



Universiteit  
Leiden  
The Netherlands

## Endoglin and the immune system: immunomodulation and therapeutic opportunities for cancer

Schoonderwoerd, M.J.A.

### Citation

Schoonderwoerd, M. J. A. (2022, May 12). *Endoglin and the immune system: immunomodulation and therapeutic opportunities for cancer*. Retrieved from <https://hdl.handle.net/1887/3303586>

Version: Publisher's Version

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

Downloaded from: <https://hdl.handle.net/1887/3303586>

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

# ENDOGLIN AND THE IMMUNE SYSTEM

IMMUNOMODULATION AND  
THERAPEUTIC OPPORTUNITIES FOR CANCER

MARK J.A. SCHOONDERWOERD

ISBN: 978-94-6423-774-0

Cover design & lay-out: Wendy Schoneveld || [www.wenziD.nl](http://www.wenziD.nl)

Printed by: ProefschriftMaken || [proefschriftmaken.nl](http://proefschriftmaken.nl)

The research described in this thesis was performed at the Leiden University medical Center

© Mark J. A. Schoonderwoerd, 2022

All rights reserved. No part of this thesis may be reproduced, stored or transmitted in any form or by any means without prior permission of the author, or the copyright-owning journals for previously published chapters.

# **Endoglin and the immune system**

Immunomodulation and therapeutic opportunities for 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 12 mei 2022  
klokke 13:45 uur

Door

Mark Johannes Adrianus Schoonderwoerd

geboren te Utrecht

Promotor: Prof. Dr. J.C.H. Hardwick

Co-promotores: Dr. L.J.A.C. Hawinkels  
Dr. M.F. Fransen

Promotiecommissie: Prof. dr. M.T.H. Goumans  
Prof. dr. F. Ossendorp  
Prof. dr. B.E. Snaar - Leiden University  
Prof. dr. J. Prakash - University of Twente  
Prof. dr. C. Bernabeu - Spanish National Research Council

# Contents

<b>CHAPTER 1</b>	General introduction	7
<b>CHAPTER 2</b>	Endoglin, the endothelium and beyond	21
<b>CHAPTER 3</b>	Endoglin expression on cancer-associated fibroblasts regulates invasion and stimulates colorectal cancer metastasis	45
<b>CHAPTER 4</b>	Fibroblast-specific endoglin knock out changes the colonic immune infiltrate and increases formation of colitis associated intestinal adenomas	71
<b>CHAPTER 5</b>	Targeting endoglin expressing cells in the tumor microenvironment does not inhibit tumor growth in a pancreatic cancer mouse model	95
<b>CHAPTER 6</b>	Targeting endoglin expressing regulatory T cells in the tumor microenvironment enhances the effect of PD1 checkpoint inhibitor immunotherapy	121
<b>CHAPTER 7</b>	Tumor draining lymph nodes are pivotal in PD-1/PD-L1 checkpoint therapy	143
<b>CHAPTER 8</b>	General discussion	157
<b>APPENDIX</b>	Nederlandse samenvatting	169
	List of publications	173
	Curriculum vitae	175
	Dankwoord	177