



Universiteit
Leiden
The Netherlands

Immunosuppression in breast cancer: a closer look at regulatory T cells

Kos, K.

Citation

Kos, K. (2023, January 11). *Immunosuppression in breast cancer: a closer look at regulatory T cells*. Retrieved from <https://hdl.handle.net/1887/3505617>

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/1887/3505617>

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

Immunosuppression in breast cancer:

a closer look at regulatory T cells

Kevin Kos

About the cover:

Immunosuppressive signals coming from the tumor microenvironment arrest successful anti-cancer immunity. Work in this thesis aims to understand how we can “break free” from specific components of tumor-associated immunosuppression to improve cancer treatment. This concept of “Breaking free” is illustrated on the cover, inspired by my passion for birds.

Cover concept: MaDedee & Kevin Kos

Layout: Ilse Modder, www.ilsemodder.nl

Printing: GildePrint Enschede, www.gildeprint.nl

ISBN: 978-94-6419-654-2

The research described in this thesis was performed at the division of Tumor biology and Immunology at the Netherlands Cancer Institute – Antoni van Leeuwenhoek hospital (NKI-AvL). The research was financially supported by the NWO Diamond Grant, KWF, and Oncode Institute. The printing of this thesis was financially supported by the NKI-AVL.

© 2022 by Kevin Kos. All rights reserved. No part of this thesis may be reproduced, stored in a retrieval system or transmitted in any form or by any means without prior permission of the author and the publisher holding the copyright of the articles contained within.

Immunosuppression in breast cancer: a closer look at regulatory T cells

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 woensdag 11 januari 2023
klokke 13:45 uur

door

Kevin Kos
geboren te Blaricum
in 1993

Promotor: Prof. Dr. K. E. de Visser

Co-promotor: Prof. Dr. J.G. Borst

Leden Promotiecommissie:

Prof. Dr. F. A. Ossendorp

Prof. Dr. S. H. van der Burg

Prof. Dr. M. Yazdanbakhsh

Prof. Dr. T. D. de Gruijl (Amsterdam UMC, location VUmc)

Dr. L. Akkari (Netherlands Cancer Institute)

TABLE OF CONTENTS

Chapter 1:	General introduction & Scope of the thesis	9
Chapter 2:	The multifaceted role of regulatory T cells in breast cancer <i>Annual Review of Cancer Biology. 2020, 5:291-310</i>	19
Chapter 3:	Tumor-associated macrophages promote intratumoral conversion of conventional CD4 ⁺ T cells into regulatory T cells via PD-1 signalling <i>Oncolmmunology. 2022, 11(1)</i>	43
Chapter 4:	Tumor-educated T _{regs} drive organ-specific metastasis in breast cancer by impairing NK cells in the lymph node niche <i>Cell Reports. 2022, 38(9):110447</i>	77
Chapter 5:	Neutrophils create a fertile soil for metastasis <i>Cancer Cell. 2021, 8;39(3):301-303</i>	123
Chapter 6:	Immune checkpoint blockade triggers T _{reg} activation which blunts therapeutic response in metastatic breast cancer <i>Unpublished</i>	131
Chapter 7:	Flow cytometry-based isolation of tumor-associated regulatory T cells and assessment of their suppressive potential <i>Methods in Enzymology. 2019, 632:259-281</i>	157
Chapter 8:	Discussion	179
Addendum:	English Summary	202
	Nederlandse samenvatting	206
	Curriculum Vitae	210
	Acknowledgments	212
	List of publications	214
	PhD portfolio	216