



Universiteit  
Leiden  
The Netherlands

## Osteoprotegerin: a double-edged sword in osteoarthritis development

Rodriguez Ruiz, A.

### Citation

Rodriguez Ruiz, A. (2022, October 19). *Osteoprotegerin: a double-edged sword in osteoarthritis development*. Retrieved from <https://hdl.handle.net/1887/3484338>

Version: Publisher's Version

[Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

License: <https://hdl.handle.net/1887/3484338>

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

# **Osteoprotegerin, a double-edged sword in osteoarthritis development**

**Alejandro Rodríguez Ruiz**

**Osteoprotegerin, a double-edged sword in osteoarthritis development**  
A. Rodríguez Ruiz

ISBN: 978-94-6458-527-8

Cover design: David Pavón

Lay-out: Publiss | [www.publiss.nl](http://www.publiss.nl)

Print: Ridderprint | [www.ridderprint.nl](http://www.ridderprint.nl)

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.

The research presented in this thesis was performed at the Department of Molecular Epidemiology, Leiden University Medical Center, Leiden, The Netherlands. This research was supported by the Dutch Arthritis Society (DAF-16-1-406 and DAF-16-1-405), and the Dutch Scientific Research council NWO/ZonMW VICI scheme (no. 91816631/528). This work was partly supported by grants from Marie Curie Initial Training Network (Euroclast, FP7-People-2013-ITN: #607447). Data are generated within the scope of the Medical Delta programmes Regenerative Medicine 4D and Improving Mobility with Technology.

Printing of this thesis has been possible thanks to the sponsorship of ChemoMetec, PeproTech, Nederlandse vereniging voor Matrix Biologie (NVMB), Tebu-bio, Sanbio Research & Diagnostics, Proefdiervrij and Medical Delta.

# **Osteoprotegerin, a double-edged sword in osteoarthritis development**

Proefschrift

ter verkrijging van  
de graad van doctor aan de Universiteit Leiden,  
op het gezag van rector magnificus prof.dr.ir. H. Bijl,  
volgens besluit van het college voor promoties  
te verdedigen op woensdag 19 oktober 2022

klokke 10.00 uur

door

**Alejandro Rodríguez Ruiz**

geboren te Valencia, Spanje  
in 1992

**Promotor:** Prof. dr. I. Meulenbelt  
**Copromotor:** Dr. Y. F. M. Ramos

**Leden promotiecommissie:** Prof. Dr. C. L. Mummery  
Prof. Dr. G. J. V. M. van Osch  
(Erasmus Medical Centre)  
Dr. T. J. de Vries  
(Academic Centre for Dentistry Amsterdam)  
Dr. J. Geurts  
(Lausanne University Hospital)

# **Table of contents**

## **Chapter 1**

General Introduction	7
----------------------	---

## **Chapter 2**

The role of <i>TNFRSF11B</i> in development of osteoarthritic cartilage	33
---	----

## **Chapter 3**

Cartilage from human-induced pluripotent stem cells: comparison with neo-cartilage from chondrocytes and bone marrow mesenchymal stromal cells	57
--	----

## **Chapter 4**

Readthrough mutation at CCAL1 locus in <i>TNFRSF11B</i> deciphers role of immobilized osteoprotegerin in subchondral bone turnover and cartilage mineralization in humans	87
---	----

## **Chapter 5**

General discussion	121
--------------------	-----

## **Addendum**

English Summary	138
Nederlandse samenvatting	141
List of Publications	144
Curriculum vitae	146
Acknowledgements	147

