

## CURRICULUM VITAE I.J.M. DE VRIES

### PERSONAL DETAILS

Name: Ingrid Jolanda Monique de Vries  
 Male/female: female  
 Date and place of birth: 19 February 1968, Beilen  
 Nationality: Dutch  
 Marital status: cohabitation agreement, two children

### BACHELOR'S

University of Higher Education Polytechnische faculteit Rotterdam en omstreken; Hoger  
 Laboratorium Onderwijs, Delft  
 Date 19 June 1991  
 Main subject Biochemistry

### DOCTORATE

University of Higher Education University Medical Center Utrecht  
 Date 25 September 1997  
 Supervisor Prof. Dr. C.A.F.M. Bruijnzeel-Koomen  
 Title of thesis T cell migration in Atopic Dermatitis

### WORK EXPERIENCE SINCE GRADUATING

1990-1991 researcher, 1 fte, tenured term, Swiss Institute for Allergy and  
 Asthma research, Davos, Switzerland  
 1991-1997 PhD project, 1 fte, fixed term, Department of Dermatology, University Medical  
 Center Utrecht, The Netherlands. Supervision 1 technician.  
 01/1993-06/1993 Visiting Scientist, Department of Hematology, University Hospital  
 08/1993-01/1994 Zurich, Zurich, Switzerland.  
 02/1994-04/1994  
 1997-2004 Post-doc, 1 fte, fixed term, Department of Tumor Immunology, Nijmegen Centre for  
 Molecular Life Sciences, Radboud University Nijmegen Medical Centre, Nijmegen,  
 The Netherlands. Supervision 2-4 technicians, 2-3 AGIKOs/PhD students, 2-3 post-  
 docs.  
 2004-2009 Staff member and from 2006 assistant professor, Department of Tumor  
 Immunology, 0.5 fte tenured; Department of Pediatric Hemato-oncology 0.5 fte  
 fixed term, Nijmegen Centre for Molecular Life Sciences, Radboud University  
 Nijmegen Medical Centre, Nijmegen, The Netherlands. Supervision 6 technicians, 4  
 AGIKOs/PhD students, 4 post-docs.  
 2009-2011 Associate professor, Department of Tumor Immunology 0.75 fte and Medical  
 Oncology 0.25 fte, Nijmegen Centre for Molecular Life Sciences, Radboud University  
 Nijmegen Medical Centre, Nijmegen, The Netherlands. Supervision 8 technicians, 4  
 AGIKOs/PhD students, 4 post-docs.

- 2011-present Professor Translational Tumor Immunology, Department of Tumor Immunology 0.75 fte and Medical Oncology 0.25 fte, Radboud Institute for Molecular Life Sciences, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. Currently supervising 7 technicians, 16 AGIKOs/PhD students, 3 post-docs.
- 2018-present Chair of the Dutch society for Immunology (NVVI)

#### BRIEF SUMMARY OF RESEARCH

I believe I can be best characterized as an investigator intrigued by the potential of immunotherapy to fight cancer without major side effects. My ambition is to translate findings from preclinical studies into new immunological approaches for the treatment of cancer patients. My track record demonstrates that I am capable of that and I have built a research line focusing on human immunotherapy, where I have not only established a clinical immunotherapy programme with all its regulatory and GMP/GLP hurdles but also created a multitude of techniques to monitor immune responses during and after therapy, not only in vitro but also in vivo. I have throughout my career, developed unique and extensive expertise in this area. Over the past five years my work has been mainly focused on the modulation of Dendritic Cells (DC) for effective DC-based cancer immunotherapeutic purposes (funded in part by a ZonMW-VIDI grant). My primary scientific interest continues along the line of DC-immunotherapy and in particular the migratory and immunomodulatory behaviour of natural DC subsets. Throughout the past period I have developed a variety of immunomonitoring tools and established a multimodal imaging toolbox for human studies. The uniqueness of my work in humans is underscored by multiple invitations for international meetings, and the numerous requests for advice. Furthermore, exploiting the developed tools resulted in high impact papers in different fields of medical research, underscoring the multidisciplinary approach of my research.

I demonstrated in the worldwide first trial, that natural DC activated with preventive vaccines are the most promising cell type for cancer immunotherapy. Hence, my basic research is focussed around DC subsets. I demonstrated that natural DC can be targeted via various molecules, take up antigens and (cross)- present them to T-cells.

I strongly believe that basic research integrated with clinical application provides great opportunities for both sites. My research thus encompasses both bench-to bedside and bedside-to-bench translational studies.

#### *My research in the past 5 years resulted in:*

1. Knowledge concerning the scarce naturally occurring DC subsets for in vivo application
2. An in vivo imaging technique for visualising therapy induced immune responses
3. In immunomonitoring assays to predict clinical outcome after DC vaccination
4. Development of in vivo tracking techniques for visualising cellular therapy and insight in employed mechanisms
5. Understanding the mechanism behind the immune modulating capacity of platinum chemotherapeutics

I have next to my basic science, massively invested (time and costs) in building up an infrastructure to perform dendritic cell based clinical trials. This has led to major successes in the past 5 years: I authored 10 papers describing investigator-driven clinical trials with a self-manufactured cellular product. Recently, my group together with the department of Pharmacy obtained a GMP factory license for the production of advanced-therapy medicinal products, an important achievement for an academic institution and essential for performing clinical trials. During the past years I have not only achieved to set up the infrastructure at the lab but also in the hospital. One of my talents is to connect the separate worlds. As basic scientist I have build up an extensive collaboration with various clinical PIs, and in a joint effort we have now an infrastructure at the clinic. Clinicians like to work with me, I'm part of the UMC. I initiate and supervise clinical trials together with MDs.

## PHD-STUDENTS

I successfully supervised more than 10 PhD students (4 passed with distinction/cum laude) and more than 60 bachelor and master students from biomedical sciences as well as medical sciences.

In my opinion, students should be supervised and coached such that they will be able to perform and design experiments, write papers and grants in a highly independent manner. To date, 2 of my master students wrote, defended and obtained a personal grant in a competitive internal RUNMC PhD round. Furthermore, three of my postdocs were able to obtain various prestigious grants, Annette Sköld: a Swedish research council grant (2012), Mangala Srinivas: a VENI (2010) and an ERC starting grant (2013), Stanleyson Hato: a Bas Mulder award (a personal grant from Alpe d'Huzes/Dutch Cancer Society (620keuro). Moreover, two of my PhD students were able to obtain a Veni (Hans Jacobs 2012 and Jurjen Tel 2013). Two of my PhD/MD students obtained prestigious KWF fellowships (Friederike Meyer Wentrup and Joost Lesterhuis).

## PRIZES AND GRANTS

- Radboudumc PhD project, Dendritic cells to prevent cancer: Immune responses against neoantigens after dendritic cell vaccination of Lynch syndrome. Principal Investigator: IJM de Vries (2019-2023, **240k€**)
- KWF 11618: Galectin-9 is required for dendritic cell function during anti-melanoma immunity. Principal Investigators: A van Spruiel, IJM de Vries (2019-2024, **628k€**)
- ONCOBIOME, Gut OncoMicrobiome Signatures (GOMS) associated with cancer incidence, prognosis and prediction of treatment response. H2020-SC1-2018-825410. Principal Investigator: EU consortium, IJM de Vries (2018-2023, **791k€**)
- DC4Balance, Dendritic Cell Targeting for Resetting Immune Balance. Health-Holland, Top Sector Life Sciences & Health. Principal Investigator: Consortium, IJM de Vries, main applicant (**1,247k€** 2018-2022)
- KWF 10673: Towards prediction of the outcome of cancer immunotherapy. Principal Investigators: CG Figdor, IJM de Vries (2017-2021, **700k€**)
- Radboud penning 2017, The Radboudpenning of Radboud UMC is awarded annually to a person who contributed through a special personal commitment to the goal of the UMC as a top knowledge center for academic medicine and health care
- NWO-ZonMw 2016, Vaccinaties met autologe, natuurlijk circulerende dendritische cellen (nDC) beladen met synthetische peptides bij patiënten met maligne melanoom stadium IIIb en IIIc: evaluatie van klinische respons, kwaliteit van leven en economische aspecten. Principal Investigator: IJM de Vries **550k€**, 2016-2021
- Dendritic cell therapy part of the Dutch Health Care system (Tijdelijke toelating basispakket), to carry out a large randomized study with natural dendritic cell vaccines. **19.867k€** euro for 5 years and 4 months.
- PROCROP, Professional cross-priming for ovary and prostate cancer H2020-PHC-2014-two-stage- 635122. Principal Investigator: EU consortium, IJM de Vries (**1,510k€**, 2015 – 2020)
- ATK, Stichting afweer tegen kanker: Natural dendritic cells for immunotherapy of chemo-naïve metastatic castration-resistant prostate cancer patients. Principal Investigator: IJM de Vries, H. Westdorp, F Witjes, W Gerritsen (**100k€**, 2015 – 2017)
- KWF 2013-6430: GMP production of PLGA beads for in vivo cell tracking. Principal Investigator: IJM de Vries, ML Zandvliet, CG Figdor (**170k€**, 2013 – 2017)
- NWO VICI: Theranostics for the development of successful natural dendritic cell vaccines to combat and prevent cancer. Principal Investigator: IJM de Vries (**1,500k€**, 2014 - 2019)

- Radboudumc JO project 2013: Multifunctional Fight against Cancer. Supervisors: IJM de Vries, J Jacobs (**228k€**, 2013 - 2017)
- Swedish Research Society 2013: Dissecting mechanisms exploited by plasmacytoid dendritic cells for antitumor immunity in therapeutically vaccinated prostate cancer patients. Supervisors: IJM de Vries, R. Kiessling (**372k€**, 2013 - 2016)
- RIO JO project 2013: Dissecting mechanisms exploited by plasmacytoid dendritic cells for antitumor immunity in prostate cancer patients. Principal Investigator: IJM de Vries, W. Gerritsen. (**133k€**, 2013 - 2016)
- NWO-ZonMW 2012:pTO 95103002: Natural circulating plasmacytoid dendritic cells: Key for antitumor immunity? Principal Investigator: IJM de Vries (**€495**, 2012 – 2016)
- BetaTrain: European Training Network for Excellence in Molecular Imaging in Diabetes, EC FP7 ITN . Principal Investigator: M Gotthardt, IJM de Vries (2012 – 2016)
- KWF 2010-4722: Vaccination of early-stage high-risk *uveal* melanoma patients with mRNA-transfected dendritic cells. Principal investigators: IJM de Vries, CJA Punt, ADA Paridaens (**539k€**, 2012 – 2016)
- KWF 2006-3699: Toll like receptor-mediated dendritic cell maturation: The key towards induction of potent anti-tumor immunity? Principal investigators: IJM de Vries, GJ Adema, CJA Punt (**200k€**, 2009 – 2011)
- NWO Vidi: Dendritic Cells en route. Principal investigator: IJM de Vries. (**800k€**, 2007 – 2012)
- NWO Aspasia. Principal investigator: IJM de Vries. (**100k€**, 2007 – 2012)
- ENCITE, European Network for Cell Imaging and Tracking Expertise, EC FP7 project (600k€, 2008 – 2012)
- Pharmachild, Long-term PHARMacovigilance for adverse effects in childhood arthritis focusing on immune modulatory drugs, EC FP7 project (**297k€**, 2011 – 2014)
- NWO-ZonMW 2008: pTO 95100106: Boosting the immune response to prevent cancer: Frameshift neopeptide-derived antigens as novel tumor specific targets for immune therapy in hereditary colorectal cancer. Principal investigators: IJM de Vries, N. Hoogerbrugge (**500k€**, 2009 – 2015)
- KWF 2009-4580: NPK project translational research (**550k€**, 2010 – 2017).
- Van der Es foundation 222, 2010: STAT6 en platinum-chemotherapie gevoeligheid. Principal investigators: WJ Lesterhuis, CJA Punt, IJM de Vries (**160k€**, 2010 – 2012)

## SELECTED PUBLICATIONS

Number of publications: 199; H-index: 49; Total times cited 6848 (web of knowledge)

### Clinical trials:

I have heavily invested in the translation of laboratory discoveries into clinical application with potential benefit for cancer patients.

1. Tel, J, et al. **De Vries, IJ**. Natural human plasmacytoid dendritic cells induce antigen-specific T-cell responses in melanoma patients. **Cancer Res**, 2013. 73(3): p. 1063-75. (IF9.130; PMID23345163)

In this paper, the worldwide first trial with plasmacytoid dendritic cells is presented showing the potency of this cell type in combating cancer. The approach tested in this paper was a result of my discovery in the lab that plasmacytoid DC were excellent cells for antigen presentation.

2. Schreibelt, G, et al. **De Vries, IJ**. Effective Clinical Responses in Metastatic Melanoma Patients after Vaccination with Primary Myeloid Dendritic Cells. **Clin Cancer Res**, 2016. 22(9): p. 2155-66. (IF10.199; PMID26712687)

Here, the potency of the other subset of blood-derived dendritic cells in combating cancer is presented. The remarkable good clinical results with both subsets solely, led to the very novel approach to combine the subsets, a strategy currently being tested in the phase 3 trial financed by the Dutch government.

#### Imaging:

Already right from the start of my DC trials, I recognised that next to measuring effects on the tumour, monitoring the behaviour of the cellular vaccine and measuring immune responses is of utmost importance. I developed a toolbox of techniques to measure and visualize immune processes in vivo and in vitro, thus developing also novel theranostics. I expect that this spin off technology will not be limited to oncology, but be helpful to advance personalized healthcare in general.

3. Aarntzen, et al. **De Vries, IJ.** Early identification of antigen-specific immune responses in vivo by [18F]-labeled 3'-fluoro-3'-deoxy-thymidine ([18F]FLT) PET imaging. **Proc Natl Acad Sci USA**, 2011. 108(45): p. 18396-9. (IF9.504; PMID22025695)

Here, I published a very useful technique to identify immunological responding patients. I collaborated with experts in the field of Nuclear Medicine to employ this innovative technique.

4. **De Vries, IJ** et al. Magnetic resonance tracking of dendritic cells in melanoma patients for monitoring of cellular therapy. **Nat Biotechnol**, 2005. 23(11): p. 1407-13. (IF35.724; PMID16258544)

This highly cited paper is my most recognised innovation in the field of Molecular Imaging and led to many invitations at renowned conferences. I had the original idea to label cells with iron for visualisation with MRI, manufactured dendritic cells under good clinical practice (GMP) and performed experiments in collaboration with MR specialists.

#### Fundamental:

To stay at the forefront of translational research it is of the utmost importance to continuously fuel the pipeline for the next implementation. Therefore, her laboratory is constantly searching for new avenues to make superior vaccines for the benefit of (cancer) patients.

5. Lesterhuis, WJ, et al. **De Vries, IJ.** Platinum-based drugs disrupt STAT6-mediated suppression of immune responses against cancer in humans and mice. **The Journal of Clinical Investigation**, 2011. 121(8): p. 3100-8. (IF13.251; PMID21765211)

The here described discovery, chemotherapy has a positive effect on the immune response, has led to a clinical trial were the DC-based cancer vaccine is combined with chemotherapy.