

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/32015> holds various files of this Leiden University dissertation.

**Author:** Akker, Erik Ben van den

**Title:** Computational biology in human aging : an omics data integration approach

**Issue Date:** 2015-02-18

# **Computational Biology in Human Aging**

**An Omics Data Integration Approach**

**Erik Ben van den Akker**

## **Computational Biology in Human Aging**

Ir. E.B. van den Akker

The cover displays a view from the north coast of Spain, a region historically known for its adept sailors and daring explorers of the world seas. In this bay, many embarked and sailed off in the unknown, driven by their curiosity, to claim new land for king and country, often with little details on their final destinations. Many parallels exist between these early scientific endeavours and current projects. In this thesis, we set out to link two worlds, epidemiology and bioinformatics, convinced that the synergy between these two fields would allow us to probe deeper for the factors contributing to healthy aging and longevity. Little was known on omics data integration in aging, but still we embarked on what was going to be a very exciting journey. Driven by our curiosity.

Financial support for the printing of this thesis was provided by the Netherlands Consortium of Healthy Ageing (NGI 050-060-810).

PhD thesis with summary in Dutch

ISBN: 978-94-6295-084-9

**© 2015 E.B. van den Akker**

All rights reserved. No part of this thesis may be reproduced, stored in a retrieval system or transmitted in any other form by any means, without the permission of the author, or when appropriate, of the publisher of the represented published articles.

**Cover design:** Proefschriftmaken.nl || Uitgeverij BOXPress

**Printed & Lay Out by:** Proefschriftmaken.nl || Uitgeverij BOXPress

**Published by:** Uitgeverij BOXPress, 's-Hertogenbosch

**Computational Biology in Human Aging**  
**An Omics Data Integration Approach**

Proefschrift

ter verkrijging van  
de graad van Doctor aan de Universiteit Leiden,  
op gezag van Rector Magnificus prof. mr. C.J.J.M. Stolker,  
volgens besluit van het College voor Promoties  
ter verdedigen op woensdag 18 februari 2015  
klokke 11.15 uur

door

**Erik Ben van den Akker**

Geboren te 's-Hertogenbosch  
in 1981

## **Promotiecommissie**

**Promotor:** Prof. Dr. P.E. Slagboom

Prof. Dr. Ir. M.J.T. Reinders  
*Delft University of Technology*

**Co-promotor:** Dr. M. Beekman

**Overige leden:** Prof. Dr. B.J. Zwaan  
*Wageningen University Research Centre*

Prof. Dr. L. Wessels  
*Netherlands Cancer Institute*  
*Delft University of Technology*

Dr. J.P. De Magalhães  
*University of Liverpool*

## Contents

<b>Chapter 1:</b>	Introduction	7
<b>Chapter 2:</b>	Integrating Protein-Protein Interaction Networks with Gene-Gene Co-Expression Networks improves Gene Signatures for Classifying Breast Cancer Metastasis	21
<b>Chapter 3:</b>	Meta-Analysis on Blood Transcriptomic Studies Identifies Consistently Co-Expressed PPI Modules as Robust Markers of Human Aging	41
<b>Chapter 4:</b>	Germ line and Somatic Characteristics of the Long-Lived Genome	61
<b>Chapter 5:</b>	A novel life span regulating locus at chr13q34 influencing serum triiodothyronine level	89
<b>Chapter 6:</b>	An R package for generic access and handling of genomic data	117
<b>Chapter 7:</b>	Discussion	125
<b>Chapter 8:</b>	Nederlandse Samenvatting	141
<b>Appendix</b>	List of Publications	152
	Curriculum Vitae	155
	Dankwoord	157

