



Universiteit
Leiden
The Netherlands

Unmasking the masters of evasion : TAP inhibition by varicellovirus UL49.5 proteins

Verweij, M.C.

Citation

Verweij, M. C. (2010, September 29). *Unmasking the masters of evasion : TAP inhibition by varicellovirus UL49.5 proteins*. Retrieved from <https://hdl.handle.net/1887/15995>

Version: Corrected 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/1887/15995>

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

Unmasking the masters of evasion:
TAP inhibition by varicellovirus
UL49.5 proteins

Cover illustration

Painted by Miranda Ebbeling (www.mibakunst.nl), adjusted by Sjoerd van den Worm.

**Unmasking the masters of evasion:
TAP inhibition by varicellovirus UL49.5 proteins**

Proefschrift

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van Rector Magnificus prof.mr. P.F. van der Heijden,
volgens besluit van het College voor Promoties
te verdedigen op woensdag 29 september 2010
klokke 15.00 uur

door

Marieke Christine Verweij

geboren te Heerjansdam
in 1982

Promotiecommissie

Promotores: prof.dr. E.J.H.J. Wiertz, UMC Utrecht
 prof.dr. A.C.M. Kroes

Copromotores: dr. M.E. Ressing, UMC Utrecht
 dr. T. van Hall

Overige leden: prof.dr. K. Früh, Oregon Health and Science University, Portland, OR, USA
 prof.dr. E.J. Snijder
 prof.dr. J.M. Middeldorp, VUMC Amsterdam

"Your only fear is possibility"

- Pete Murray

let's go get lost, hunny

Table of contents

Chapter 1	General introduction 'Herpesviruses and immunity: the art of evasion'	9
	Layman's introduction to herpesviruses	26
	Outline of the thesis	27
Chapter 2	The varicellovirus UL49.5 protein blocks the transporter associated with antigen processing (TAP) by inhibiting essential conformational transitions in the '6+6 TM' TAP core complex	37
Chapter 3	Signaling of a varicelloviral factor across the endoplasmic reticulum membrane induces destruction of the peptide-loading complex and immune evasion	69
Chapter 4	Structural and functional analysis of the TAP-inhibiting UL49.5 proteins of varicelloviruses	95
Chapter 5	Varicellovirus UL 49.5 proteins differentially affect the function of the transporter associated with antigen processing, TAP	123
Chapter 6	The capacity of UL49.5 proteins to inhibit TAP is widely distributed amongst members of the genus <i>Varicellovirus</i>	153
Chapter 7	Herpesvirus-encoded immune evasion molecules cross species barriers to inhibit mouse MHC I-restricted antigen presentation	181
Chapter 8	CD8 ⁺ T cell responses against TAP-deficient cells are readily detected in the human population	205
Chapter 9	Two mechanistically distinct immune evasion proteins of cowpox virus combine to avoid antiviral CD8 ⁺ T cells	231
Chapter 10	General discussion	257
	Nederlandse samenvatting	269
	List of publications	274
	Curriculum vitae	277

