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## **Immunological aspects of conventional and new treatments for cervical cancer, an immunopharmacological approach**

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## LIST OF ABBREVIATIONS

ACT	Adoptive cell transfer	PBMC	Peripheral blood mononuclear cells
ATREG	Activated regulatory T-cell	PD-1	Program death 1
APC	Antigen presenting cell	PD-2	Program death 2
BT	Brachytherapy	PD-L	Program death ligand
CBA	Cytometric bead array	PHA	Phytohemagglutinin
CGOA	Center for Gynecologic Oncology Amsterdam	PRR	Pattern recognition receptor
CD	Cluster of differentiation	SI	Stimulation index
CHDR	Centre for Human Drug Research	SLP	Synthetic Long Peptide
CIN	Cervical intraepithelial neoplasia	TAM	Tumor associated macrophages
CTL	CD8 <sup>+</sup> Cytotoxic T lymphocyte	TGF	Tumor growth factor
CTLA-4	Cytotoxic T-lymphocyte Antigen 4	TH CELL	CD4 <sup>+</sup> T-helper
DC	Dendritic cell	TIL	Tumor infiltrating T-cells
EBRT	External beam radiation therapy	TIM	Tumor infiltrating myeloid cells
EGFR	Epidermal growth factor receptor	TIM-3	T cell immunoglobulin mucin 3
FOXP3	Forkhead box p3	TLR	Toll-like receptor
GMDSC	Granulocytic myeloid derived suppressor cell	TNF	Tumor necrosis factor
HLA	Human Leukocyte Antigen	TREG	Regulatory T-cell
HPV	Human Papilloma Virus	VEGF	Vascular endothelial growth factor
HRHPV	High-risk human Papilloma Virus		
ICS	Intracellular cytokine staining		
IFN	Interferon		
IL	Interleukin		
LC	Langerhans cells		
LST	Lymphocyte stimulation test		
LUMC	Leiden University Medical Center		
M1	Macrophage type 1		
M2	Macrophage type 2		
MOABS	Monoclonal antibodies		
MMDSC	monocytic myeloid derived suppressor cell		
MDSC	Myeloid derived suppressor cell		
MRM	Memory Response Mix		
MLR	Mixed Lymphocyte Reaction		
NTREG	Naïve regulatory T-cell		
NK	Natural Killer		



## **CURRICULUM VITAE**

Hélène van Meir was born on the 20th of September 1981 in Goes. From the age of 10, she went to the girls-only boarding school Sint-Bavo humaniora in Ghent, Belgium, from which she graduated in 1999. In the same year she started with Pharmacy at the Catholic University of Leuven, Belgium, and switched to medical school at the Leiden University the year after. During her study, she worked as an allocation officer at the Eurotransplant International Foundation. She performed her graduation project at the department of Cardiac Surgery and Pediatric Cardiology at the Leiden University Medical Center, under supervision of Prof. dr. Hazekamp. She studied the use of bovine jugular vein graft for the reconstruction of the right ventricular outflow tract in a pediatric population at the Leiden University Medical Center and Centre Hospitalier Universitaire Vaudoise, Lausanne, Switzerland. In 2008 she obtained her medical degree (cum laude) and started working as a physician at the Department of Obstetrics and Gynecology at the Bronovo Hospital, The Hague. In 2009 she was appointed as a research physician in the Vascular Medicine research group at the Centre for Human Drug Research (CHDR). She focused on the integration of immunology in clinical pharmacology, and participated in several research projects, supervised by prof. dr. A.F. Cohen and prof. dr. J. Burggraaf. The studies in this thesis were performed in close collaboration with the departments of Clinical Oncology (prof. dr. S.H. van der Burg) and Gynecology (dr. M.I.E. van Poelgeest) of the Leiden University Medical Center and the Center for Gynecological Oncology Amsterdam (prof. dr. G.G. Kenter). Whilst working as a research physician at CHDR, she was trained as a clinical pharmacologist and obtained her degree in clinical pharmacology in 2016.

Since October 2012, Hélène performs her residency training in Obstetrics and Gynecology at the HMC Bronovo Hospital, The Hague and the Leiden University Medical Center, under supervision of dr. C.A.G. Holleboom and Prof. dr. J.J.M. van Lith.

## LIST OF PUBLICATIONS

- Impact of (chemo)radiotherapy on immune cell composition and function in cervical cancer patients. **H. van Meir**, R.A. Nout, M.J.P. Welters, N.M. Loof, M.L. de Kam, J.J. van Ham, S. Samuels, G.G. Kenter, A.F. Cohen, C.J.M. Melief, J. Burggraaf, M.I.E. van Poelgeest, S.H. van der Burg. *OncoImmunology* 2017;1,e1267095
- The identification of patients at high risk for recurrent disease after treatment for early-stage cervical cancer. **H. van Meir**, I.J. du Burck, M.L. de Kam, M.J.P. Welters, S.H. van der Burg, J.B.M.Z. Trimbos, C.D. de Kroon, M.I.E. van Poelgeest. *Eur. Journal Gynaecol. Oncol* 2017 Jan;38(1):25-32
- Vaccination during myeloid cell depletion by cancer chemotherapy fosters robust T cell responses. M.J.P. Welters\*, T.C. van der Sluis\*, **H. van Meir\***, N.M. Loof, V.J. van Ham, S. van Duikeren, S.J. Santegoets, R. Arens, M.L. de Kam, A.F. Cohen, M.I.E. van Poelgeest, G.G. Kenter, J.R. Kroep, J. Burggraaf, C.J.M. Melief, S.H. van der Burg. *Science Translational Medicine*. 2016 Apr 13;8(334):334ra52 (\* Authors contributed equally)
- Population pharmacokinetic model characterizing 24-hour variation in the pharmacokinetics of oral and intravenous midazolam in healthy volunteers. A. van Rongen, L. Kervezee, M. Brill, **H. van Meir**, J. Den Hartigh, H.J. Guchelaar, J.H. Meijer, J. Burggraaf, F. van Oosterhout. *Clinical Pharmacology and Therapeutics: Pharmacometrics & Systems Pharmacology*. 2015 Aug;4(8):154-64
- The need for improvement of the treatment of advanced and metastatic cervical cancer, the rationale for combined chemo-immunotherapy. **H. van Meir**, G.G. Kenter, J. Burggraaf, J.R. Kroep, M.J.P. Welters, C.J.M. Melief, S.H. van der Burg, M.I.E. van Poelgeest. *Anticancer Agents in Medicinal Chemistry*. 2014 Feb;14(2):190-203
- Braken in de zwangerschap: niet altijd hyperemesis gravidarum. **H. van Meir**, H.T.C. Nagel, O.R. Guicherit, L.Th. Vlasveld. *Dutch Journal of Obstetrics and Gynecology*. 2010;10:394-397



Arterio-arterial anastomoses do not prevent the development of twin anemia-polycythemia sequence. **H. van Meir**, F. Slaghekke, E. Lopriore, W.J. van Wijngaarden. *Placenta*. 2010 Feb;31(2):163-5

Klinische Les uit de Tropen: een Surinaamse Vrouw met Schistosoma Mansoni van het Ovarium. **H. van Meir**, T. van Meer, A.A.W. Peters. *Dutch Journal of Obstetrics and Gynecology*. 2008;121:168-70

Right ventricular outflow tract reconstruction with the bovine jugular vein graft: 5 years' experience with 133 patients. N. Sekarski, **H. van Meir**, M.E. Rijlaarsdam, P.H. Schoof, D.R. Koolbergen, J. Hruda, L.K. von Segesser, E.J. Meijboom, M.G. Hazekamp. *Annals of Thoracic Surgery*. 2007 Aug;4(2):599-605



**On ne voit bien qu'avec le cœur; l'essentiel est invisible pour les yeux.**

It is only with the heart that one can see rightly; what is essential is invisible to the eye.

*(Antoine de Saint-Exupéry, Le petit Prince, 1943)*