CDKN1a/p21 Plays Critical Role in Suppressing Stem Cell Regenerative Potential during Aging

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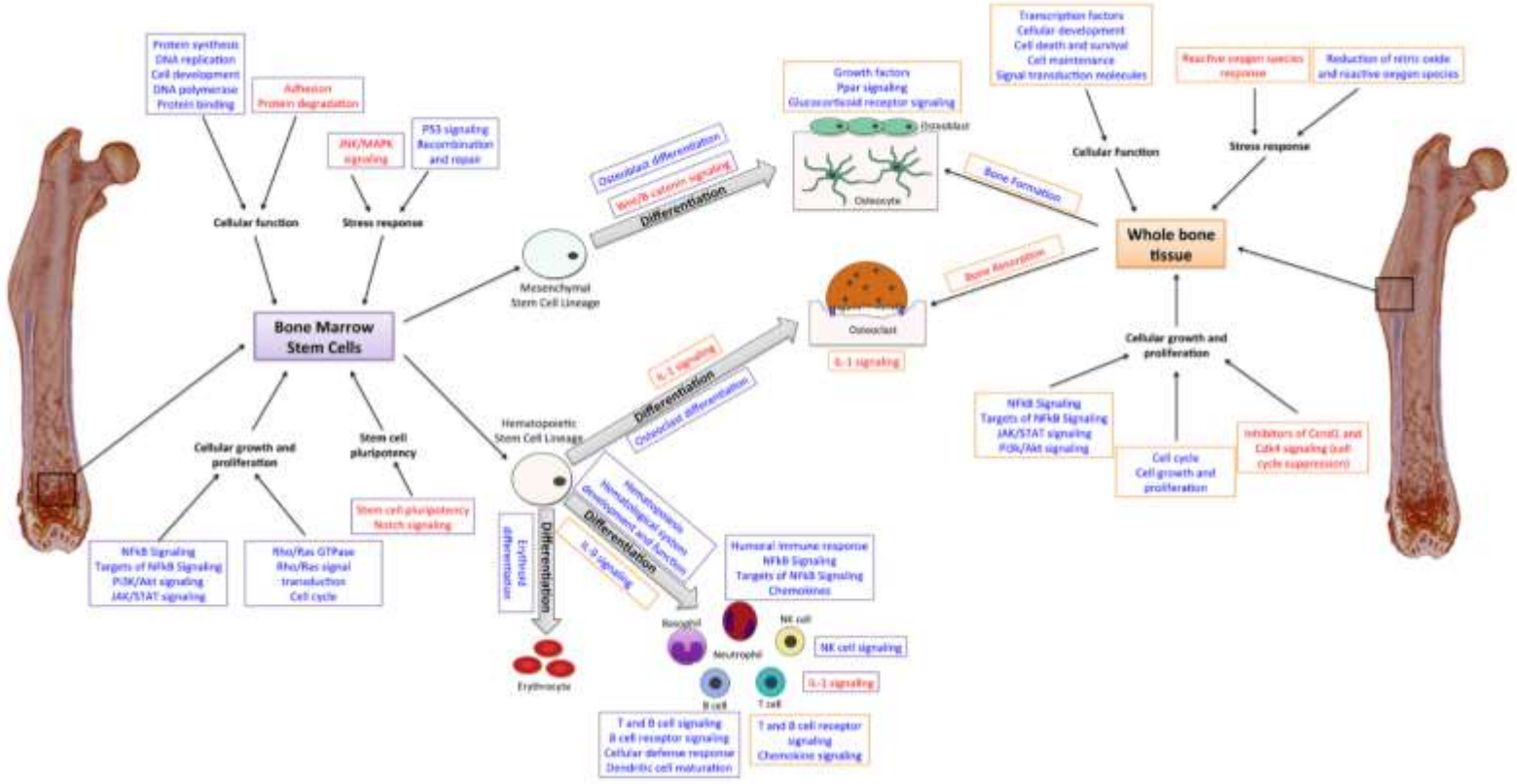
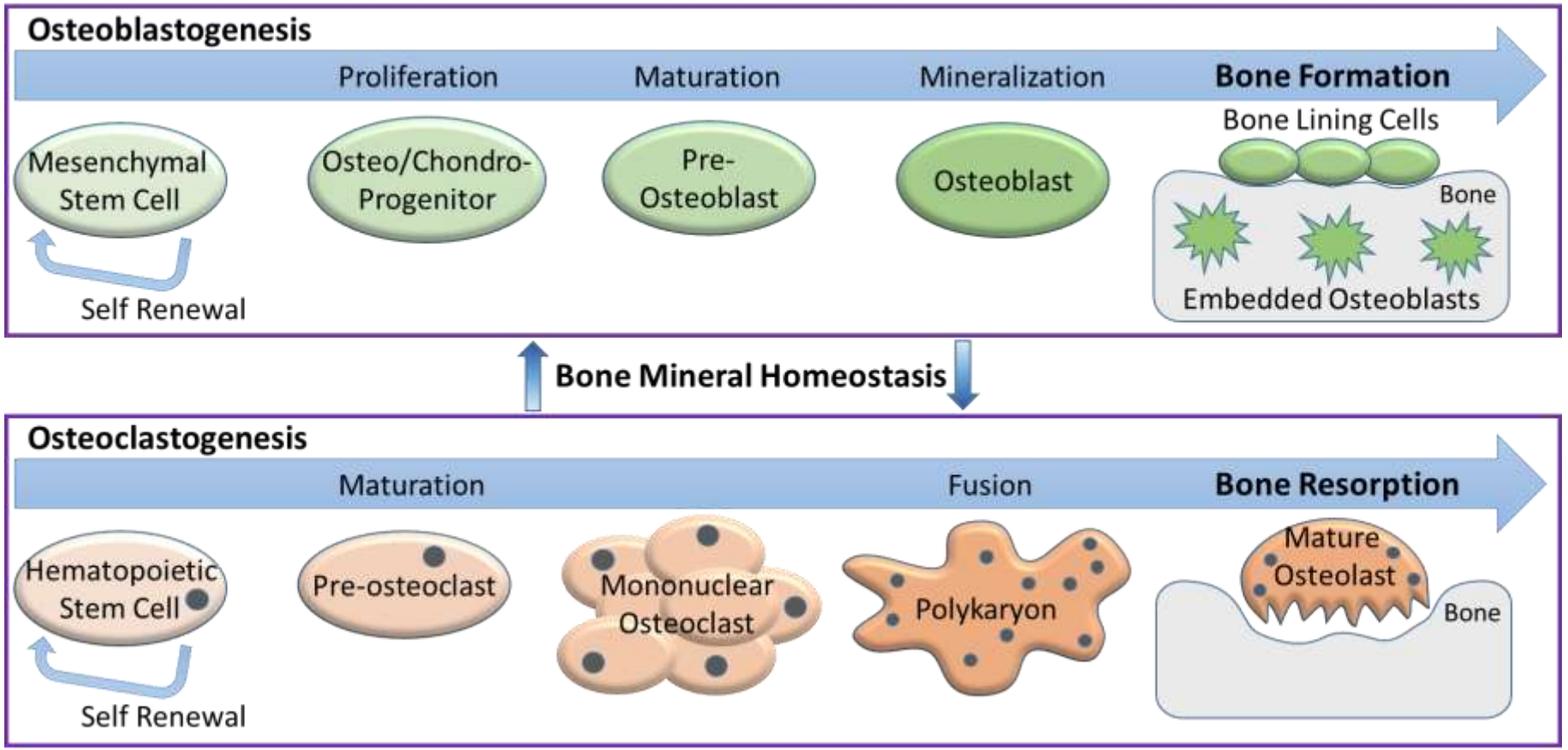
Bone in Spaceflight



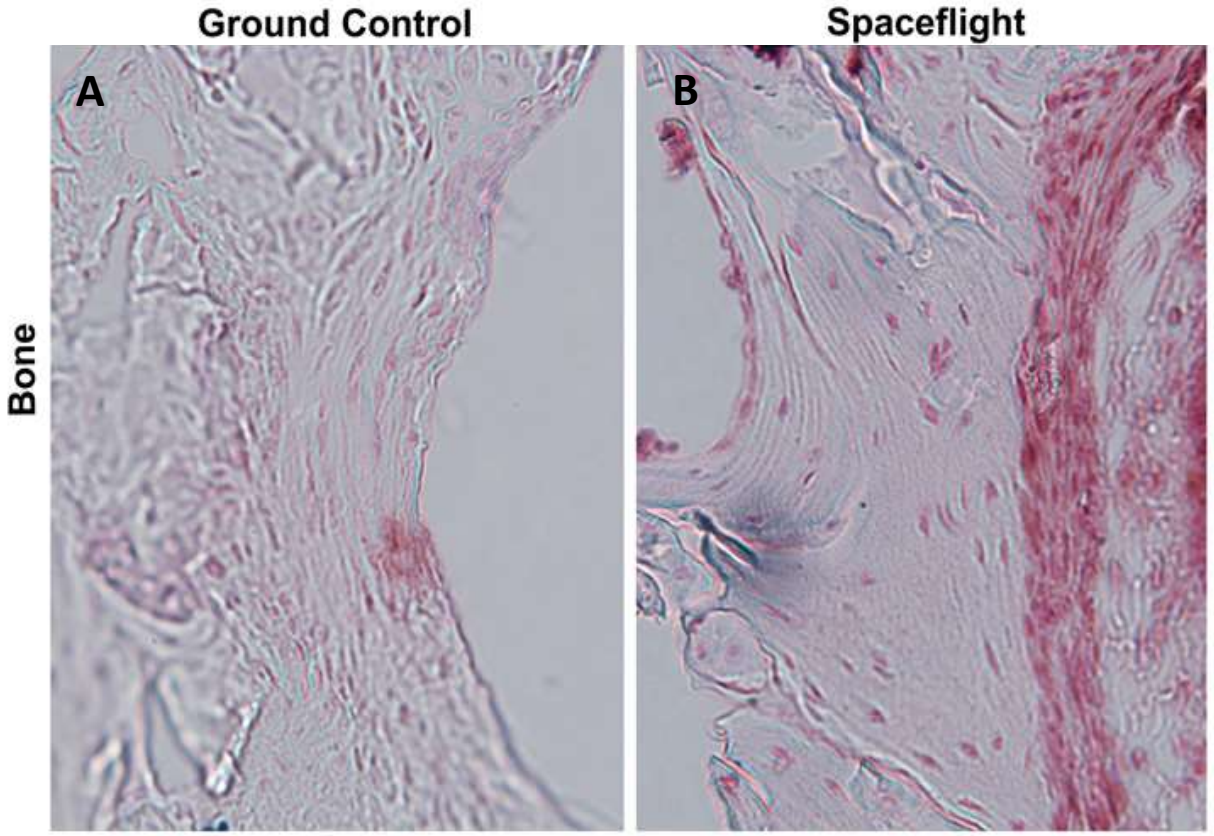
Spaceflight results in significant down-regulation of key genes required for mesenchymal and hematopoietic stem cell differentiation into terminally differentiated linages.

Bone Regulation



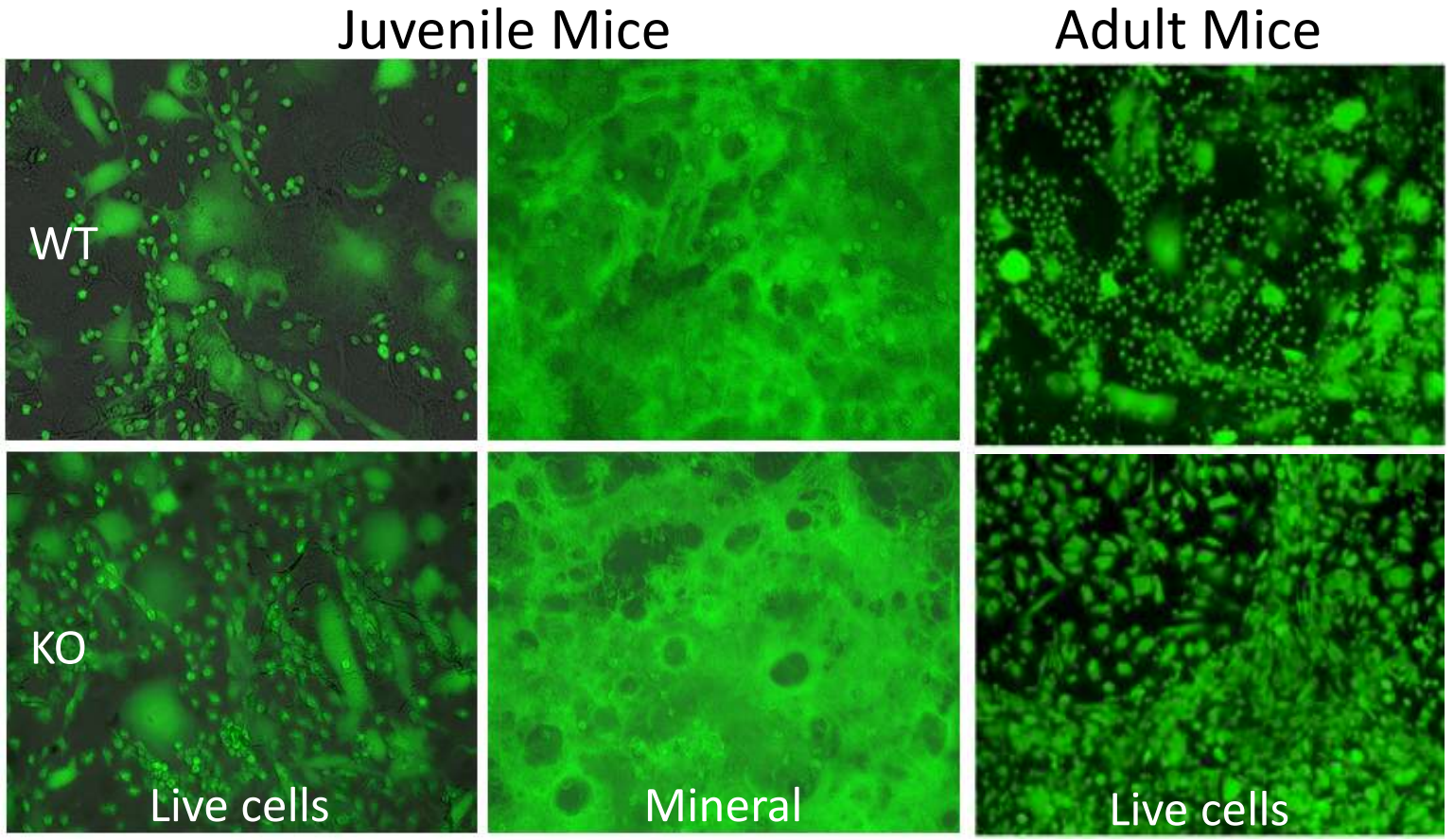
Bone mineral homeostasis is a balance between bone formation by osteoblasts and bone resorption by osteoclasts.

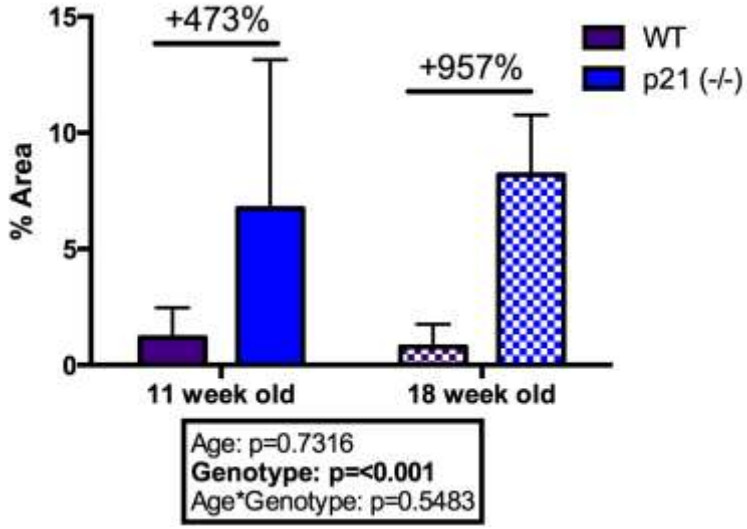
CDKN1a/p21



- Spaceflight mice showed increased CDKN1a/p21 in osteoprogenitor cells
- CDKN1a/p21 is a potent cell cycle arrest molecule
- CDKN1a/p21 knockout (KO) mice exhibit regenerative abilities similar to amphibians
- Ongoing studies will study the effect of age on proliferation and differentiation

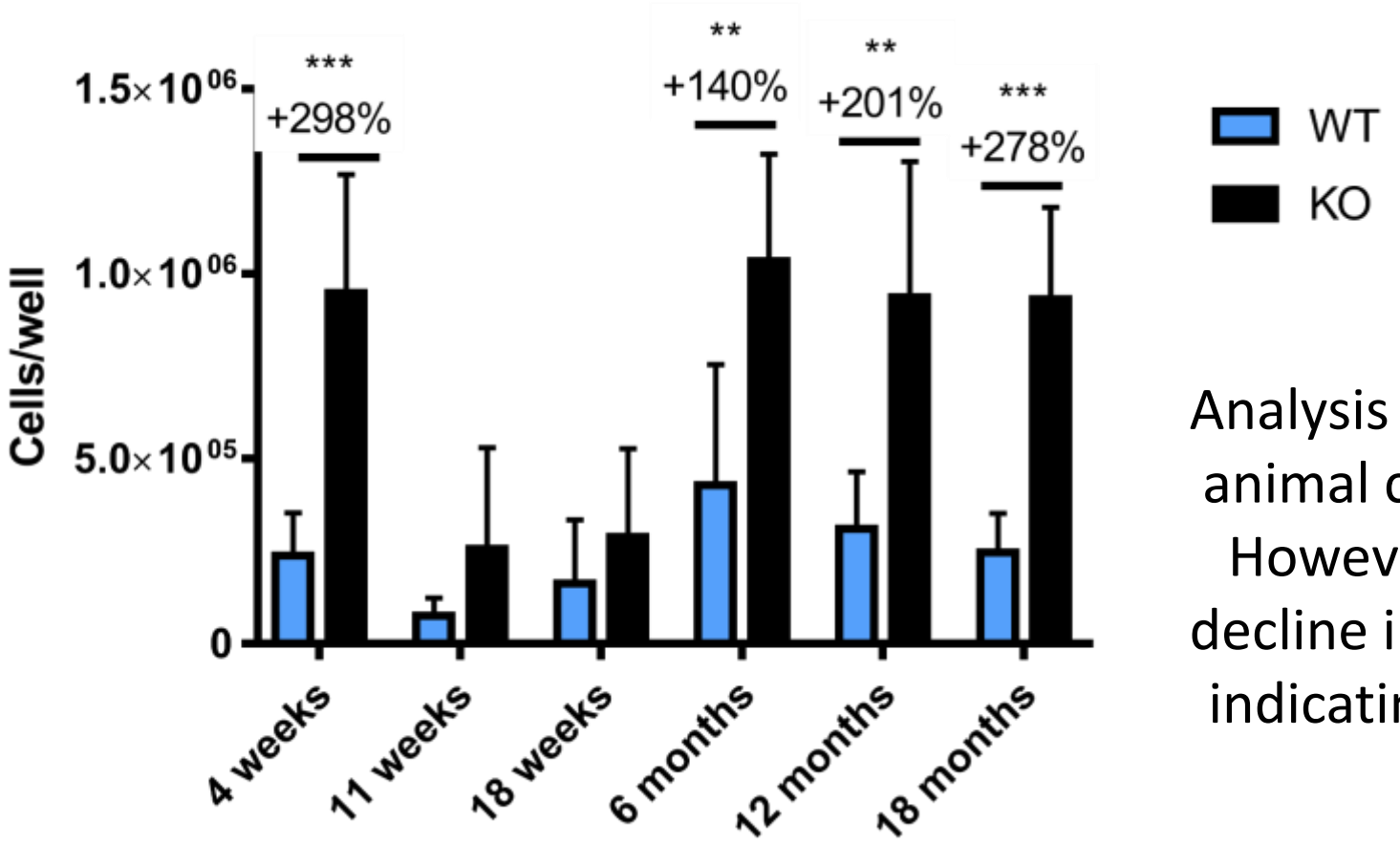
Aging Comparison- WT vs KO





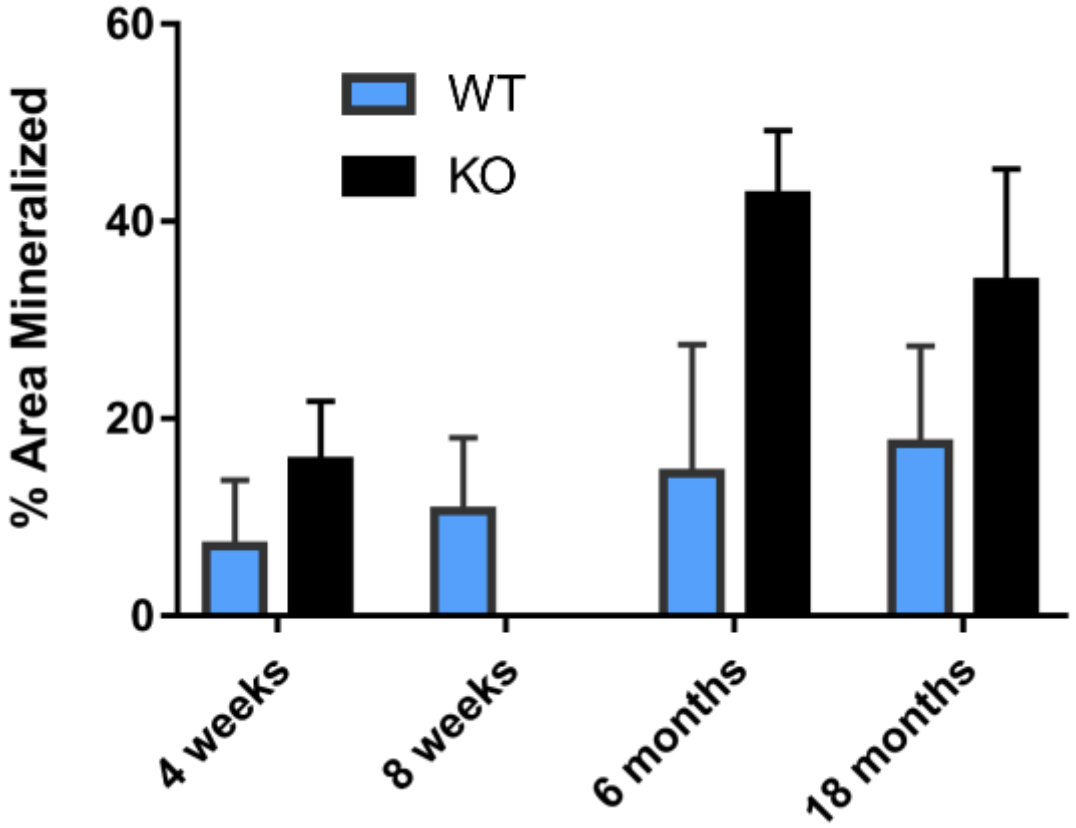
Calcein staining shows increased cell numbers and mineral in KO cultures compared to WT.

Aging Comparison- WT vs KO



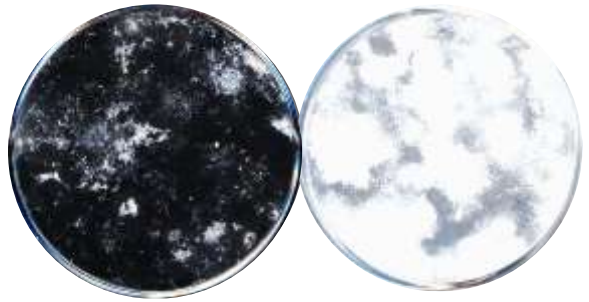
Analysis of osteoblastic cultures indicate WT animal cell counts peak at 6 months of age. However, KO cells do not exhibit a similar decline in cell number past 6 months of age, indicating a **difference in proliferation and regenerative potential**.

Aging Comparison- WT vs KO



4-week KO vs 6-month KO

18-month WT vs 18-month KO



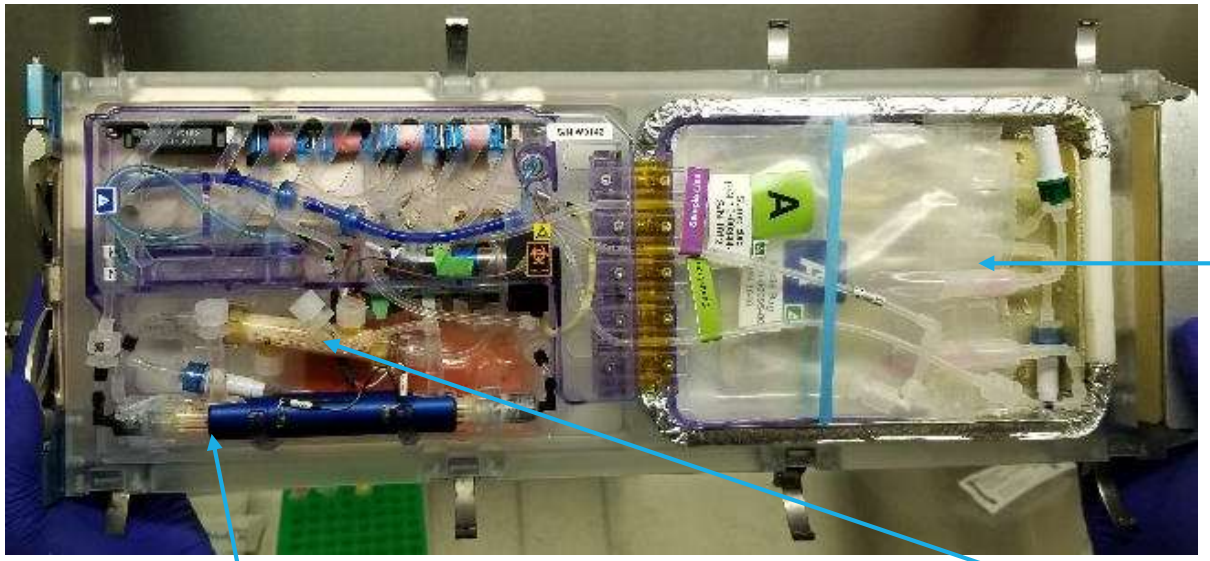
In addition to increased proliferation rates, deletion of CDKN1a/p21 in juvenile and adult mice resulted in **increased differentiation capacity** exhibited by increased formation of mineralized nodules.

CS-03 Flight Aims

1. To assess the in-vitro **proliferation, differentiation, and mineralization capacity** of BMSCs isolated from p21 KO and WT animals in microgravity versus 1g controls
2. To determine the **cellular mechanisms** associated with alterations in osteoprogenitor differentiation potential in p21 KO mice vs WT
3. To investigate the **signal transduction pathways** which are responsible for CDKN1a/p21 in microgravity and therefore inhibition of in vitro bone formation in space

Bioculture System

Photo credit: NASA/Dominic Hart

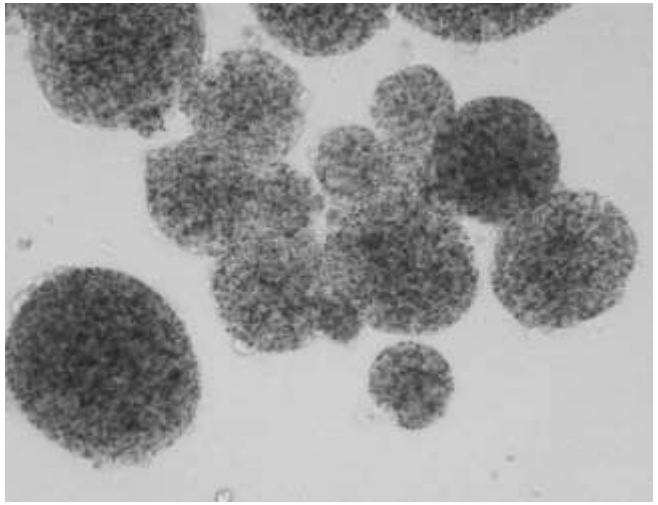


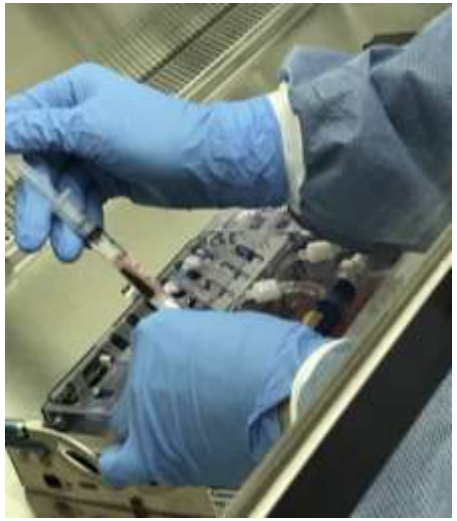
Media, sump, fixative, and sample bags

Main Hollow-fiber Bioreactor

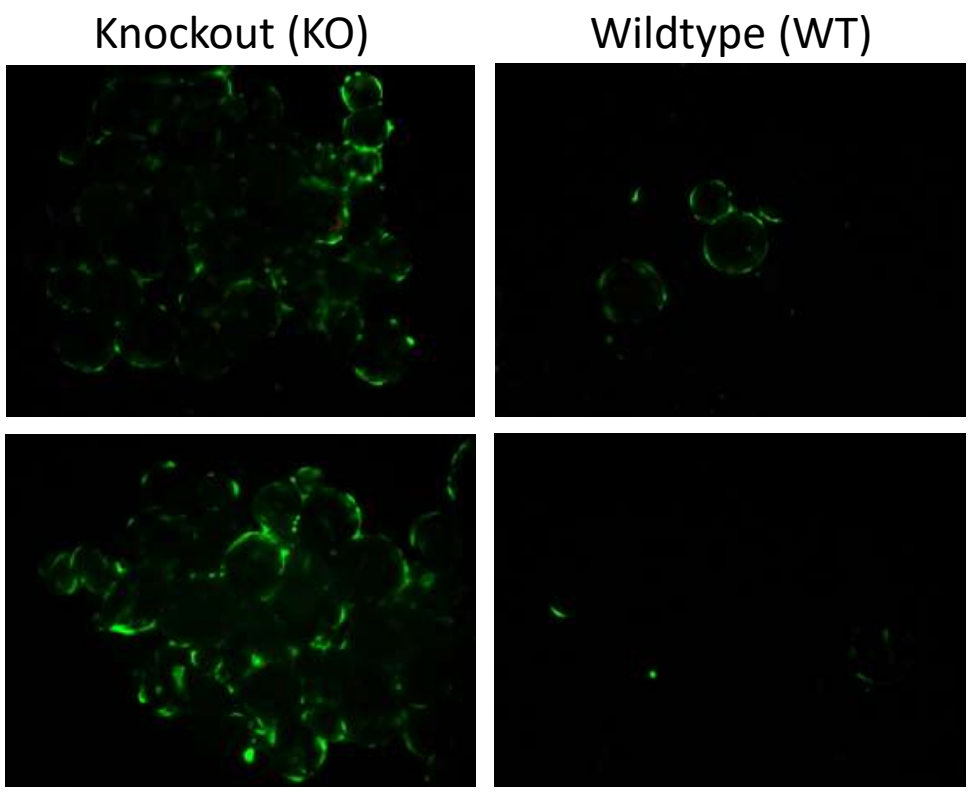
Secondary Growth Factor Bioreactor

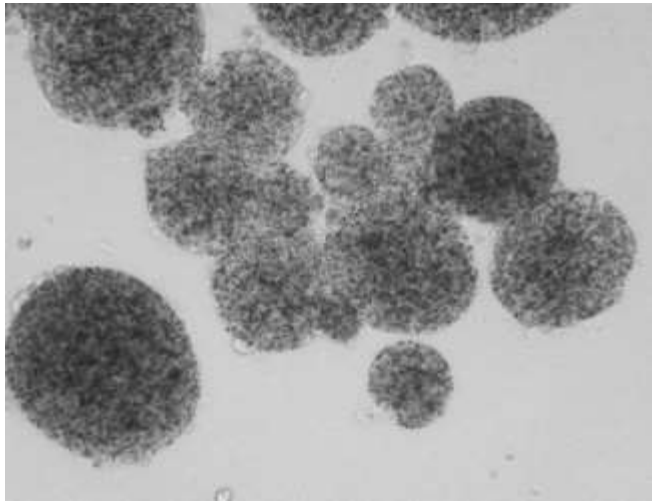
Bioculture System- Osteoblastogenesis on Beads

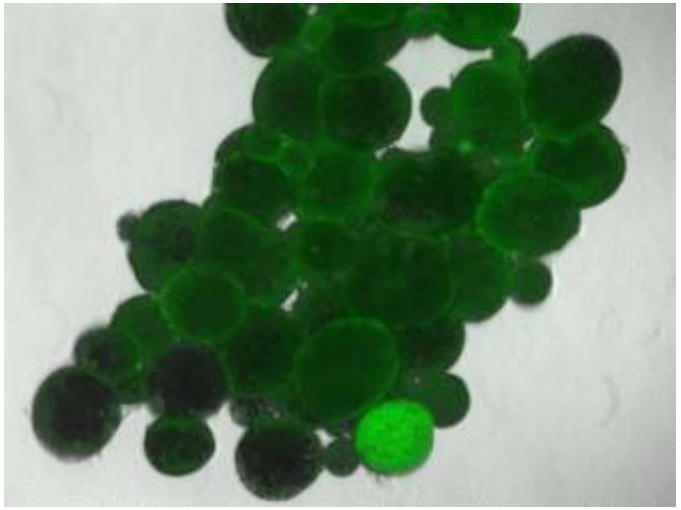




Osteoblastogenesis Using Gelatin Beads

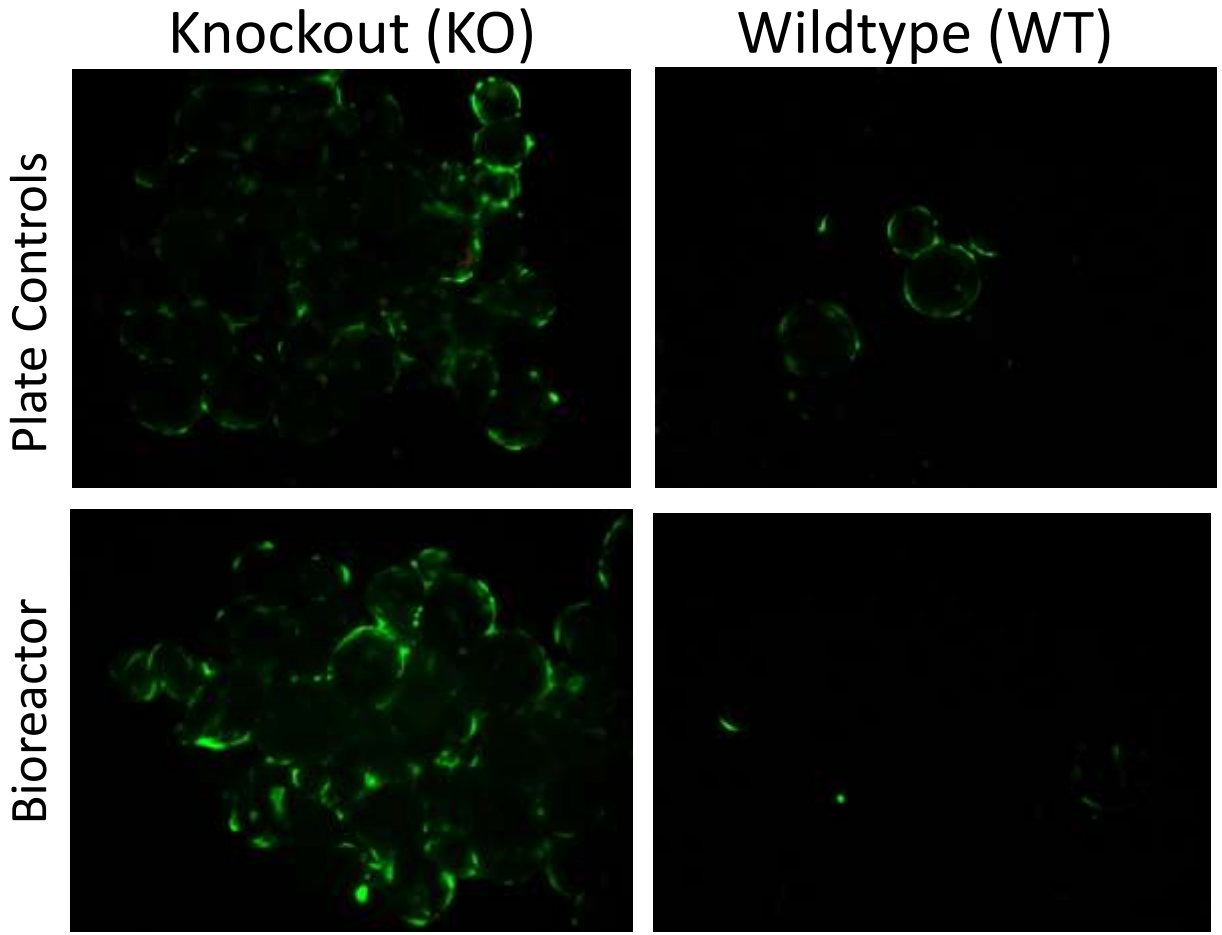


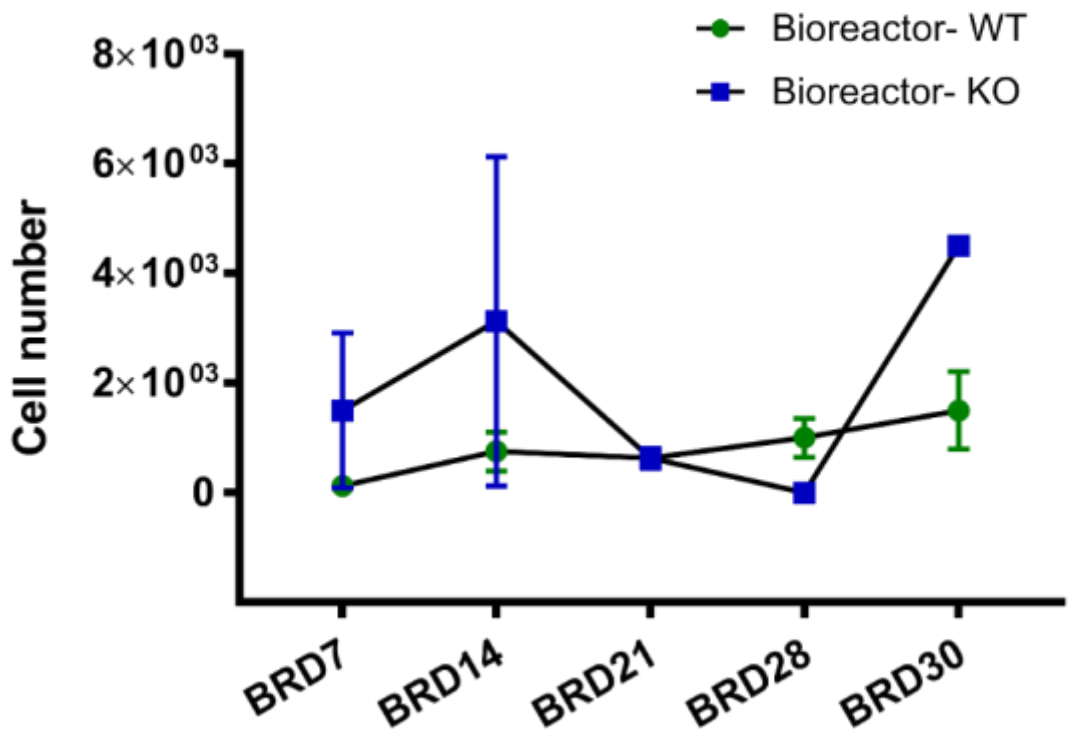


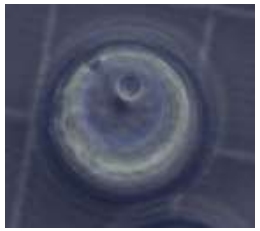


Global **E**ukaryotic **M**icrocarriers mineralized by cells as shown by calcein stain (above)

Osteoblastogenesis Using Gelatin Beads

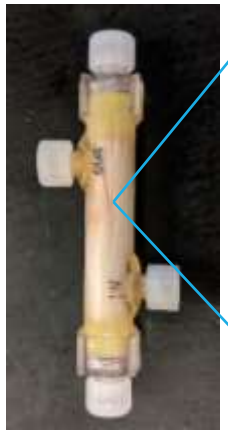


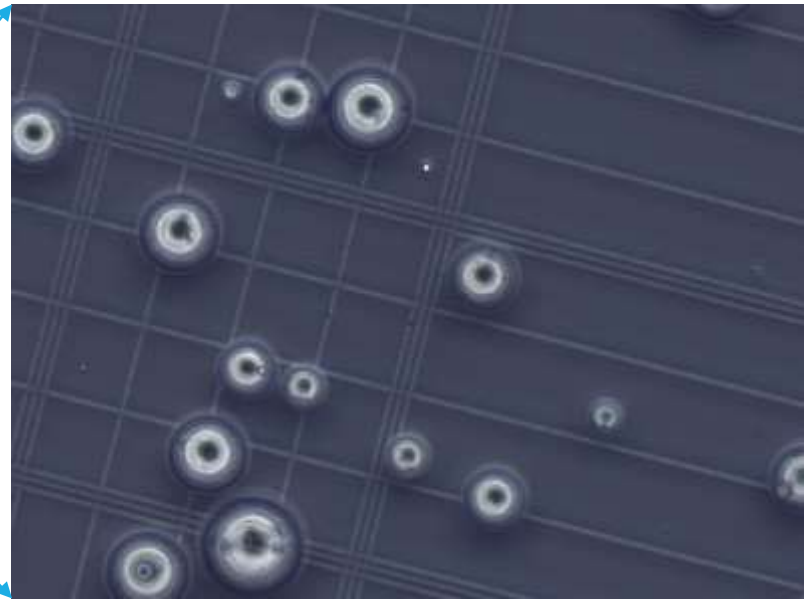




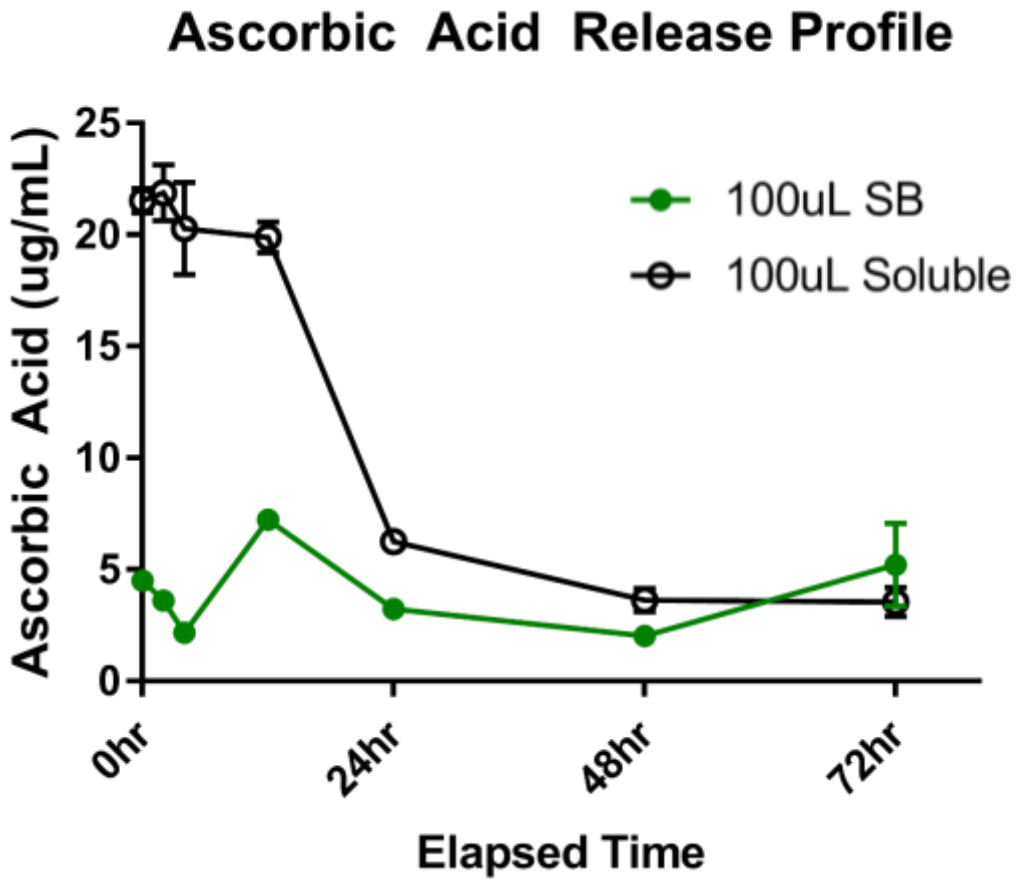
"That's no moon"

Growth Factor *StemBeads*





StemCultures



Dr. Eduardo Almeida & Dr. Elizabeth Blaber

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- The Bone and Cell Signaling Laboratory at NASA Ames Research Center
- Bioculture System Team
- StemCultures

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