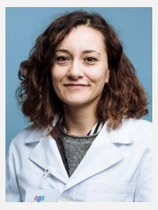
Dissecting the Role of Cellular Senescence in Hematopoietic Stem Cells during Aging



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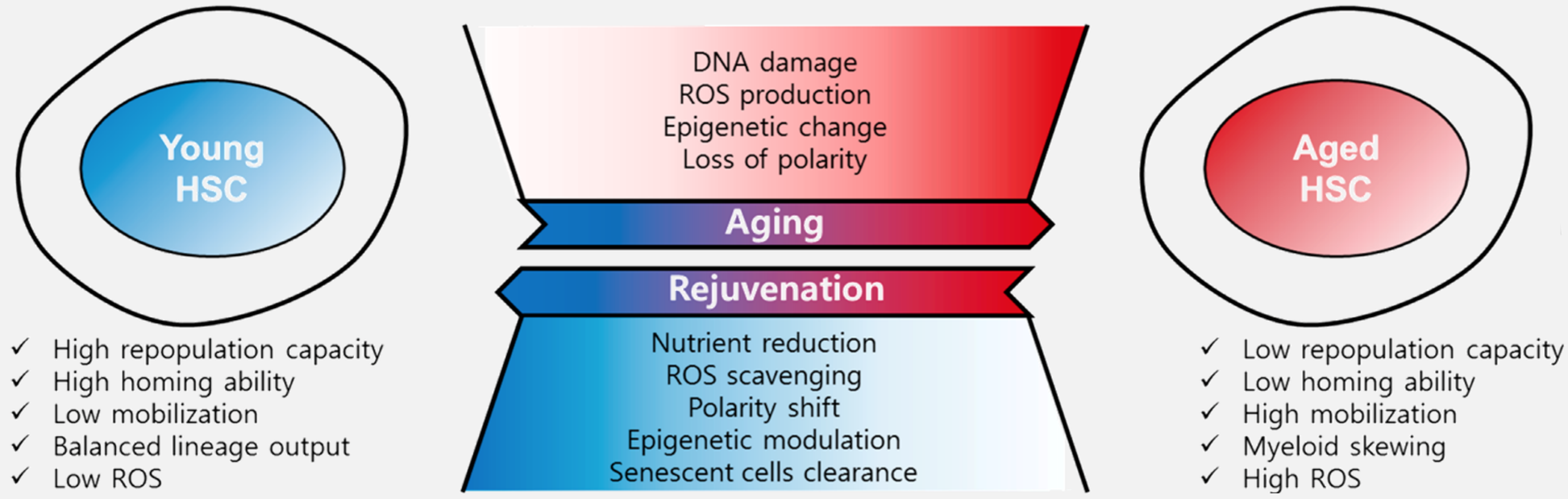
Research Background: mechanisms driving aged hematopoiesis

Senescence: *the biological process of deterioration with age.*



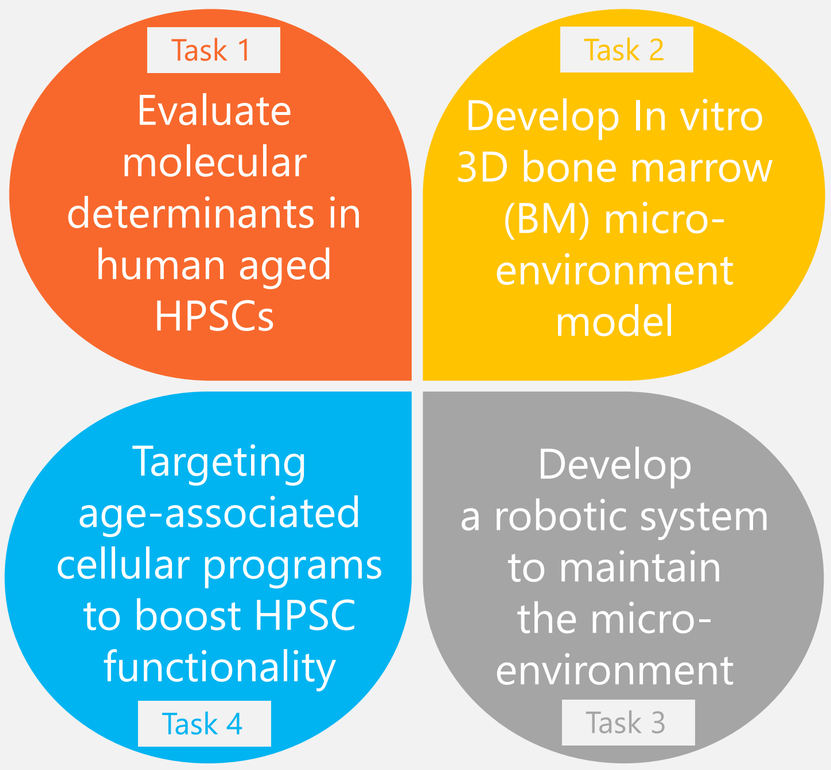
Working Hypothesis and the Long-Term Goal

HYPOTHESIS
Cellular programs contribute to human HPSC dysfunctions during aging thus affecting their long-term functionality

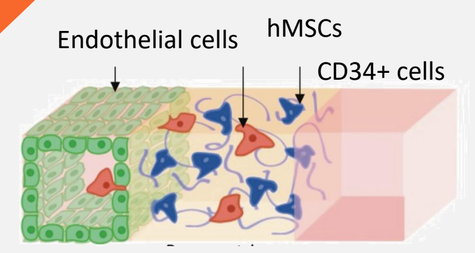
INVESTIGATE
Accumulation of DNA damage, establishment of cellular senescence, altered metabolism, Epigenetic changes

SOLUTION
By targeting the identified age-associated cellular programs strategies to ameliorate HPSC functions will be devised

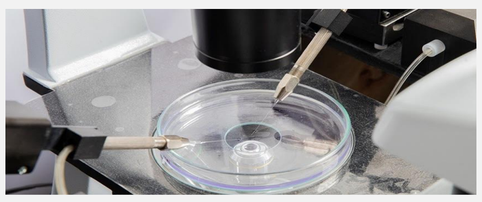
Methods and Techniques



Combine flow cytometry and imaging

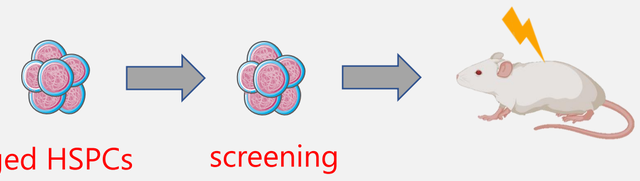


Fabricate bone marrow organ on a chip



Robotic system for liquid handling

Hematopoietic reconstitution



Novelty

- 1st study to analyze molecular pathways driving aged HSPCs
- High-throughput automated bonemarrow on a chip platform
- 1st approach using 3D models to screen for *rejuvenating* drugs

Challenge(s)

- Individual variability
- Fine-tuning co-culture conditions
- Compound priority based on gene expression data

Alternative(s)

- Test multiple donors, ...
- Use bone-like rigid scaffolds, ...
- Perform genetic inhibition of targets

Impact

- Biology: Improved long-term functionality of aged HPSCs
- Technology: Automated 3D system or realistic in vitro studies
- Healthy Longevity: reduced chronic inflammation & frailty

Progress

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