Exploring senescent chondrocytes during aging: sleeper AGEnts of osteoarthritis

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Stellingen behorend bij het proefschrift getiteld

Exploring senescent chondrocytes during aging: Sleeper AGEnts of osteoarthritis

1. Identifying senescence endotypes through blood-based metabolites, rather than relying on trial-and-error approaches, is essential to enhance clinical trial success and enable more effective, personalized treatments. **(This thesis)**

2. Sports that exert high-impact mechanical stress on joint tissues can induce chondrocyte senescence, increasing the risk of developing osteoarthritis. **(This thesis)**

3. To understand cellular senescence in tissues composed of post-mitotic cells like chondrocytes or neurons, the field must move beyond proliferative cell models and prioritize systems that accurately reflect the unique biology of post-mitotic cells. **(This thesis; Sapieha, P. et al. Trends in cell biology, 2018, 28(8), 595-607.)**

4. Human joint-on-chip systems faithfully mimic the physiologically relevant bone-cartilage interface in vitro and can be experimentally perturbed to model osteoarthritis-like damage. As such, they represent a promising alternative to traditional mouse models, aligning with the 3Rs principle and growing societal demand for more ethical and human-relevant research approaches. **(This thesis; Lin, Z. et al. Frontiers in bioengineering and biotechnology, 2019, 7: 411.)**

5. Miniaturized human neo-cartilage organoids offer a scalable and physiologically relevant platform for high-throughput drug testing, enabling sufficient sample sizes for statistically relevant outcomes. **(This thesis)**

6. The accumulation of senescent cells and their secretory phenotype (SASP), that occurs due to mechanical and cellular stress, drives osteoarthritis risk particularly in preserved articular cartilage. **(This thesis; McCulloch, Kendal et al. Aging cell, 2017, 16.2: 210-218)**

7. Osteoarthritis and cellular senescence represent distinct biological processes. **(This thesis)**

8. Triiodothyronine (T3) contributes to terminal maturation of chondrocytes, a hallmark of osteoarthritis pathophysiology. This underscores the thyroid hormone signaling pathway as a promising target for disease-modifying therapies in osteoarthritis. **(This thesis; Korthagen, N. M., et al. Arthritis Research & Therapy, 2024, 26.1: 91; Zhao, Jinlong, et al. Scientific Reports, 2024, 14.1: 13924)**

9. Increased funding for interdisciplinary research is crucial; it fosters innovative approaches and can significantly advance progress within established research fields. **(This thesis)**

10. "Success is not final, failure is not fatal: It is the courage to continue that counts." - **Winston Churchill** *Scientific research is filled with setbacks, uncertainties, and slow progress. Embracing resilience and continuing to push forward despite challenges during a PhD journey is what ultimately drives meaningful contributions to the field.*