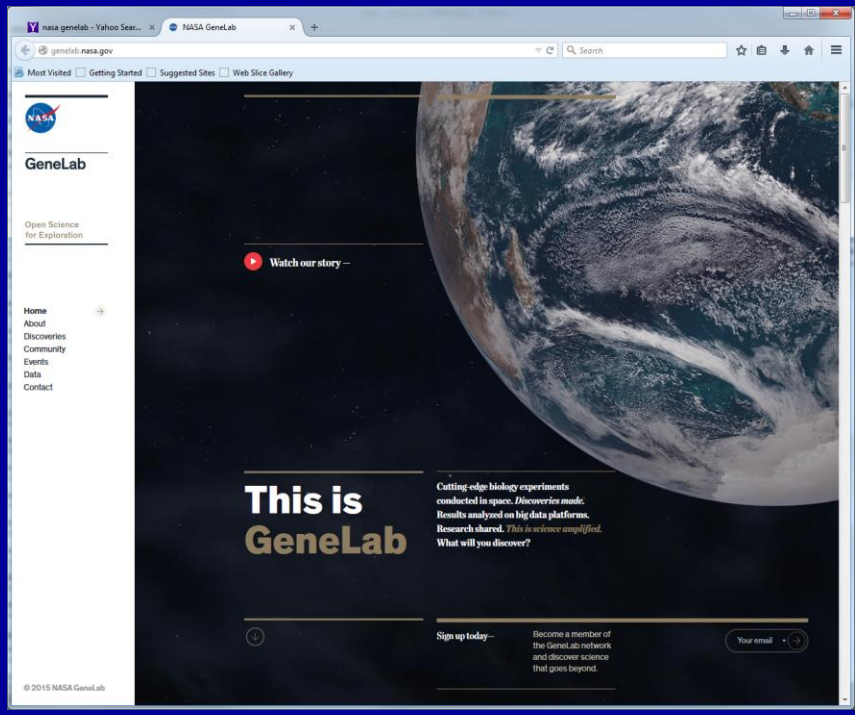
Ground based spaceflight analog (Radiation)



The **NASA Space Radiation Laboratory** provides a ground-based facility to study the effects/mechanisms of damage from space radiation exposure



Omics studies are essential in NASA life sciences research



Objectives - Micro-7 experiment

Aim #1. Investigate changes of miRNA and RNA expression in G1 human fibroblasts in space.

Aim #2. Investigate cellular responses to bleomycin-induced DNA damage in G1 human fibroblasts in space.

Aim #3. Detect the DNA damage in cells from direct exposure to space radiation.

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Transient gene and microRNA expression profile changes of confluent human fibroblast cells in spaceflight

Ye Zhang,[*,†,‡,1] Tao Lu,[*,§,1] Michael Wong,[*] Xiaoyu Wang,[¶] Louis Stodieck,[‖] Fathi Karouia,[#,**] Michael Story,[¶] and Honglu Wu[*,2]

PLOS ONE

Cellular responses and gene expression profile changes due to bleomycin-induced DNA damage in human fibroblasts in space

Tao Lu[1,2☯], Ye Zhang[3☯], Yared Kidane[1,4], Alan Feiveson[1], Louis Stodieck[5], Fathi Karouia[6], Govindarajan Ramesh[7], Larry Rohde[2], Honglu Wu[1]*

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Life Sciences in Space Research

journal homepage: www.elsevier.com/locate/lssr

Detection of DNA damage by space radiation in human fibroblasts flown on the International Space Station

Tao Lu[a,b], Ye Zhang[c], Michael Wong[a], Alan Feiveson[a], Ramona Gaza[a,d], Nicholas Stoffle[a,d], Huichen Wang[e], Bobby Wilson[f], Larry Rohde[b], Louis Stodieck[g], Fathi Karouia[h,i], Honglu Wu[a,*]

Aim 1. Gene and microRNA expression profile changes in space

- Gene expressions were analyzed with microarray containing 47k probes
- miRNA expressions were analyzed with microRNA array containing 3k probes

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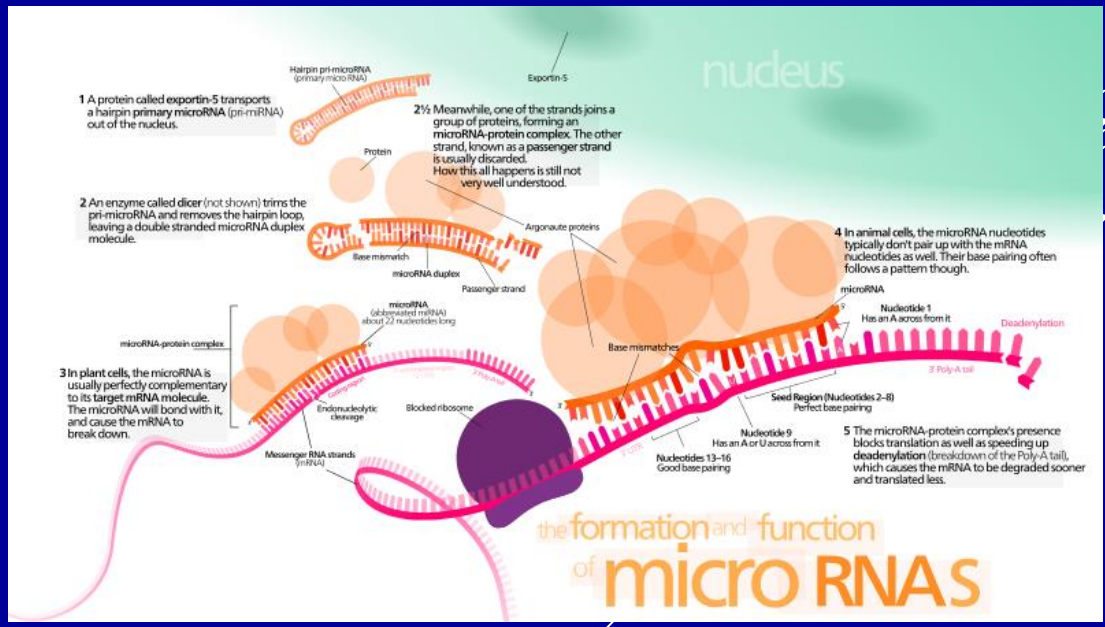
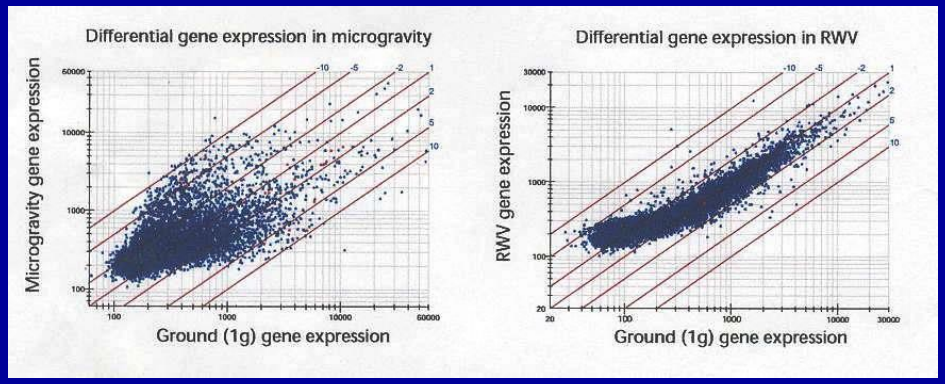
A **micro RNA** (abbreviated **miRNA**) is a small non-coding RNA molecule (containing about 22 nucleotides) found in plants, animals and some viruses, that functions in RNA silencing and post-transcriptional regulation of gene expression.



From Wikipedia

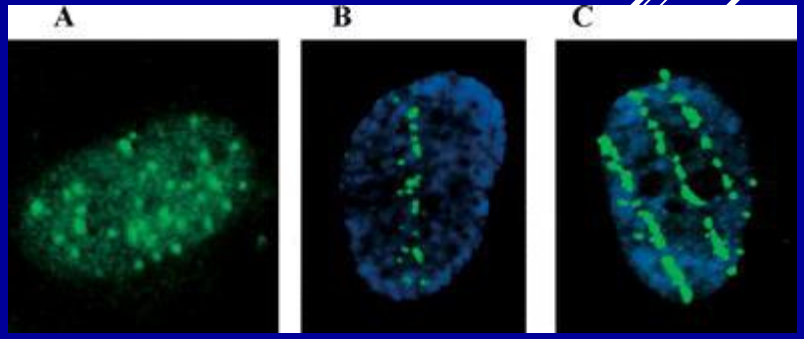
Human fibroblasts

- A fibroblast is a type of cell that synthesizes the extracellular matrix and collagen, the structural framework (stroma) for animal tissues, and plays a critical role in wound healing. Fibroblasts are the most common cells of connective tissue in animals.
- Confluent fibroblasts are slow growing or non-proliferating (90% in G1 phase based on DNA content analysis), can stay healthy without medium change for a long time (30 days tested).
- Most of the cells that have been flown to space were proliferating cells. However, most cells in an adult divide slowly.
- The cell line (AG1522) has been investigated extensively for cellular and DNA damages by low- and high-LET radiation.

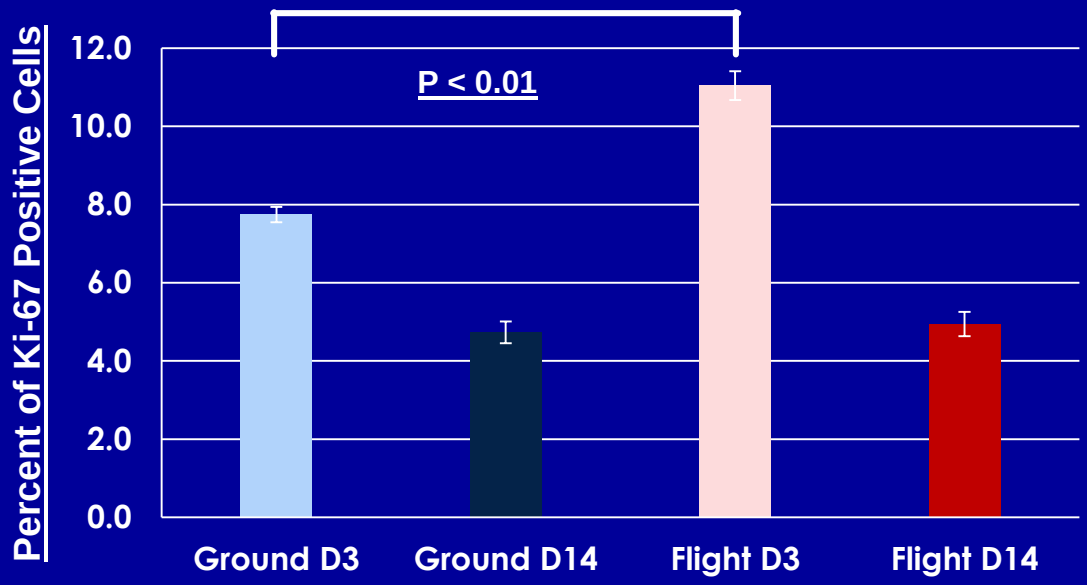


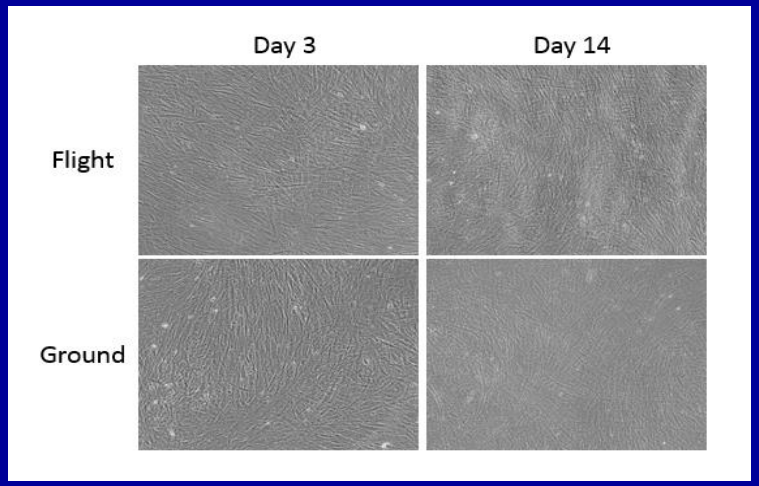
Gene expressions in human renal cortical cells.
Hammond et al. Nature Medicine 1999

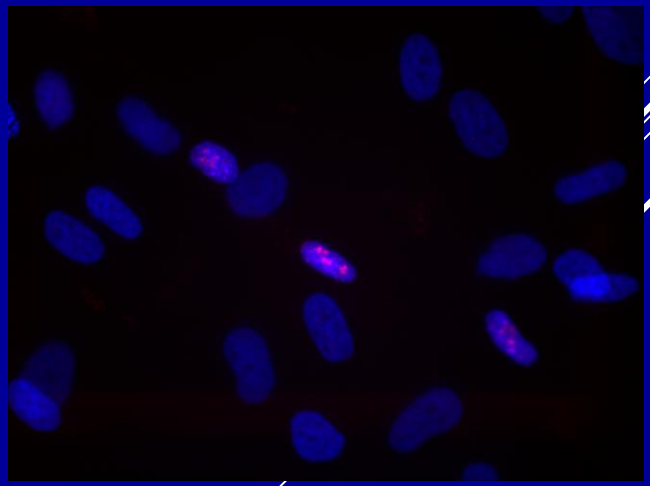
DNA damage in human fibroblast cells by γ rays, and Si and Fe ions. Desai et al. Rad. Res. 2005



Cells proliferated faster in space on Day 3



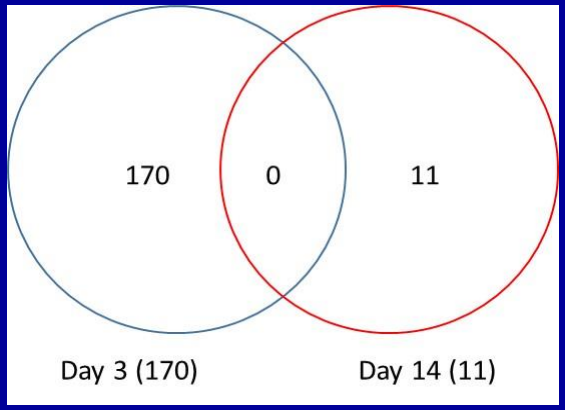




Ki-67 staining

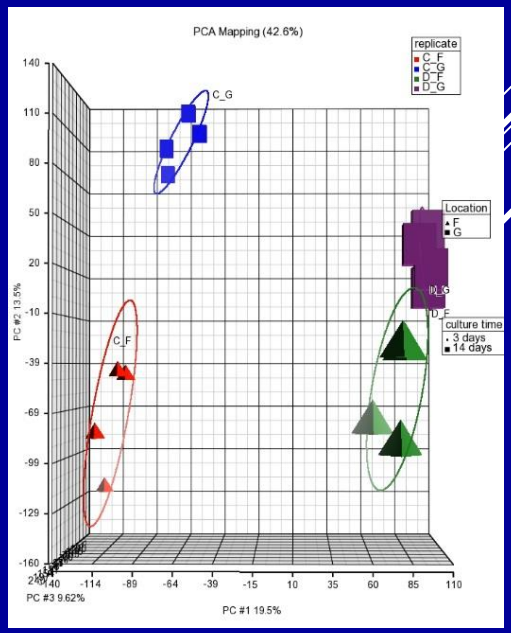
MICROARRAY RESULTS – DAY 3 AND DAY 14

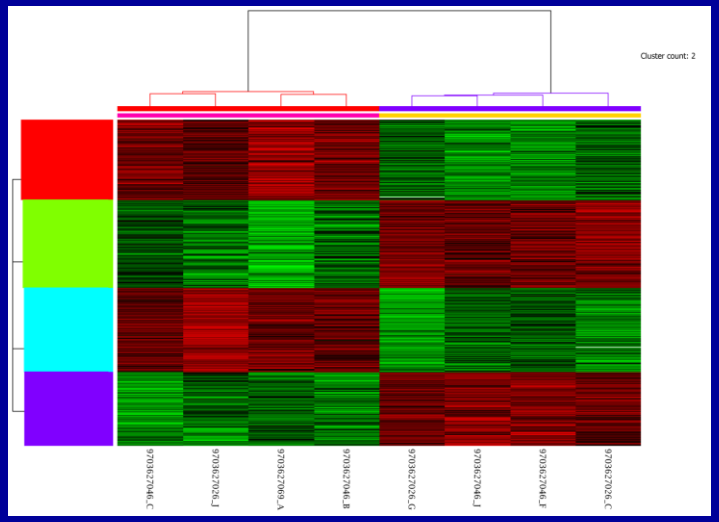
Number of genes having significant expression changes in the flight samples in comparison to the ground controls on Day 3 and Day 14



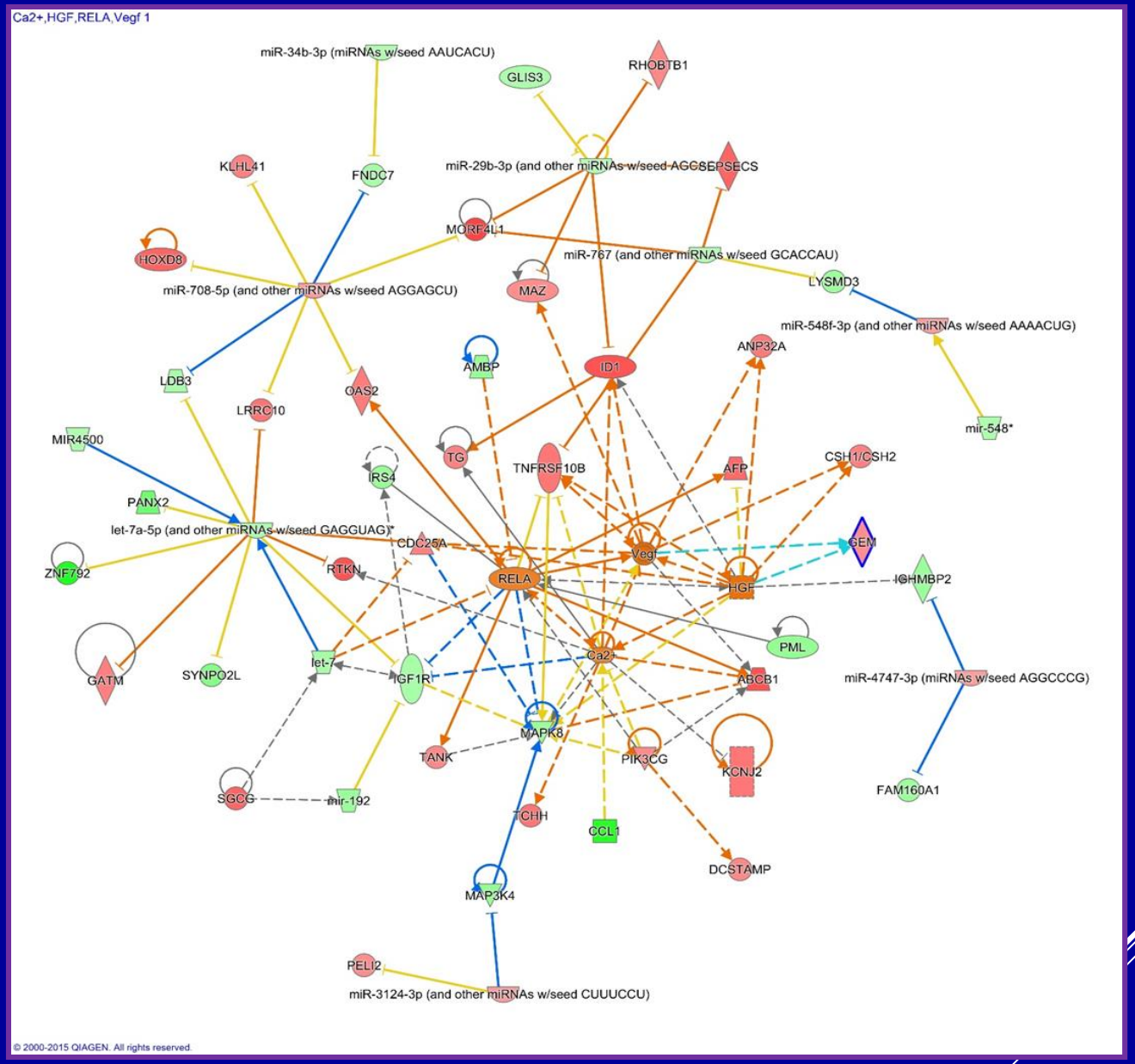
Venn diagram

PCA Analysis





Heat map



Faster proliferation of cells in space is associated with activation of NF-κB which triggers a number of growth factors.

Genes and miRNA with altered expressions in space

NF-κB

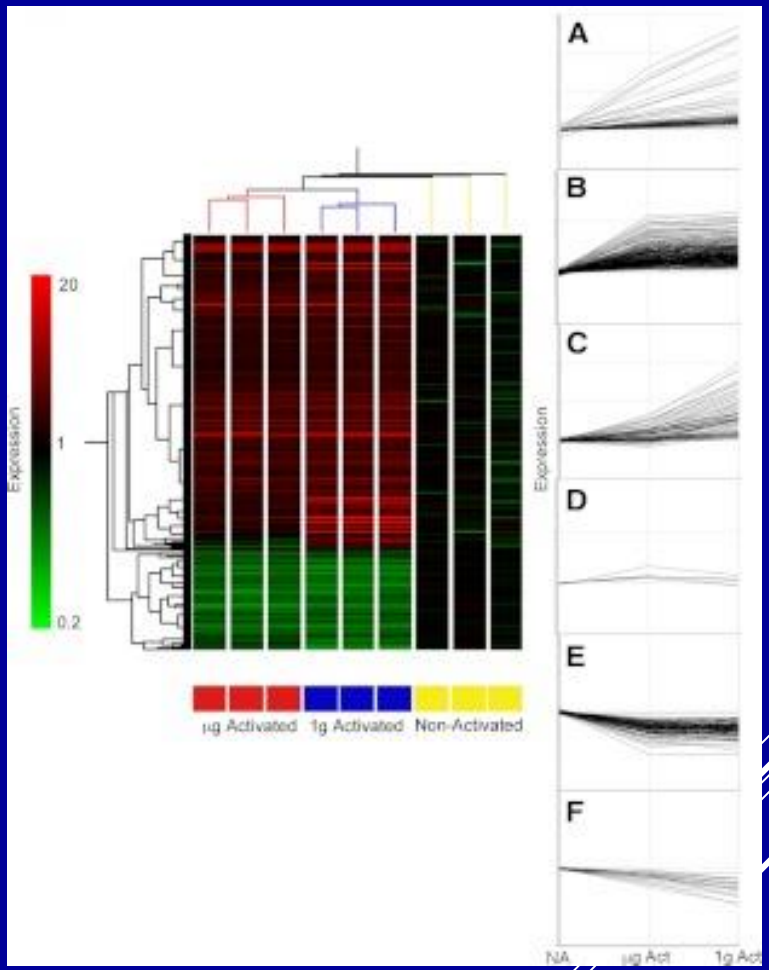
- NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) is a protein complex that controls transcription of DNA, cytokine production and cell survival.
- Involved in cellular responses to stimuli such as stress, free radicals, and radiation.
- Involved in inflammatory and innate immune response.
- Involved in cancer development.

Let-7

- The human let- 7 family plays a role in development, stem cell biology, aging, and metabolism.
- Loss of let-7 expression is associated with the development of poorly differentiated, aggressive cancers.
- Radiation exposures up-regulate the expression of Let-7 miRNA.
- Let-7 significantly impacts the radiation response in mammalian cells.

Summary of RNA and miRNA expressions

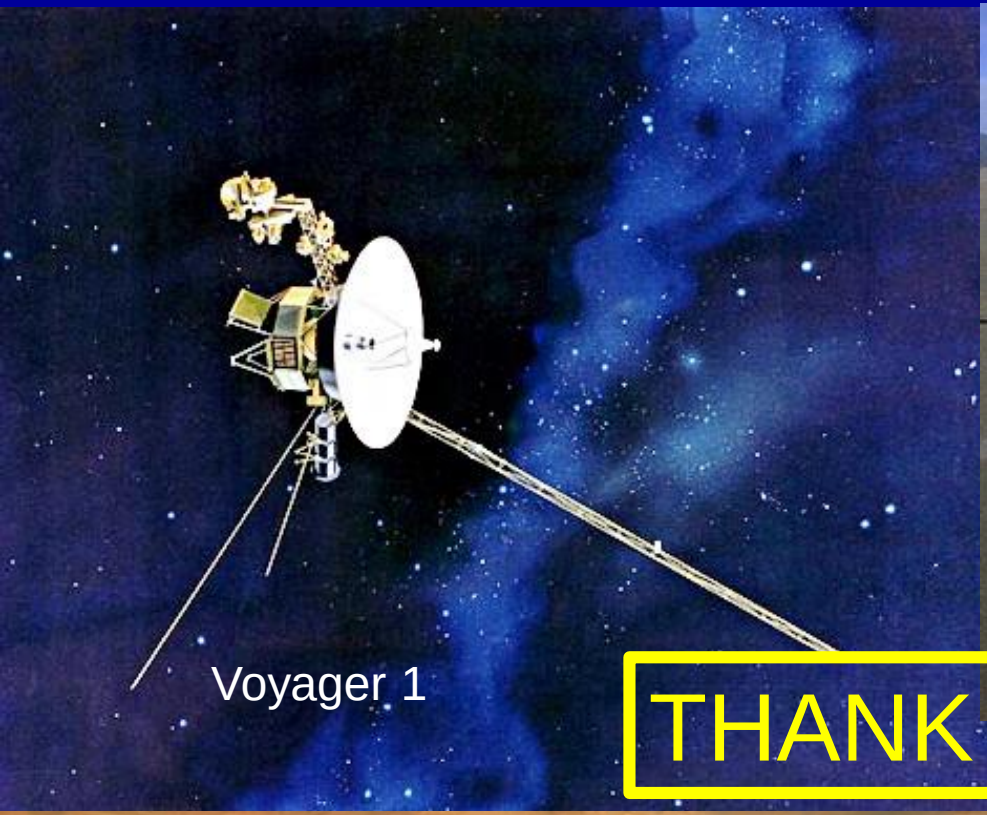
- Spaceflight has effects on gene and miRNA expressions only in proliferating human fibroblasts, but not on the resting cells.
- Human fibroblasts proliferate faster in space than on the ground, which is related to the activation of the NF-κB pathways.



T cell activation is inhibited by microgravity, but no gene expression changes were reported in the non-activated cells in space (Chang … Hughes-Fulford et al. 2012)

Conclusions

- Under stress, human fibroblast cells proliferate faster in order to stay. Such a process involves the NF-κB network.

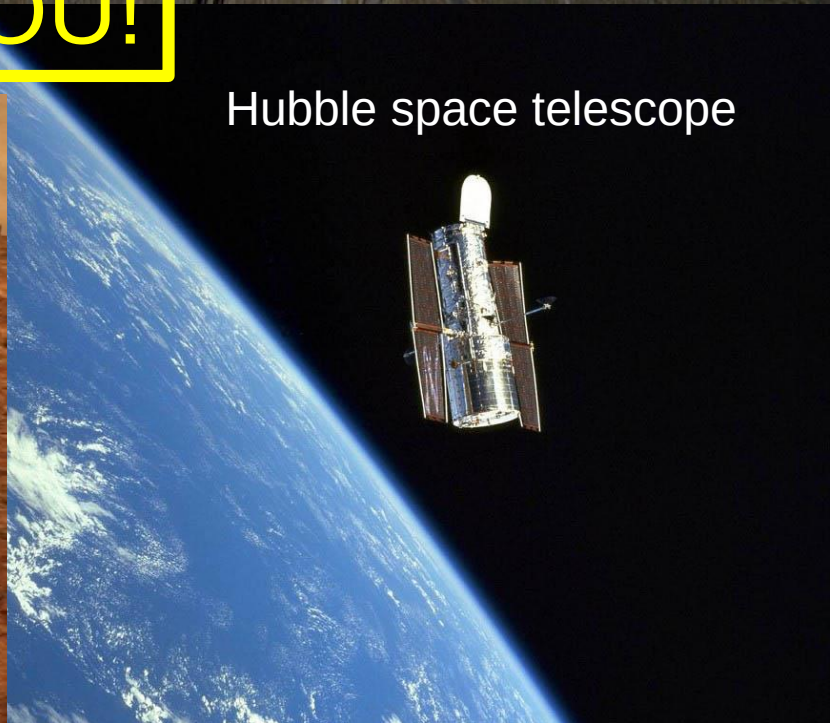


Voyager 1

Radio telescope

THANK YOU!

Curiosity rover



Hubble space telescope