



Universiteit
Leiden

The Netherlands

Role of metabolic pathways and sensors in regulation of dendritic cell-driven T cell responses

Pelgrom, L.R.

Citation

Pelgrom, L. R. (2022, February 23). *Role of metabolic pathways and sensors in regulation of dendritic cell-driven T cell responses*. Retrieved from <https://hdl.handle.net/1887/3275848>

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/1887/3275848>

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

**Role of metabolic pathways and sensors in regulation
of dendritic cell-driven T cell responses**

LEONARD R. PELGROM

Colofon

Role of metabolic pathways and sensors in regulation of dendritic cell-driven T cell responses, Leonard R. Pelgrom

Provided by thesis specialist Ridderprint, ridderprint.nl

Printing: Ridderprint

Layout and design: Mila Slappendel, persoonlijkproefschrift.nl

Cover design: Elise Metekohy

ISBN: 978-94-6458-023-5

Copyright 2022 © Leonard Pelgrom

The Netherlands. All rights reserved. No parts of this thesis may be reproduced, stored in a retrieval system or transmitted in any form or by any means without permission of the author.

Role of metabolic pathways and sensors in regulation of dendritic cell-driven T cell responses

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 23 februari 2022 klokke 11:15 uur

door

Leonard Reinier Pelgrom

geboren te Haarlem in 1988

Promotor

Prof.dr. M. Yazdanbakhsh

Co-promotor

Dr. B. Everts

Leden promotiecommissie

Prof. dr. C. van Kooten

Prof. dr. I.J.M. de Vries, Radboud Universitair Medisch Centrum, Nijmegen, Nederland

Prof. dr. J.G. Borst

Dr. J. Van den Bossche, Amsterdam Universitair Medisch Centrum, locatie VUmc, Amsterdam, Nederland

Dr. B. Guigas

Table of contents

	List of abbreviations	6
Chapter 1	General introduction	9
Chapter 2	Dendritic cells are what they eat: how their metabolism shapes T helper cell polarization	17
Chapter 3	Analysis of TLR-Induced Metabolic Changes in Dendritic Cells Using the Seahorse XFe96 Extracellular Flux Analyzer	33
Chapter 4	Cell-Intrinsic Glycogen Metabolism Supports Early Glycolytic Reprogramming Required for Dendritic Cell Immune Responses	49
Chapter 5	Butyrate Conditions Human Dendritic Cells to Prime Type 1 Regulatory T cells via both Histone Deacetylase Inhibition and G Protein-Coupled Receptor 109A Signaling	79
Chapter 6	Metabolic control of type 2 immunity	111
Chapter 7	Protein O-GlcNAcylation and low glycolysis underpin Th2 polarization by dendritic cells	135
Chapter 8	LKB1 expressed in dendritic cells governs the development and expansion of thymus-derived regulatory T cells	175
Chapter 9	mTORC1 signalling in antigen-presenting cells of the skin restrains CD8+ T cell priming	225
Chapter 10	General discussion	273
	Nederlandse samenvatting	300
	Curriculum vitae	305
	List of publications	306
	Acknowledgements	308

List of abbreviations

2-DG	2-deoxyglucose
AMP	Adenosine monophosphate
AMPK	AMP-activated protein kinase
ATP	Adenosine triphosphate
CTLs	Cytotoxic T cells
DCs	Dendritic cells
BDMCs	Bone marrow-derived DCs
GMDCs	BMDCs generated using GM-CSF
cDC1s	Type 1 conventional DCs
cDC2s	Type 2 conventional DCs
moDCs	Monocyte-derived DCs
pDCs	Plasmacytoid DCs
ECAR	Extracellular acidification rate
FAO	Fatty acid oxidation
GPRs	G protein-coupled receptors
HBP	Hexosamine biosynthesis pathway
HDACs	Histone deacetylases
HDM	House dust mite
IFN	Interferon
IL	Interleukin
LCs	Langerhans cells
LKB1	Liver kinase B1
mTOR	Mechanistic target of rapamycin
mTORC1	mTOR complex 1
OCR	Oxygen consumption rate
OGT	O-GlcNAc transferase
OGA	O-GlcNAcase
OXPHOS	Oxidative phosphorylation
PLC- β 1	Phospholipase C beta-1
PYG	Glycogen phosphorylase
RA	Retinoic acid
RALDH	Retinaldehyde dehydrogenase
SCFAs	Short-chain fatty acids
SEA	Soluble egg antigens
ST	ST045849

List of abbreviations

TG	Thiamet G
TGF β 1	Transforming growth factor beta-1
Th cells	T helper cells
Th2 cells	T helper 2 cells
TNF	Tumor necrosis factor
Tregs	Regulatory T cells
Tr1	IL-10-producing type 1 Tregs
iTregs	Induced/in vitro Tregs
pTregs	Tregs generated in the periphery
tTregs	Tregs generated in the thymus
UDP-GlcNAc	Uridine diphosphate N-acetylglucosamine
XF	Extracellular flux

