

Exploring senescent chondrocytes during aging: sleeper AGEnts of osteoarthritis

Boone, I.

Citation

Boone, I. (2025, October 17). Exploring senescent chondrocytes during aging: sleeper AGEnts of osteoarthritis. Retrieved from https://hdl.handle.net/1887/4273547

Version: Publisher's Version

Licence agreement concerning inclusion of doctoral

License: thesis in the Institutional Repository of the University

of Leiden

Downloaded from: https://hdl.handle.net/1887/4273547

Note: To cite this publication please use the final published version (if applicable).

Exploring senescent chondrocytes during aging:

Sleeper AGEnts of osteoarthritis

Ilja Boone

Exploring senescent chondrocytes during aging: Sleeper AGEnts of osteoarthritis

I. Boone, MSc

ISBN: 978-94-6522-660-6 © 2025 Ilja Boone

Copyright of each chapter is with the publisher of the journal in which the work has appeared. No part of this thesis may be reproduced, stored in retrieval system or transmitted in any form by any means, without the permission of the author, or when appropriate, of the publisher of the represented published articles.

This research was financially supported by by VOILA – SMARTage (nr LSHM18093), the Dutch Scientific Research council NWO/ZonMW VICI scheme (no. 91816631/528) and was performed in the framework of the Medical Delta program Regenerative Medicine 4D: Generating complex tissues with stem cells and printing technology and Improving Mobility with Technology.

Medical Delta and the Dutch Society for Matrix Biology are gratefully acknowledged for financial support for the printing costs of this thesis

Cover design: Demy van der Jagt

Lay-out: Ilja Boone/Demy van der Jagt

Printing: Ridderprint

Exploring senescent chondrocytes during aging:Sleeper AGEnts of osteoarthritis

Proefschrift

ter verkrijging van

de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof.dr.ir. H. Bijl,
volgens besluit van het college voor promoties
te verdedigen op vrijdag 17 oktober 2025
klokke 11.30 uur

door

Ilja Boone

geboren te Dordrecht in 1994 **Promotor** Prof. dr. I. Meulenbelt

Co-promotor Dr. Y.F.M. Ramos

Commissieleden Prof. dr. P. Slagboom

Prof. Dr. G. Kloppenburg

Dr. C.C. van Donkelaar

Department of Biomedical Engineering, Orthopaedic Biomechanics,

Eindhoven University of Technology

Dr. P. L. J. de Keizer

Center for Molecular Medicine, Division of Laboratories, Pharmacy and

Biomedical Genetics, University Medical Center Utrecht

Table of contents

Chapter 1	Introduction	7
Chapter 2	Identified senescence endotypes in aged cartilage are reflected in the blood metabolome	21
Chapter 3	Development of reliable and high-throughput human biomimetic cartilage and bone models to investigate senescence and develop personalized treatments for OA	57
Chapter 4	Quantitative high-resolution synchrotron 3D analysis of aged human osteochondral explants to identify morphological changes in cartilage during osteoarthritis	81
Chapter 5	Capturing essential physiological aspects of interacting cartilage and bone tissue –a human osteochondral unit-on-a-chip model	101
Chapter 6	Inhibiting purinergic signaling as an anti-senescence strategy in human biomimetic osteochondral explants, a potential treatment for OA related senescence	121
Chapter 7	Reversing detrimental effects of OA-related terminal maturation in high-throughput in vitro and biomimetic ex vivo human models	137
Chapter 8	General discussion and future perspective	155
Chapter 9	Appendix	169
	Nederlandse samenvatting	170
	List of publications	174
	Curriculum Vitae	175
	Dankwoord	176