

University of Groningen

## Regeneration of irradiated salivary glands by stem cell therapy

Lombaert, Isabelle Madeleine Armand

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*

Publisher's PDF, also known as Version of record

*Publication date:*

2008

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Lombaert, I. M. A. (2008). *Regeneration of irradiated salivary glands by stem cell therapy*. s.n.

### Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

### Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Copyright © 2008 by Isabelle M.A. Lombaert. All rights reserved.

No part of this book may be reproduced or transmitted in any forms or by any means without permission from the author.

The research described in this thesis was conducted in the Department of Cell Biology, Section Radiation & Stress Cell Biology and Stem Cell Biology, University Medical Center Groningen (UMCG), University of Groningen (RUG), the Netherlands.

This research project was financially supported by the Koningin Wilhelmina Fonds (KWF, Dutch Cancer Society) Grant RUG2003-2909, the European Union FP-6 contract 503436, and Amgen, Inc.


**ISBN** 978-90-367-3370-0  
**Page layout** Isabelle M.A. Lombaert  
**Cover design** "The divergent world of a stem cell" - unknown artist  
**Printed by** Drukkerij van Denderen B.V., Groningen, The Netherlands


The printing of this thesis was financially supported by:

The **Groningen University Institute for Drug Exploration** (GUIDE), The Netherlands 

**Harlan Netherlands B.V.**, Horst, The Netherlands

**Amgen B.V.**, Breda, The Netherlands

**Constructies Busseniers** (Fabricatie en plaatsing deuren en ramen), Van Rooiestraat 30-36, 2170 Antwerpen-Merksem, Belgium, [www.cbaramen.be](http://www.cbaramen.be), [cbaramen@telenet.be](mailto:cbaramen@telenet.be), RAMEN - DEUREN   
☎+32(0)36459528 Fax +32(0)36459018

**NV Van de Walle & Kleinzoorn** (Glashandel), Dendermondsesteenweg 28, 9070 Destelbergen, Belgium, [philip.dewilde@skynet.be](mailto:philip.dewilde@skynet.be), ☎+31(0)92281602 FAX +32(0)92284421 

**DE VREESE NV** (Nieuw en verbouwingen), Florastraat 65, 9840 De Pinte, Belgium, [www.aannemingendevreese.com](http://www.aannemingendevreese.com) ☎+31(0)475230.850 Fax +32(0)9282.74.54 *DE VREESE NV*

[devreese.pascal@skynet.be](mailto:devreese.pascal@skynet.be)

**BD Biosciences**, Alphen aan den Rijn, The Netherlands 

**Leica Microsystems**, Rijswijk, The Netherlands 

**Dutch Cancer Society** 



rijksuniversiteit  
 groningen

## REGENERATION OF IRRADIATED SALIVARY GLANDS BY STEM CELL THERAPY

Proefschrift

ter verkrijging van het doctoraat in de  
Medische Wetenschappen  
aan de Rijksuniversiteit Groningen  
op gezag van de  
Rector Magnificus, dr. F. Zwarts,  
in het openbaar te verdedigen op  
woensdag 16 april 2008  
om 16.15 uur

door

**Isabelle Madeleine Armand Lombaert**

geboren op 7 december 1979  
te Gent, België

**Promotores**

**Prof. dr. G. de HAAN**

**Prof. dr. H.H. KAMPINGA**

**Copromotores**

**Dr. R.P. COPPES**

**Beoordelingscommissie Prof. dr. C.L. MUMMERY**

**Prof. dr. S.M. BENTZEN**

**Prof. dr. P. LAMBIN**

*REAL SUCCESS IS FINDING YOUR LIFEWORK IN THE WORK THAT YOU LOVE.  
(DAVID McCULLOUGH (1933-))*

## TABLE OF CONTENTS

<b>CHAPTER 1</b>	<b>General Introduction and Aim of the Thesis</b>	<b>9</b>
<b>CHAPTER 2</b>	<b>Mobilization of Bone Marrow Stem Cells by Granulocyte Colony-Stimulating Factor Ameliorates Radiation-Induced Damage to Salivary Glands</b> <i>Clinical Cancer Research 12 [6], 1804-1812 (2006)</i>	<b>35</b>
<b>CHAPTER 3</b>	<b>Cytokine Treatment Improves Parenchymal and Vascular Damage of Salivary Glands after Irradiation</b> Submitted	<b>53</b>
<b>CHAPTER 4</b>	<b>Rescue of Salivary Gland Function after Stem Cell Transplantation in Irradiated Glands</b> Submitted	<b>69</b>
<b>CHAPTER 5</b>	<b>The Adult Mouse Submandibular Gland Stem/Progenitor Cell - its Localization and Fate after Post-irradiation Transplantation</b>	<b>93</b>
<b>CHAPTER 6</b>	<b>Palifermin Prevents Radiation Damage to Salivary Glands by Expansion of the Stem/Progenitor Pool</b> Submitted	<b>113</b>
<b>CHAPTER 7</b>	<b>General Discussion and Perspectives</b>	<b>129</b>
	<b>REFERENCES</b>	<b>143</b>
	<b>DUTCH SUMMARY</b>	<b>161</b>
	<b>ACKNOWLEDGEMENTS</b>	<b>167</b>
	<b>CURRICULUM VITAE</b>	<b>175</b>
	<b>APPENDIX - COLOR FIGURES</b>	<b>183</b>