

Curriculum Vitae

Surname: van de Ven
Name: Rieneke
Title: PhD
Date of birth: February 19th 1980
Place of birth: Hapert
Address: Boomsluiterskade 269
City: Den Haag
Postal code: 2511 VJ
Country: The Netherlands
Telephone number: +31(0)70-3632191
Cell phone: +31(0)6-42057844
E-mail: R.vandeven@Vumc.nl (work) / rieneke@uconl.com (private)
Gender: female
Nationality: Dutch



Work experience and education:

August 2009 – present



Postdoc
Dept. of Medical Oncology, Div. of Immunotherapy
VU University medical center, Amsterdam, NL.

Principle investigator: Dr. Tanja D. de Gruijl
Project: Mechanisms of tumor-induced immune tolerance

The aim of this project is to examine how tumor cells control the immune response. I study the effects of tumor supernatants and suppressive cytokines on dendritic cell (DC) development, DC functions and on the skewing of, and the suppressive effects on, T cells. Furthermore, within (tumor-draining) human lymph node samples, DC subsets are extensively phenotyped and are functionally analyzed to discriminate between immune-activating and immune-regulating LN DC subsets.

October 2007 – June 2009



Scientific researcher
Dept. of Pathology, VU University medical center, Amsterdam, NL in collaboration with Solvay Biologicals, Weesp, NL.



Supervision: Tanja D de Gruijl and Pauline Breedveld
Project: test a human skin explant system for its applicability to screen adjuvant efficiency.

I compared the DC-activating potential of the (influenza)vaccine adjuvants aluminum hydroxide (AIOH) (Alhydrogel ®) and immune-stimulating complexes (ISCOMs) (Matrix-M ®) and a panel of novel adjuvants. Clear differences in potent DC-activation could be discriminated upon intradermal adjuvant injection. This system could be used to screen for very potent DC-activating new compounds taking into account the effects on the surrounding tissue. This could result in the selection of adjuvants for further development, which can induce both a humoral antibody-mediated response and a (memory) cell-mediated response. Solvay Biologicals has filed a patent based on the results from this project.

April 2003 - March 2009



PhD student (defended 4th of April 2009)
Dept. of Pathology, VU University medical center, Amsterdam, NL.

Principle Investigator: Prof. Dr. Rik J. Scheper, PhD
Supervision: Dr. Tanja D. de Gruijl, PhD en Dr. George L. Scheffer, PhD
Thesis title: The contribution of ABC transporters to dendritic cell development and function.

Within this project, I characterized the expression of ATP-binding cassette (ABC) transporters on DC. These transporters have previously been described to play a role in clinical drug resistance (MDR). I analyzed whether the presence and/or activity of specific transporters during different developmental stages of DC interfered with DC development or functions. I found that the multidrug resistance protein 1 (MRP1;ABCC1) is required for optimal DC differentiation (van de Ven et al., JI 2006) and that MRP4 (ABCC4) is needed for human skin DC migration (van de Ven et al., Blood 2008). Beside that, the breast cancer resistance protein (BCRP;ABCG2) was found to accelerate Langerhans cell differentiation when introduced into CD34+ DC precursor cells (manuscript in preparation). In addition to characterizing ABC transporter expression, the effects of cytotoxic drugs on DC development were addressed. I observed that, whereas short term addition of cytostatic drugs can promote and accelerate DC differentiation, which resulted in a patented new culture method for the generation of DC *in vitro* within 3 days (DC Prime B.V.), chronic exposure of DC precursor cells to cytotoxic drugs can render these cells irresponsive to differentiating cytokines (manuscripts in preparation).

**April 2006 – August 2006**

Work-placement for my thesis research in the lab of Prof. DT Curiel.
Division of Human Gene Therapy, University of Alabama at Birmingham, USA.

Supervision: Prof. Dr. David T. Curiel, MD. PhD.

As part of my PhD project, I arranged a work visit with the collaborative lab of Prof. David Curiel to expand my horizons by learning how to clone and rescue adenoviruses. Adenoviruses were made encoding shRNA sequences against ABC transporters. In addition, I analyzed which in house adenoviruses were effective in transducing human DC. This work visit has resulted in two manuscripts, of which one is published in Blood (van de Ven et al. 2008) and the second in the Journal of Immunotherapy (van de Ven et al., in press 2009).

**1998 –2002**

Master degree in Biomedical Sciences
Faculty of Biosciences, Math and Informatics, University of Amsterdam, NL

Date of Master degree; November 7th 2002.
Specialization: Immunology and Oncology

**January 2002 – August 2002**

Student placement for Masters degree.
Lymphocyte Activation Laboratory, Cancer Research UK, London, UK.

Supervision: Dr. Doreen A. Cantrell

Subject: Investigate the function and signal transduction pathway of the enzyme protein kinase D (PKD).
For this project, I transduced Jurkat T cells with different mutants of PKD and studied the effects of truncated PKD on its cellular localization. Additionally, upstream adaptor molecules regulating PKD activity were analyzed. This work involved tissue culture, cell transduction, molecular biological assays and confocal microscopy.

**February 2001 – August 2001**

Student placement for Masters degree.
Department of Immunology, Netherlands Cancer Institute, Amsterdam, NL.

Supervision: Prof. Dr. Ada M. Kruisbeek, PhD.

Subject: Intracellular signal transduction via co-stimulatory receptors on T cells.
This project involved the identification of proteins binding to the intracellular portions of a number of co-stimulatory receptors (such as CD28, CTLA-4, OX40 and ICOS) using chemical cross-linking to gather initial leads. This work involved a variety of basic molecular biological and biochemical tools and assays. As we identified the redox-scavenger molecule thioredoxin to interact with CTLA-4, further analysis was done on the effects of reactive oxygen species on T cell activation.

**1992–1998**

High school education (VWO)
Rythovius college, Eersel, NL.

Exam subjects (and grades): Dutch (8), English (8), Latin (8), Math (7), Biology (7), Chemistry (7), Physics (7).

References:

Dr. Tanja de Gruijl, PhD; TD.deGruijl@VUmc.nl / phone: +31 (0)20 4444063
Prof. Rik Scheper, PhD; R.J.Scheper@VUmc.nl / phone: +31 (0)20 4444031
Prof. David Curiel, MD, PhD; Curiel@uab.edu / phone: +1 205 934 8627

Awards:

- Eli Lilly AACR Scholar in Training Award 2006
American Association for Cancer Research Annual meeting. Washington D.C. USA, 2006.

Grants:

- Student Travel grant from the Dutch Cancer Society (KWF) (2001) for the placement with Dr. D.A. Cantrell at Cancer Research UK, London.
- Grant for Academics from the Dutch Cancer Society (KWF) (2006) for the work-placement with Prof. Dr. D.T. Curiel at the University of Alabama in Birmingham, Birmingham, USA.
- Travel grant from the Netherlands Society for Scientific Research (NWO) (2006) for the work-placement with Prof. Dr. D.T. Curiel at the University of Alabama in Birmingham, Birmingham, USA.
- Placement grant from the Netherlands Society for Immunology (Nvvi) (2006) for the work-placement with Prof. Dr. D.T. Curiel at the University of Alabama in Birmingham, Birmingham, USA.

Memberships:

- The Netherlands Society for Immunology (Nvvi) since 2003
- The American Association for Cancer Research (AACR) since 2006

Certificates:

- Certificate to work with radioactive materials level 5B.
- Certificate to write research protocols and work with research animals (article 9).

Postdoctoral courses:

- Advanced Immunology
- Trends in tumor-immunology
- Basic oncology
- Transport processes in health and disease

Techniques:

- Cell culture, DC culture from monocytes, the MUTZ3 cell line and murine bone marrow cells, PBMC isolation from blood, isolation of epidermal and dermal human skin DC, T helper assays, T cell priming, *in vitro* trans-well and human skin explant migration assays, flowcytometry, FACS-sort, ELISA, Western blot, mixed leukocyte reactions, immunocytochemistry, drug-transporter activity tests, drug cytotoxicity tests (XTT), molecular cloning, propagation and isolation of adenoviruses, *in vitro* adenoviral and retroviral cell transduction, *in situ* adenoviral transduction of human skin DC, (Lightcycler) PCR, low-density microarray.

Publication list:

R van de Ven, JJ Lindenberg, D Oosterhoff, MP van den Tol, RA Rosalia, M Murakami, M Everts, GL Scheffer, RJ Scheper, TD de Gruijl and DT Curiel (2009) *Selective transduction of mature DC in human skin and lymph nodes by CD80/CD86-targeted fiber-modified adenovirus-5/3*, J.Immunotherapy, in press.

R van de Ven, J de Groot, AW Reurs, PGJTB Wijnands, K van de Wetering, JD Schuetz, TD de Gruijl, RJ Scheper and GL Scheffer (2009), *Unimpaired immune functions in the absence of Mrp4 (Abcc4)*, Immunol Lett 124, p81-7.

R van de Ven, GL Scheffer, AW Reurs, JJ Lindenberg, R Oerlemans, G Jansen, JP Gillet, JN Glasgow, A Pereboev, DT Curiel, RJ Scheper and TD de Gruijl (2008) *A role for multidrug resistance protein 4 (MRP4 ; ABCC4) in human dendritic cell migration*. Blood 112; 2353-2359.

SJAM Santegoets, S Gibbs, K Kroeze, R van de Ven, RJ Scheper, C Borrebaeck, TD de Gruijl and M Lindstedt (2008) *Transcriptional profiling of human skin-resident Langerhans cells and CD1a+ dermal dendritic cells: differential activation states suggest distinct functions*. J.Leuk.Biology 84 (1); 143-151.

R van de Ven, MJ de Jong, AW Reurs, AS Schoonderwoerd, G Jansen, JH Hooijberg, TD de Gruijl, GL Scheffer and RJ Scheper (2006) *Dendritic cells require multidrug resistance protein 1 (ABCC1) activity for differentiation*. J. Immunology 176 (9); 5191-5198.

Reviews:

R van de Ven, R Oerlemans, JW van der Heijden, GL Scheffer, TD de Gruijl, G Jansen and RJ Scheper (2009), *ABC transporters and immunity: novel therapeutic targets in autoimmunity and cancer*, J. Leuk. Biol, in press (Epub ahead of print).

R van de Ven, GL Scheffer, RJ Scheper and TD de Gruijl (2009), *The ABC of dendritic cell development and function*, Trends in Immunol. 30(9); p421-9.