Altered gravity platforms in space research

Two applications of *in vitro* space simulations models

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Overview

- Space environment
- Space simulation models
- Immune system
- Skin – wound healing
- Hypergravity project
Space Environment

Altered gravity
- Acute:
  - Space motion sickness
  - Adaptation process
- Chronic:
  - Deterioration of multiple physiological systems

Ionizing radiation
- Acute:
  - Solar particle events: increased dose, high energy protons
- Chronic:
  - Galactic cosmic rays: highly charged, energetic atomic nuclei (HZE) particles

Psychological stress
- Acute:
  - Adrenal gland releases adrenaline and cortisol
  - Fight-or-flight
  - Goal: restore allostasis
- Chronic:
  - Prolonged exposure to cortisol
  - Maladaptive
Space Environment

Mechanisms?

Countermeasures?
Space simulation model

Limitations ISS/spaceflight studies:

• Small sample sizes
• ISS missions vs. interplanetary missions
  • Duration
  • Space radiation field
• Effect of spaceflight stressors alone vs. in combination

⇒ Development of *in vitro* model to investigate cellular responses to the combined spaceflight environment
Ground Control to Major T-Cell
T-Cells as models for space immune dysfunction

T-Cells
Key regulators of the cellular immune response
Kill infected cells
Activate other immune cells
Provide memory immunity

Space immune dysfunction
Reduced T-Cell activity
Diminished cell numbers
Increased reactivity (e.g. Allergies)
Interaction between μG and radiation

Ground Control to Major T-Cell Methodology

Stimulated Jurkat Cells

Altered Gravity
Ionizing Radiation
Stress hormones

CD4+ T-Cell extraction
CD4+ T-Cells stimulated

Altered Gravity
Ionizing Radiation
Stress hormones

IL-2 Concentration
IL-2 gene expression

Flow cytometry
Cytokine profiling
Proteomics
Transcriptomics
Astronauts report delayed cutaneous wound healing during spaceflight

• Interference in complex process of wound healing leads to defective repair

• Fibroblast migration to wound site and interaction with ECM is crucial for wound healing process

➢ Investigate migration capacity and ECM protein expression of fibroblasts exposed to simulated spaceflight environment
Human primary dermal fibroblasts ➔ major cellular component of the dermis

Simulated spaceflight stressors:
- Random Positioning Machine for micro- and partial gravity simulation
- Ionizing radiation, high- vs. low LET
- Hydrocortisone exposure in the medium
Wound healing in space
Preliminary results

- Altered gravity
- Ionizing radiation
- Psychological stress

Graphs showing:
- Open wound area (%)
- Relative wound closure (%) over time for different conditions:
  - Control
  - HC 100nM
  - HC 1000nM

Graphs for different gravity levels:
- 1g
- μg

Graphs for different radiation doses:
- 0Gy
- 0.1Gy
- 0.5Gy
- 2Gy
Long-duration spaceflight

Case report of skin sensitivity after one-year space mission

- Erythema and skin sensitivity
- Gravity-dependent areas
- Interruption of post-flight activities

→ Development of effective countermeasures

[Law et al. 2020]
Hypergravity exposure using the **Large Diameter Centrifuge (LDC)**.

- Investigate the potential of hypergravity to **counteract** spaceflight-induced **delayed wound healing**

- Document **space-related defects** in wound healing and a possible interplay with elevated stress levels experienced in space

- **ESA’s Large Diameter Centrifuge**
  - 8m diameter
  - Up to 20 times Earth’s gravity
Conclusion

Better risk assessment for deep-space exploration

• More insights into possible interaction effects of spaceflight stressors
  • Synergistic, antagonistic, or additive effects

Better insights into gravity dependent fibroblast functions related to wound healing

• Reveal altered cellular functioning
  • Indication for possible countermeasure development
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