Osteoblastic cellular functions during spaceflight_1

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http://www.osteoblasticcellularfunctions.spaceflight.com
Osteoblastic cellular functions during spaceflight

by

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Osteoblastic cellular functions during Spaceflight
Osteoblasts are bone forming cells

- Osteoblasts are mononucleated cells derived from mesenchymal progenitor cells
- They are important for new bone formation after a fracture or during bone remodelling
- Osteoblasts are responsible for calcification of the bone

Principal Proteins found in Bone Collagenens
- Collagen type I
- Collagen type V

Noncollagen proteins
- osteonectin
- osteocalcin
- osteopontin
- bone sialoprotein
- bone morphogenetic proteins (BMPs)
- osteoprotegerin
- proteoglycans
Osteoblast cells in space

- without gravity bone demineralize
- bone formation is reduced
- and bone resorption is increased
- maturation of precursors to osteoblasts is delayed

Consequence: bone loss/osteoporosis
Methodology

NHOst

- FS
  - Gene expression
- GC37°C
- GCAT
  - Protein expression
- Mechanical

MRO

- DNA damage
- Cell Morphology
- Cytoskeleton
- Gene expression
- Protein expression
Osteoblastic cellular functions during Spaceflight
cellular functions of osteoblast cells

- proliferation
- production of extracellular matrix
- bone mineralisation
- regulation of osteoclastogenesis
Confounding factors for a space experiment:

- Growth matrix
- Temperature
- Vibrations
- Radiation
Influence of the growth matrix

Comparison between OB growth on flask versus cytodex

We compared the expression of various bone markers of osteoblast cells growing in a normal tissue culture flask and on collagen based microcarriers:

Results: no significant difference between the two was found.
Influence of temperature on gene expression

We examined the expression of various bone markers by osteoblast cells grown at 37 degree and the temperature profile obtained from the flight samples. Result: temperature has a significant influence on CD44 expression.
Change of actin and tubulin after 3 days of hypothermia

After 72h of hypothermia the intensity of actin increased while tubulin didn’t seem to be affected.

Conclusion: hypothermia affects the cytoskeleton and therefore will affect gene expression.

Figure 1: Fixed NHOS cells were stained with Anti-α-Tubulin-FITC; tubulin (green), Alexa Fluor®635 Phalloidin; actin (red), and DAPI; nucleus (blue). Change in cell cytoskeleton during control and hypothermia was viewed under confocal laser scanning microscope at 40x magnification (scale bar: 75µm after 12h, 24h, 72h and 5 days of treatment.
influence of mechanical stress on gene expression (3 days)
we tested the effect of mechanical stress on the expression of osteoblast markers and found that mechanical stress influences the expression of osteoblast markers positively. Mechanical stress is considered a positive stressor for osteoblast cells.
Influence of radiation on osteoblasts

DNA damage measured with Acridine Orange and propidium iodide
Osteoblastic cellular functions during Spaceflight
Changes of osteoblastic markers during spaceflight

spaceflight significantly influenced the expression of cell surface markers, indicating reduced cell matrix interaction
Microgravity-readapted osteoblast cells
changes in osteoblastic function

• bone and matrix markers
• cell morphology
• cytoskeleton
• cell signaling pathway
changes in bone and matrix markers
changes in gene and protein expression

We investigated osteoblast cells after they returned from space. The microgravity exposed and re-adapted cells cell showed similar expression levels of osteoblast markers than normal non-spaceflight exposed cells.
changes in cell morphology and cytoskeleton

SEM of the normal osteoblasts. Cells are elongated; nuclei are oval, centrally located, with prominent nucleoli. Plasmalemma with moderate amount of pores; x 3,000.

SEM of the postflight osteoblasts. The cells are enlarged, with irregular contours, numerous long and thin processes, extremely eccentric nucleus; x 2,000.
SEM of the normal osteoblasts. Cells are elongated; nuclei are oval, centrally located, with prominent nucleoli. Plasmalemma with moderate amount of pores; x 3,000.
SEM of the postflight osteoblasts. The cells are enlarged, with irregular contours, numerous long and thin processes, extremely eccentric nucleus; x 2,000.
Changes in cell signaling pathways
Functional annotation chart from DAVID Bioinformatics Resources

- Cell cycle: 10.73%
- Ubiquitin mediated proteolysis: 1.9%
- T cell receptor signaling pathway: 2.4%
- Calcium signaling pathway: 1.52%
- Wnt signaling pathway: 1.14%
- Others: 1.39%
- Unclassified: 80.83%
osteoblastic cellular functions during space flight and long term changes in microgravity re-adapted osteoblast cells
1. Change in bone function markers
2. Loss of cell-cell interaction and cell-matrix
3. Change in cell morphology and cytoskeleton
4. Premature aging
5. Resistance to apoptosis and increased life-span of the spaceflown osteoblasts
1. Change in bone function markers
function markers

2. loss of cell-cell interaction and cell-matrix

3.
3. change in cell morphology and cytoskeleton
and cytoskeleton

4.

premature aging

5.
5. resistance to apoptosis and increased life-span of the spaceflown osteoblasts
1. Change in bone function markers

2. Loss of cell-cell interaction and cell-matrix

3. Change in cell morphology and cytoskeleton

4. Premature aging

5. Resistance to apoptosis and increased life-span of the spaceflown osteoblasts
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