



Universiteit  
Leiden  
The Netherlands

## **PI3K signaling and adherens junctions in invasive lobular breast cancer**

Klarenbeek, S.

### **Citation**

Klarenbeek, S. (2021, April 15). *PI3K signaling and adherens junctions in invasive lobular breast cancer*. Retrieved from <https://hdl.handle.net/1887/3154437>

Version: Publisher's Version

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

Downloaded from: <https://hdl.handle.net/1887/3154437>

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

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/3154437> holds various files of this Leiden University dissertation.

**Author:** Klarenbeek, S.

**Title:** PI3K signaling and adherens junctions in invasive lobular breast cancer

**Issue date:** 2021-04-15

# **PI3K signaling and adherens junctions in invasive lobular breast cancer**

**Sjoerd Klarenbeek**

### *Colofon*

PI3K signaling and adherens junctions in invasive lobular breast cancer

Sjoerd Klarenbeek

ISBN: 978-94-6419-158-5

Cover image: Sophia Anastasia | [www.sophia-anastasia.com](http://www.sophia-anastasia.com)

Layout and design: Lara Leijtens | [persoonlijkproefschrift.nl](http://persoonlijkproefschrift.nl)

Printing: Gildeprint Enschede | [gildeprint.nl](http://gildeprint.nl)

The research described in this thesis was performed at the division Molecular Pathology of the Netherlands Cancer Institute, Amsterdam, the Netherlands and UMC Utrecht, The Netherlands. The research was financially supported by the European Research Council, the European Union Seventh Framework Programme, Top Institute (TI) Pharma, the Netherlands Organization for Scientific Research (NWO), the Dutch Cancer Society (KWF), the Oncode Institute, the UMC Cancer Center, and the Association for International Cancer Research (AICR). The printing of this thesis was financially supported by the Netherlands Cancer Institute, Amsterdam, The Netherlands.

© Copyright, Sjoerd Klarenbeek, 2021

All rights reserved. No part of this book may be reproduced in any form or by any means without permission of the author and the publisher holding the copyright of the articles.

PI3K signaling and adherens junctions in invasive lobular breast cancer

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 donderdag 15 april 2021  
klokke 15.00 uur

door

Sjoerd Klarenbeek

geboren te Oss

in 1977

Promotor: Prof. dr. J. Jonkers  
Copromotoren: Prof. dr. K.E. de Visser  
Dr. P.W.B. Derksen

Promotiecommissie: Prof. dr. H. Irth (voorzitter)  
Prof. dr. J.A. Bouwstra (secretaris)  
Prof. dr. F.A. Ossendorp (Universiteit Leiden)  
Prof. dr. J. Wesseling (Universiteit Leiden)  
Prof. dr. E.H.J. Danen (Universiteit Leiden)

## TABLE OF CONTENTS

Chapter 1	<b>General introduction</b>	7
Chapter 2	<b>Genetically engineered mouse models of PI3K signaling in breast cancer</b> <i>Molecular Oncology 7, 146-164 (2013)</i>	31
Chapter 3	<b>A preclinical mouse model of invasive lobular breast cancer metastasis</b> <i>Cancer Research 73, 353-363 (2013)</i>	75
Chapter 4	<b>Response of metastatic mouse invasive lobular carcinoma to mTOR inhibition is partly mediated by the adaptive immune system</b> <i>Oncoimmunology 9, 1724049 1-14 (2020)</i>	109
Chapter 5	<b>PTEN loss in E-cadherin-deficient mouse mammary epithelial cells rescues apoptosis and results in development of classical invasive lobular carcinoma</b> <i>Cell Reports 16, 2087-2101 (2016)</i>	155
Chapter 6	<b>Loss of p120-catenin induces metastatic progression of breast cancer by inducing anoikis resistance and augmenting growth factor receptor signaling</b> <i>Cancer Research 73, 4937-4949 (2013)</i>	201
Chapter 7	<b>p120-catenin is critical for the development of invasive lobular carcinoma in mice</b> <i>Journal of mammary gland biology and neoplasia 21, 81-88 (2016)</i>	243
Chapter 8	<b>General discussion and future perspectives</b>	265
Appendices	<b>English summary</b>	280
	<b>Nederlandse samenvatting</b>	284
	<b>Curriculum vitae</b>	288
	<b>List of publications</b>	290
	<b>Acknowledgements</b>	294