

MSc Infection & Immunity

Appendix 3

Senior staff CV's

Def vs NVAO 180908

(equal to Def vs NVAO 080708)

Name

Carla Baan

CV

Carla C. Baan, PhD, is senior investigator and Head of the Laboratory of Nephrology and Transplantation and a transplant immunologist at Erasmus University, Rotterdam, The Netherlands. Her position involves the supervision of doctorate research related to the role of cytokines and T-cells in organ failure and post transplantation. Additionally, she is responsible for the discovery and implementation of immunological and molecular biological techniques relevant to transplantation research. Dr Baan obtained her doctorate from Erasmus University. Dr Baan has served as the primary author for 29 peer-reviewed articles and has contributed to 60 additional publications. She serves as a reviewer for the *American Journal of Transplantation*, *Transplantation Proceedings (member of the editorial board)*, *Transplantation*, the *Journal of Heart and Lung Transplantation*, *Transplant International*, *Human Immunology* and *Transplant Immunology*. Dr Baan has extensive speaking experience including over 60 presentations. She is a member of the council of the European Society for Organ Transplantation, member of the International Society of Heart and Lung Transplantation, the International Cytokine Society, the Dutch Transplantation Society, the Dutch Immunology Society and the Dutch Nephrology Society.

Selected Publications

- Baan CC, Balk AH, van Riemsdijk IC, Vantrimpont PJ, Maat AP, Niesters HG, Zondervan PE, van Gelder T, Weimar W. Anti-CD25 monoclonal antibody therapy affects the death signals of graft-infiltrating cells after clinical heart transplantation. *Transplantation*. 2003; 75(10): 1704-10.
- Lemos FBC, IJzermans JNM, Zondervan PE, Peeters AMA, van den Engel S, Mol WM, Weimar W, Baan CC. Differential expression of heme oxygenase-1 and vascular endothelial growth factor in cadaveric and living donor kidneys after ischemia-reperfusion. *J Am Soc Nephrol*. 2003;14(12): 3278-87
- Baan CC, Peeters AMA, Lemos FB, Uitterlinden A, Doxiadis I, Claas FHJ, IJzermans JMN, Roodnat JI, Weimar W. Fundamental role of HO-1 in the self-protection of renal allografts. *Am Journal of Transplantation* 2004;4(5):811-8.
- Holweg CTJ, Uitterlinden A, Weimar W, Baan CC. Gene polymorphisms in heart transplantation: Overview and discussion of the current literature. *J Heart Lung Transplant* 2004; 23(9):1017-26.
- Baan CC, van der Mast BJ, Klepper M, Mol WM, Peeters AMA, Korevaar SS, Balk AHMM, Weimar W. Differential effect of calcineurin inhibitors, anti-CD25 antibodies and rapamycin on the induction of FOXP3 in human T-cells. *Transplantation* 2005;80:110-7.
- van der Mast BJ, Rischen-Vos J, de Kuiper P, Vaessen LM, van Besouw NM, Weimar W. Calcineurin inhibitor withdrawal in stable kidney transplant patients decreases the donor-specific cytotoxic T lymphocyte precursor frequency. *Transplantation*. 2005;80:1220-5.
- Dijke IE, Velthuis JH, Balk AH, Korevaar SS, Maat AP, Weimar W, Baan CC. Donor-specific cytotoxic hyporesponsiveness associated with high interleukin-10 messenger RNA expression in cardiac allograft patients. *J Heart Lung Transplant*. 2006;25:955-64.
- Baan CC, Weimar W. Targeting the IL-15 pathway to prevent rejection after organ transplantation. *Transplantation Rev* 2006;20:28-33.
- Velthuis JHL, Mol WM, Weimar W, Baan CC. CD4⁺ CD25^{bright+} regulatory T cells can mediate donor non-reactivity in long-term immunosuppressed kidney allograft patients, *American Journal of Transplantation* 2006 (*in press*).

PhD Students

Ph.D projects finished:

- The tumor necrosis factor (TNF)- α system in organ failure and transplantation, thesis of IC van Riemsdijk-van Overbeeke (2000, co-promotor).
- Cytokines and graft function in heart transplant recipients, thesis of Dr HA de Groot-Kruseman (2002, co-promotor).
- Gene polymorphisms in heart transplantation, thesis of Dr CTJ Holweg (2003, co-promotor)
- Cytokine gene polymorphisms in liver transplantation, thesis of Dr MC Warlé (2004)

Current Ph.D projects:

- Regulatory cells after organ transplantation; thesis project of Ing IE Dijke (start 2003)
- Immunological monitoring of tapering immunosuppression; thesis project of Drs J van de Wetering (start 2003)
- The influence of immunosuppressive medication on the development of immune regulation; thesis project Drs TK Hendrikx (start 2004)
- mTOR inhibition after kidney transplantation. Thesis project of Drs EAFJ van Gorp (start 2004)
- Induction of regulatory T-cells for tolerance. V Sewgobind (start 2006)
- The immunomodulatory role of mesenchymal stem cells in organ transplantation. Thesis project of Drs M Crop (start 2006)

(International) Awards

- Aves Award 1998 of the International Society for Heart and Lung Transplantation entitled: Anti-CD25 therapy reveals the redundancy of the intra-graft cytokine network after clinical heart transplantation
- Best Dutch Transplantation Article, Award 2000, entitled: Anti-CD25 therapy reveals the redundancy of the intra-graft cytokine network after clinical heart transplantation. Transplantation 1999;67:870-876.
- International Young Investigator Award 2001 of the American Society of Transplantation entitled: Blockade of the IL-2R α chain affects the death signals of graft infiltrating lymphocytes after clinical heart transplantation.
- Supervisor of the study by AMA Peeters entitled "Heme oxygenase-1 promoter gene polymorphism is associated with graft survival of kidney donors" awarded with the International Young Investigator Award 2003 of the American Society of Transplantation and
- the Young Investigators Award 2003 of the European Society for Organ Transplantation

Current Research Topic

Clinical Transplantation Immunology

International Collaboration

Prof dr IV Hutchinson, University of Southern California, USA

Dr I Anegon, INSERM, Nantes, France,

Dr A Bushell, University of Oxford, England

Name

Irma A.J.M. Bakker-Woudenberg, PhD

CV

Born 11 juni 1949 in Utrecht.

June 1968 : Diploma Gymnasium-beta, R.K. Lyceum O.L.V. ter Eem, Amersfoort.

1968-1975: MSc degree Biology (cum laude), study program Biochemistry, University of Utrecht, Faculty Natural Sciences, with specializations Medical Microbiology, Immunology, Haematology.

1975-1980: PhD degree in Clinical Microbiology & Antimicrobial Therapy, Erasmus University Rotterdam, Faculty of Medicine and Health Sciences, Promotor: Prof.dr. M.F. Michel.

Thesis: Efficacy of Antimicrobial Therapy in the Compromised Host, an experimental study.

Year PhD 1980

1980-1985: Assistant professor.

Since 1985: Associate professor, senior staff member of the Department of Medical Microbiology & Infectious Diseases, Erasmus University Medical Centre Rotterdam (EMC), The Netherlands.

Responsibilities :Research and supervising research projects. Field of research: Antibiotic pharmacodynamics and antibiotic delivery systems in infectious diseases in relation to therapeutic efficacy and emergence of antibiotic resistance. Teaching and curriculum development in Medical Microbiology and Infectious Diseases. Management.

Selected publications

- Bakker-Woudenberg I.A.J.M. **M.T. ten Kate, L.E.T. Stearne-Cullen, M.C. Woodle (1995) Efficacy of gentamicin or ceftazidime entrapped in liposomes with prolonged blood circulation and enhanced localization in *Klebsiella pneumoniae* infected lung tissue.** J. Infect. Dis. 171: 938-947.
- **Bakker-Woudenberg I.A.J.M.** (1995) Delivery of antimicrobials to infected tissue macrophages. Adv. Drug Deliv. Rev. 17: 5-20.
- Hagen T.L.M. ten, W. v. Vianen, H.F.J. Savelkoul, H. Heremans, W.A. Buurman, **I.A.J.M. Bakker-Woudenberg** (1998) Involvement of T-cells in enhanced resistance to *Klebsiella pneumoniae* septicemia in mice treated with liposome-encapsulated muramyl tripeptide phosphatidylethanolamine or gamma interferon. Infect. Immun. 66: 1962-1967.
- Schiffelers R.M., G. Storm, M.T. ten Kate, L.E.T. Stearne-Cullen, J.G. den Hollander, H.A. Verbrugh, **I.A.J.M. Bakker-Woudenberg** (2001) In vivo synergistic interactions of liposome -co-encapsulated gentamicin and ceftazidime. J. Pharmacol. Exp. Ther. 298: 369-375.
- Becker M.J., S. de Marie, M.H.A.M. Fens, H.A. Verbrugh, **I.A.J.M. Bakker-Woudenberg** (2003) Effect of amphotericin B treatment on kinetics of cytokines and parameters of fungal load in neutropenic rats with invasive pulmonary aspergillosis. J. Antimicrob. Chemother. 52: 428-434.
- **Bakker-Woudenberg I.A.J.M.**, R.M. Schiffelers, G. Storm, M.J. Becker, L. Guo (2005) Long-circulating sterically stabilized liposomes in the treatment of infections. Methods Enzymol. 391:228-260.
- Vianen W. van, S. de Marie, M.T. ten Kate, R.A.A. Mathot, **I.A.J.M. Bakker-Woudenberg** (2006) Caspofungin: antifungal activity in vitro, pharmacokinetics, and effects on fungal load and animal survival in neutropenic rats with invasive pulmonary aspergillosis.

- J. Antimicrob. Chemother. 57: 732-740.
- **Bakker-Woudenberg I.A.J.M.**, M.T. ten Kate, W.H.F. Goessens, J.W. Mouton (2006) Effect of treatment duration on pharmacokinetic/pharmacodynamic indices correlating with therapeutic efficacy of ceftazidime in experimental *Klebsiella pneumoniae* lung infection. Antimicrob. Agents Chemother. 50: 2919-2925.
 - Goessens W.H.F., J.W. Mouton, M.T. ten Kate, A.J. Bijl, A. Ott, **I.A.J.M. Bakker-Woudenberg** (2007) Role of ceftazidime dose regimen on the selection of resistant *Enterobacter cloacae* in the intestinal flora of rats treated for an experimental pulmonary infection. J. Antimicrob. Chemother. 59: 507-516.
 - de Steenwinkel J.E.M., W. van Vianen, M.T. ten Kate, H.A. Verbrugh, M.A. van Agtmael, R.M. Schiffelers, **Irma A.J.M. Bakker-Woudenberg** (2007) Targeted drug delivery to enhance efficacy and shorten treatment duration in disseminated *Mycobacterium avium* infection in mice. J. Antimicrob. Chemother. 60: 1064-1073.

PhD students

- Robert Roosendaal. Thesis: Therapeutic effect of antibiotics in the compromised host. Erasmus University Rotterdam, 1988.
- Pernela Melissen. Thesis: Free and liposome-encapsulated immunomodulators stimulating the non-specific resistance against bacterial infections. Erasmus University Rotterdam, 1993.
- Els van Etten. Thesis: Liposomal amphotericin B for invasive fungal infections. An experimental study in the leukopenic host. Erasmus University Rotterdam, 1995.
- Timo ten Hagen. Thesis: Immunomodulation in gram-negative septicemia. Liposome-encapsulated MTPPE and IFN- γ in *Klebsiella pneumoniae* infection in mice, efficacy and mechanisms. Erasmus University Rotterdam, 1996.
- Raymond Schiffelers. Thesis: Liposomal targeting of antimicrobial agents to bacterial infections. Erasmus University Rotterdam, 2001.
- Martin Becker. Thesis: Experimental and clinical studies on invasive pulmonary aspergillosis: pathophysiology, diagnosis and management. Erasmus University Rotterdam, 2004.
- Wendy van de Sande. Thesis: Genetic variability, antigenicity and antifungal susceptibility of *Madurella mycetomatis*. Erasmus University Rotterdam, 2007.
- Jurriaan de Steenwinkel. 2005-current. Tuberculosis, targeted drug delivery to shorten treatment duration and to prevent resistance and latency, role of endemic strains.
- Sanne van den Berg. 2008-current. Novel therapeutic approaches in severe infections caused by (multi-drug) resistant *Staphylococcus aureus*.

(International) Awards

1987 Recipient of the W.R.O. Goslings Award – Research in Infectious Diseases. Infectious Diseases Society of the Netherlands and Flanders. Research grant in the field of experimental infections.

2005 Recipient of the ESCMID / AstraZeneca Award 'Turning the Tide of Resistance'. Research grant in the field of antibiotic resistance.

Current Research Grant Support

- Merck Research laboratories, Rahway, USA. Study: Therapeutic efficacy of Caspofungin in the inhalation model of invasive pulmonary aspergillosis in persistently neutropenic rats. Research support E 64.701,- .

- Pfizer Inc., New York, USA. Study: Therapeutic efficacy of Voriconazole alone or in combination with Anidulafungin in an inhalation model of invasive pulmonary aspergillosis in persistently neutropenic rats. Research support E 94.765,- .
- Top Institute Pharma. Study: Antibodies against *Klebsiella pneumoniae* as an alternative non-antibiotic-based antimicrobial strategy. Research support E 411.000,- .
- Top Institute Pharma. Study: New antibiotics to fight antimicrobial resistance. Research support E 500.000,- .
- Top Institute Pharma. Study: Protective human antibodies against multi-drug resistant *Staphylococcus aureus*. Research support E 572.000,- .

Current Research Topics

- Tuberculosis, targeted drug delivery to shorten treatment duration and to prevent resistance and latency, role of endemic strains.
- Fungal infections, innovative therapeutic intervention in invasive pulmonary aspergillosis in the immunocompromised host.
- Factors involved in the enhancement of mutations leading to extended-spectrum-beta-lactamase resistance in *Klebsiella pneumoniae*.
- New antibiotics to fight antimicrobial resistance in bacterial and fungal infections.
- Protective human antibodies against antibiotic-resistant *Klebsiella pneumoniae* and *Staphylococcus aureus* as an alternative non-antibiotic-based antimicrobial strategy.
- Beta-lactam resistance in *Pseudomonas aeruginosa*, factors important to the emergence of resistance, mechanisms of resistance and prevention.

International Collaboration

- Cameron Douglas. Merck Research Laboratories, Rahway, NJ, USA.
- Rogelio Hernandez-Pando. National Institute of Medical Sciences and Nutrition Salvador Zubiran, Dept. Experimental Pathology. Mexico city, Mexico.

Name

Alex van Belkum

CV

Alex van Belkum is Professor of Molecular Microbiology in the Department of Medical Microbiology and Infectious Diseases at Erasmus MC, Rotterdam, The Netherlands. His research interests cover diagnostic, epidemiological and fundamental aspects of infectious diseases. Molecular diagnostic methods are developed and implemented in routine applications. Epidemiological typing methods are being developed as well and applied for the elucidation of routes of bacterial spread, population structure, dynamics and genetics. Fundamental research is in the field of human nasal colonisation by *Staphylococcus aureus*, the basics of *Campylobacter jejuni* induced post infectious neurological complications, the biology of the mycetoma causing fungal organism *Madurella mycetomatis*, and animal models for the study into pathogenesis and therapy of infections.

Selected Publications

- Belkum Alex van, Braak Nicole van den, Godschalk Peggy, Ang Wim, Jacobs Bart, Gilbert Michel, Wakarchuk Warren, Verbrugh Henri and Endtz Hubert (2001) "A *Campylobacter jejuni* gene associated with immune mediated neuropathy". *Nature Medicine*, 7, 752-753. (IF 30)
- Boer Jan Willem den, Yzerman Ed, Belkum Alex van, Vlaspolder Fer and Breukelen Fred (1998) "Legionnaire's disease and saunas". *Lancet* 351, 114. (IF 25)
- Wertheim Heiman, Vos Greet, Leeuwen Willem van, Belkum Alex van, Verbrugh Henri, Nouwen Jan (2005) "The role of nasal carriage in *Staphylococcus aureus* infection. *Lancet Infectious Diseases* 5, 751-762. (IF 10)
- Belkum Alex van, Alphen Loek van, Scherer Stewart and Verbrugh Henri (1998) "Short sequence repeats in prokaryotic genomes", *Microbiology and Molecular Biology Reviews* 62, 275-293. (IF 15)
- Sande Wendy van de, Janse Dirk Jan, Hira Vishal, Goedhart Heidy, Zee Ruurd van der, Ahmed Abdalla, Ott A, Verbrugh H, Belkum Alex van (2006) "Translationally controlled tumor protein from *Madurella mycetomatis*, a marker for tumorous mycetoma progression". *Journal of Immunology* 177, 1997-2005. (IF 7)
- Houliston Scott, Endtz Hubert, Yuki Nobuhiro, Li Jianjun, Jarrell Harold, Koga Michiaki, Belkum Alex van, Karwaski Marie-France, Wakarchuk Warren, Gilbert Michel (2006) "Identification of a sialate O-acetyltransferase from *Campylobacter jejuni*: demonstration of direct transfer to the C-9 position of terminal alpha-2,8-linked sialic acid." *Journal of Biological Chemistry* 281, 11480-11486. (IF 7)
- Godschalk Peggy, Heikema Astrid, Gilbert Michel, Komagamine Tomoko, Ang Wim, Glerum Jobine, Brochu Denis, Li Jiangjun, Yuki Nobuhiro, Jacobs Bart, Belkum Alex van, Endtz Hubert (2004) "The crucial role of *Campylobacter jejuni* genes in anti-ganglioside antibody induction in Guillain-Barre Syndrome". *Journal of Clinical Investigation* 114, 1659-1665. (IF 15)
- Melles Damian, Gorkink Raymond, Boelens Helene, Snijders Susan, Peeters Justine, Moorhouse Michael, Spek Peter van der, Leeuwen Willem van, Simons Guus, Verbrugh Henri, Belkum Alex van (2004) "Natural population dynamics and expansion of pathogenic clones of *Staphylococcus aureus*". *Journal of Clinical Investigation* 114, 1732-1740. (IF 15)
- Wertheim Heiman, Vos Margreet, Ott Alewijn, Belkum Alex van, Voss Andreas, Kluytmans Jan, Keulen Peter van, Vandenbroucke-Grauls Christina, Meester Marlene, Verbrugh Henri

(2004) "Risk and outcome of nosocomial *Staphylococcus aureus* bacteremia in nasal carriers versus non-carriers". *Lancet* **364**, 703-705. (IF 25)

- Bogaert Debbie, Belkum Alex van, Sluijter Marcel, Luijendijk Ad, Groot Ronald de, Rumke Hans, Verbrugh Henri, Hermans Peter (2004) "Colonisation by *Streptococcus pneumoniae* and *Staphylococcus aureus* in healthy children". *Lancet* **363**, 1871-1872. (IF 25)
- Daubersies Pierre, Thomas Alan, Millet Pascal, Brahimi Karima, Langermans Jan, Ollomo Benjamin, Ben Mohamed Lbachir, Slierendregt Bas, Eling Wijnand, Belkum Alex van, Meis Jacques, Guerin-Marchand Claudine, Cayphas Sylvie, Cohen Joe, Gras-Masse Helene and Druilhe Pierre (2000) Protection against *Plasmodium falciparum* malaria in chimpanzees by immunization with the conserved pre-erythrocytic liver-stage 3 antigen. *Nature Medicine* **6**, 1258-1263. (IF 30)

PhD Students

- Nicole Renders (PhD thesis 2000; Bacterial colonization of the respiratory tract in cystic fibrosis patients)
- Nicole van den Braak (PhD thesis 2001; Glycopeptide resistant enterococci in The Netherlands: surveillance and genome analysis)
- Willem van Leeuwen (PhD thesis 2002; Binary typing of *Staphylococcus aureus*)
- Abdalla Ahmed (PhD thesis 2003; Molecular and biological studies on *Madurella mycetomatis* infections in man and mice)
- Jan Nouwen (PhD thesis 2004: Determinants, risks and dynamics of *Staphylococcus aureus* nasal carriage)
- John Hays (PhD thesis 2006: Studies into the genetic diversity and complement resistance phenotype of *Moraxella catarrhalis*)
- Peggy Godschalk (PhD thesis 2007: Bacterial determinants of the pathogenic routes leading to *Campylobacter*-induced Guillain-Barré Syndrome)

(International) Awards

2003 Astra Zeneca Award in Infectious Disease Research (\$50.000,--)

Current Research Grant Support

- Revolving Fund Erasmus MC (Development and application of methods suited for high-speed diagnosis of nasal carriage of (methicillin resistant) *Staphylococcus aureus*) €50.000,-- research support.
- STW Raman spectroscopy (1 FTE technician for four years)
- EUR Trustfund (Nasal carriage of *Staphylococcus aureus*: inoculation of site directed mutants in the noses of (non)carrying volunteers) €30.000,- research support
- STW (MLPA as a new method for the high speed diagnosis of infectious agents) €120.000,- research support
- MLDS (Studies into gastro-enteritis and its sequelae caused by *Campylobacter jejuni* using organo-enzymatically synthesised lipo-oligosaccharide mimics) €105.000,- research support.
- EU FP6 (Partner in: Role of mobile genetic elements in the spread of antimicrobial drug resistance) €160.000,- research support.
- EU FP6 (Partner in: Novel prevention and treatment possibilities for otitis media through the comprehensive identification of antigenic proteins) €355.000,- research support
- Ministry of LNV (Characterisation of MRSA ST 398: the pig associated clone) €75.000,- research support.

- Top Institute Pharma (Protective human antibodies against multi-drug resistant *Staphylococcus aureus*) €397.000,- research support
- Top Institute Pharma (New antibiotics to fight antimicrobial resistance) €500.000,- research support

Current Research Topics

See above

International Collaboration

See list of publications

Name

Prof. Dr. Robbert Benner

CV

Rob Benner, PhD, is a full professor of immunology (since 1979) and head of the Department of Immunology, Erasmus MC (since 1985). The department has over 140 members, a.o. 4 full professors, 4 internists-immunologist, 16 other permanent academic staff members, postdocs, PhD students, technicians and supporting staff. His main scientific interests are the cellular and molecular regulation of the immune response. He is author and co-author of over 200 articles in refereed international journals, promotor of over 60 PhD theses, and (co-)inventor of over 100 patents. Since 1998, the Department has filed over 200 patents and has spawned four spin-out biotech companies based on these patents (Dynamics BV, SkinTec BV, Biotempt BV, EBI-anti-sepsis BV).

Selected Publications

- Wolters EAJ, Benner R. Functional separation *in vivo* of both antigens encoded by H-2 subregion and non-H-2 loci. *Nature*. 1979; 279: 642-643.
- Wolters EAJ, Benner R. Different target antigens for T-cell subsets acting synergistically *in vivo*. *Nature*. 1980; 286: 895-896.
- Bianchi ATJ, Hooijkaas H, Benner R, Tees R, Nordin AA, Schreier, MH. Clones of helper T cells mediate antigen-specific H-2 restricted DTH. *Nature*. 1981; 290: 62-63.
- Bianchi ATJ, Bril H, Benner R. Alloantigen-specific suppressor T cells suppress also the *in vivo* immune response to 'bystander' alloantigens. *Nature*. 1983; 301: 614-616.
- Benner R, Wolters EAJ, Bril H, Molendijk A, Oudenaren A van. Regulation of delayed type hypersensitivity to host histocompatibility antigens during Graft-versus-Host reactions. *Immunol Rev*. 1985; 88: 25-57.
- Khan NA, Khan A, Savelkoul HFJ, Benner R. Inhibition of diabetes in NOD mice by human pregnancy factor. *Hum Immunol*. 2001; 62: 1315-1323.
- Khan NA, Khan A, Savelkoul HFJ, Benner R. Inhibition of septic shock in mice by an oligopeptide from the β -chain of human chorionic gonadotrophin hormone. *Hum Immunol*. 2002; 63: 1-7.
- Benner R, Khan NA. Dissection of systems, cell populations and molecules. Review. *Scand J Immunol*. 2005; 62: 62-66.

PhD Students

Schrijver IA.

Bacterial peptidoglycan in rheumatoid arthritis and multiple sclerosis.

Thesis, Erasmus University Rotterdam, the Netherlands (2000; 5 January)

Supervisors: Benner R, Laman JD.

ISBN 90-73436-51-6.

Boonstra PA.

Modulation of T helper cell activity by ultraviolet B irradiation. Analysis of cytokines and genetic susceptibility factors.

Thesis, Erasmus University Rotterdam, the Netherlands (2000; 25 October)

Supervisors: Benner R, Savelkoul HFJ.

ISBN 90-73436-53-2.

Nawijn MChr.

Regulation of cell-fate decisions in T lymphocyte differentiation.

Thesis, Erasmus University Rotterdam, the Netherlands (2000; 6 December)

Supervisors: Savelkoul HFJ, Benner R, Hendriks RW.

ISBN 90-73436-54-0.

Companjen AR.

Modulation of pro-inflammatory cytokines in normal and inflamed skin.

Thesis, Erasmus University Rotterdam, the Netherlands (2000; 3 October)

Supervisors: Benner R, Laman JD, Prens EP.

ISBN 90-73436-57-5.

Blokland SCA van.

The salivary glands in Sjögren's syndrome: pathogenetic aspects of the initiation of sialoadenitis.

Thesis, Erasmus University Rotterdam, the Netherlands (2000; 19 December)

Supervisors: Benner R, HA Drexhage, Versnel MA.

ISBN 90-73436-58-3.

Dik WA.

Lung disease of the preterm infant: mediators involved in fibroproliferation and fibrogenesis.

Thesis, Erasmus University Rotterdam, the Netherlands (2002; 22 May)

Supervisors: Benner R, Versnel MA, Zimmerman LJI.

ISBN 90-73436-60-5.

Burg M van der.

Recombination processes during human B-cell differentiation.

Thesis, Erasmus University Rotterdam, the Netherlands (2002; 19 June)

Supervisors: Dongen JJM van, Benner R, Langerak AW.

ISBN 90-73436-61-3.

Brok HPM.

Experimental autoimmune encephalomyelitis in the common marmoset: a novel model for multiple sclerosis.

Thesis, Erasmus University Rotterdam, the Netherlands (2002; 28 June)

Supervisors: Benner R, Hart LA 't, Bontrop RE.

ISBN 90-9015887-1.

Middendorp S.

Btk at the Pre-B cell receptor checkpoint.

Thesis, Erasmus University Rotterdam, the Netherlands (2004; 19 May) *cum laude*

Supervisors: Benner R, Hendriks RW.

ISBN 90-73436-66-4.

Visser L.

Immune modulation in MS models by peptidoglycan, CD97 and CD44.

Thesis, Erasmus University Rotterdam (2005; 11 May)

Supervisors: Benner R, Laman JD.

ISBN 90-73436-69-9.

Awards

- 1980 Steven Hoogendijk Prize 1980 of the Bataafsch Genootschap, Rotterdam
- 2004 Ad Fontes medallion of the Erasmus University Rotterdam
- 2005 Companion in the Order of the Dutch Lion

Current Research Topic

Gene regulation by oligopeptides and its clinical applicability

Name

Dr. Andre Boonstra
Laboratory of Gastroenterology and Hepatology

CV

Andre Boonstra studied Biology at the University of Groningen (1988-1993). After receiving his degree he worked at the National Institute for Public Health and the Environment (RIVM), the Netherlands, and started his PhD project in 1996 at the department of Immunology of the Erasmus MC in Rotterdam. During his PhD period he visited DNAX Research Institute, USA to study the development of regulatory T cells. He successfully defended his thesis entitled "Modulation of T helper cell activity by ultraviolet B irradiation -analysis of cytokines and genetic susceptibility factors" in 2000, and returned to DNAX Research Institute, USA as a post-doctoral fellow to study the function of myeloid and plasmacytoid dendritic cells and their effect on Th cell development. In 2002, he moved to the National Institute for Medical Research, London to focus on the immunology of tuberculosis infections. In September 2006 he became a staff member at the Department of Gastroenterology and Hepatology of the Erasmus MC in Rotterdam, and his current research focusses on the immunology of hepatitis C infections.

Selected Publications

Boonstra A, Rasjbaum R, Holman M, Marques R, Asselin-Paturel C, Pereira J, Bates EEM, Akira S, Vieira P, Liu Y-J, Trinchieri G, O'Garra A. Macrophages and myeloid DC, but not plasmacytoid DC, produce IL-10 in response to MyD88- and TRIF-dependent TLR signals, and TLR-independent signals. *J. Immunol.* Dec 1, 2006.

Boonstra A, Asselin-Paturel C, Gilliet M, Crain C, Trinchieri G, Liu Y-J, O'Garra A. Flexibility of mouse classical and plasmacytoid-derived dendritic cells in directing T helper type 1 and 2 cell development: dependency on antigen dose and differential Toll-like receptor ligation. *J Exp Med.* 2003. 197: 101-109.

Gilliet M, Boonstra A, Paturel C, Antonenko S, Xu X, Trinchieri G, O'Garra A, Liu Y-J. The development of murine plasmacytoid dendritic cell precursors is differentially regulated by Flt3-ligand and granulocyte/macrophage colony-stimulating factor. *J Exp Med.* 2002. 195: 953-958.
Asselin-Paturel C, Boonstra A, Dalod M, Durand I, Yessaad N, Dezutter-Dambuyant C, Vicari A, O'Garra A, Biron C, Brière F, Trinchieri G. The major type I interferon producing cells in the mouse are immature antigen-presenting cells exhibiting plasmacytoid morphology. *Nature Immunol.* 2001. 2: 1144-1150.

PhD Students

Mark Claassen (2005-2008)

Current Research Topics

Viral hepatitis is a major global health problem with more than 500 million patients chronically infected. Both chronic hepatitis B and C lead to liver cirrhosis, liver failure and hepatocellular carcinoma, accounting for approximately 1 million deaths annually. The importance of developing adequate therapy for these diseases is obvious and the Rotterdam Liver Unit is one of the foremost groups in the world to develop such treatments. Taking full advantage of recent knowledge acquired in clinical and immunological medicine, our studies combine epidemiological and fundamental research in a cross-disciplinary approach while collaborating with the most experienced centers in the field of viral hepatitis.

In the laboratory, our research is mainly devoted to understanding the apparently inadequate immune response of chronic viral hepatitis. Gaining better understanding of these mechanisms, will eventually contribute to innovations in treatment regimens.

Our research is focused on the immunology of chronic HCV infections, and studies the role of dendritic cells, NK cells and regulatory T cells on the chronicity of infections with hepatitis virus. In these studies, both peripheral and intrahepatic HCV specific immune responses are characterized.

International Collaboration

Dr. A. O'Garra and Dr. G. Kassiotis. National Institute for Medical Research, London, UK

Dr. Y-J Liu. M.D. Anderson Cancer Center, Houston, USA

Dr. G. Trinchieri. NIH/NIAID, Bethesda, USA

Name

Charles Achim Bernard Boucher, MD, PhD

Place of birth	Amsterdam
Date of birth	January 16, 1958
Nationality	Dutch

Education & Training

1993	Ph.D.-degree University of Amsterdam, Faculty of Medicine . Thesis: "Characterisation of human immunodeficiency viruses during zidovudine treatment"
1991	Board certification clinical microbiologist
1987-1991	Medical microbiologist training Academic Medical Centre, University of Amsterdam
1987	Medical degree (MD), <i>cum laude</i>
1986	Fellow Royal Dutch Academy of Sciences(Ter Meulen fonds) Department of Paediatrics, School of Medicine, Yale University, USA
1983-1987	Medical internships
1983	Doctoraal degree
1977-1983	Study Medicine, University of Amsterdam, Faculty of Medicine
1977	Gymnasium Beta
1970-1977	Barlaeus Gymnasium, Amsterdam

Present position and Assignments

- Professor in virology Department of virology Erasmus Medical Center , Erasmus University Rotterdam, the Netherlands
- Associate Professor in Virology, Department of Medical Microbiology, Faculty of Medicine, University Medical Center Utrecht (UMCU), the Netherlands
- Coordinator of a European Network of 32 countries entitled Europe HIV Resistance. A Network to control spread of HIV drug resistance supported by the European Commission.
- Scientific director Virology Education Utrecht, the Netherlands

Professional and scientific experience

2006	Chief editor of the journal Reviews in Antiviral Therapy.
2006 - 2010	Coordinator Grant from European Commission European Pan Network on HIV Drug Resistance named "EuropeHIVResistance"
2005 - 2009	Partner in "ViroLab" an European Commission funded project.
2005 - 2006	Coordinator of Unite More an European Commission funded project.
2002 - 2005	Coordinator Grant from European Commission European Network for SPREAD of drug resistant HIV.
2001-2004	Visiting associate professor, School of Medicine, Stanford University
1997-2001	Coordinator Grant from the European Commission. European Network for Evaluation of AIDS therapy ENVA'
1995-	Associate professor in Virology, Department of Medical Microbiology, University Medical Centre Utrecht, head Prof. Dr. J. Verhoef.

Education and teaching

- 2007 Copromoter van M. Huigen
- 2007 Co-promotor van Dr. A.M.J Wensing *Transmission of drug resistant HIV* Universiteit van Utrecht
- 2006 Co-promotor van Dr. N. van Maarseveen. *Evolution of protease inhibitor resistance.* Universiteit van Utrecht.
- 2001 Co-promotor van Dr. J.C. Stuart, *HIV and the immune system during highly active antiretroviral therapy.* Universiteit van Utrecht
- 2000 Co-promotor van Dr. W Keulen. *Evolution of drug-resistant HIV-1 Variants.* Universiteit van Utrecht.
- 1999 Co-promotor van Dr. M. Nijhuis. *Fitness of HIV-1 during Antiretroviral therapy.* Universiteit van Utrecht.
- 1998 Co-promotor van Dr. A.M. Been-Tiktak *Clinical and Virological Evaluation of Ateviridine and Delavirdine. Nonnucleoside Reverse Transcriptase Inhibitors.* Universiteit van Utrecht
- 1996 Co-promotor van M.D. de Jong, proefschrift *Drug-failure in HIV-1 infection causes and Implications for Therapeutic strategies,* Universiteit van Amsterdam

Organisational Activities

- Initiator and member of the Organising committee of the International Workshop on HIV-Drug Resistance:
1992 Noordwijk, the Netherlands, 1993 Noordwijk, the Netherlands, 1994 Kuai, Hawaii, USA
1995 Sardinia, Italy, 1996 Whistler, Canada, 1997 St. Petersburg, USA, 1998 Baveno / Lake Maggiore, Italy, 1999 San Diego, USA, 2000 Barcelona Spain, 2001 Scotsdale USA
2002 Sitges Spain, 2003 Cabo Mexico, 2004 Seville Spain, 2005 Quebec, USA, 2006 Sitges, Spain, 2007
- Initiator and member of the Organising committee of the Annual International workshop on HIV Pharmacology:
2000 Noordwijk the Netherlands, 2001 Noordwijk the Netherlands, 2002 Washington, USA
2003 Cannes France, 2004 Rome Italy, 2005 Quebec Canada, 2006 Lisboa Portugal, 2007 Budapest Hungary, 2008 New Orleans USA
- Organiser of the Dynamics of HIV Infection Meeting 1995 Arden Conference Centre, Harriman, New York, USA.
- International Editor of 'Timely Topics in Medicine SIDA', <http://www.prous.com/ttmsida>; the AIDS Cyber Journal.
- Guest-editor Antiviral Therapy
- Co-chair 6th Annual International Discussion Meeting on HIV Dynamics and Evolution, Atlanta, Georgia, USA, March 26-29, 1999. Session: Dynamics and evolution of HIV antiviral resistance.
- Chair during the NAM symposium on "Emerging Therapies for HIV Infection: new targets and sustainable strategies" in London on May 9th 2003.

Scientific reviewer for:

Journal of Infectious Disease, AIDS, Antiviral Research, Antimicrobial Agents

and Chemotherapy, Journal of Virology, Proceedings National Academy of Sciences, Journal of AIDS, Antiviral Therapy, Lancet, Bioinformatics.
NWO grants, ZonMw
Member scientific advisory board dutch AIDS foundation
Member scientific board Dutch HIV stichting

Peer reviewed publications (since 2000)

- Hazenberg MD, Stuart JW, Otto SA, Borleffs JC, Boucher CA, de Boer RJ, Miedema F, Hamann D. T-cell division in human immunodeficiency virus (HIV)-1 infection is mainly due to immune activation: a longitudinal analysis in patients before and during highly active antiretroviral therapy (HAART). *Blood*. 2000 Jan 1;95(1):249-55.
- Back, N.K.T., van Wijk, A., Remmerswaal, D., van Montfort, M., Nijhuis, M., Schuurman, R., and Boucher, C.A. In vitro tipranavir susceptibility of HIV-1 isolates with reduced susceptibility to other protease inhibitors. *AIDS*. (2000). 14 (1): 101-102.
- P.Clevenbergh, J. Durant, P. Halfon, P. del Giudice, V. Mondain, N. Montagne, J.M. Schapiro, C.A.B. Boucher and P. Dellamonica - Persisting long-term benefit of genotype-guided treatment for HIV-infected patients failing HAART. The Viradapt study: week 48 follow up. *Antiviral Therapy* (2000), 5: 65-70.
- Orendi JM, Nottet HS, De Vos NM, Visser MR, Snippe H, Boucher CA, Verhoef J. Hydroxyurea interferes with antigen-dependent T-cell activation in vitro. *Eur J Clin Invest*. 2000 Feb;30(2):162-6.
- European Paediatric Hepatitis C Virus Infection Network, Tovo, P-A., Pembrey, L.J. and Newell, M-L.. Persistence Rate and Progression of Vertically Acquired Hepatitis C Infection. *The Journal of Infectious Diseases* (2000). 181: 419-24.
- Hazenberg, M.D., Otto, S.A., Cohen Stuart, J.W.T., Verschuren, M.C.M., Borleffs, J.C.C., Boucher, C.A.B., Coutinho, R.A., Lange, J.M.A., Rinke de Wit, T.F., Tsegaye, A., van Dongen, J.M. van, Hamann, D., de Boer, R.J., Miedema, F. Increased cell division but not thymic dysfunction rapidly affects the T-cell receptor excision circle content of the naive T cell population in HIV-1 infection. *Nature Medicine*, 2000, 6 (8), 1036-1042
- Cohen Stuart JW, Hazebergh MD, Hamann D, Otto SA, Borleffs JC, Miedema F, Boucher CA, de Boer RJ. The dominant source of CD4+ and CD8+ T-cell activation in HIV infection is antigenic stimulation. *J Acquir Immune Defic Syndr*. 2000 Nov 1;25(3):203-11.
- L.J.R. van Elden, G.A. van Essen, C.A.B. Boucher, M. Nijhuis, A.M. van Loon, - Nieuwe antivirale middelen voor de preventie en behandeling van influenza. *Nederlands Tijdschrift voor Medische Microbiologie*, 8^e jaargang, december 2000, no. 4, 124-128.
- Para. Michael, F. , David V. Glidden, Robert W. Coombs, Ann. C. Collier, John H. Condra, Charles Craig, Roland Bassett, Randi Leavitt. Baseline Human Immunodeficiency Virus Type 1 Phenotype, Genotype, and RNA Response after Switching from Long-Term Hard-Capsule Saquinavir to Indinavir or Soft-Gel-Capsule Saquinavir in AIDS Clinical Trials Group Protocol 333, *The Journal of Infectious Diseases*, 2000; 182; 733-43
- Marée, A.F.M., Keulen, W., Boucher, C.A.B., Boer, R.J. de. Estimating Relative Fitness in Viral Competition Experiments. *Journal of Virology* (2000), 74 (23) : 11067-11072
- Sevin, A.D., DeGruttola, Nijhuis, M., Schapiro, J.M., Foulkes, A.S., Para, M.F., Boucher, C.A.B. Methods for Investigation of the Relationship between Drug-Susceptibility Phenotype and Human Immunodeficiency Virus Type 1 Genotype with Applications to AIDS Clinical Trials Group 333. *The Journal of Infectious Diseases*, (2000) 182 : 59-67
- Vaerenbergh, Kristien van, Kristel van Laethem, Jan Albert, Charles, A.B. Boucher, Bonaventura Clotet, Marco Florida, Jan Gerstoft, Bo Heideman, Claus Nielsen, Christophe

Pannecouqou, Luc Perrin, Maria F. Pirillo, Lidia Ruiz, Jean-Claude Schmit, Francois Schneider, Anne Schoolmeester, Rob Schuurman, Hans J. Stellbrink, Lieven Stuyver, Jan van Lunzen, Barbara van Remoortel, Eric van Wijngaerden, Stefano Vella, Myriam Witvrouw, Sabine Yerley, Erik de Clercq, Jan Desmyter, Anne-Mieke Vandamme. Prevalence and Characteristics of Multinucleoside-Resistant Human Immunodeficiency Virus Type 1 among European Patients Receiving Combinations of Nucleoside Analogues. *Antimicrobial Agents and Chemotherapy*, Aug. 2000, p. 2109-2117.

- Frost SD, Nijhuis M, Schuurman R, Boucher CA, Brown AJ. Evolution of lamivudine resistance in human immunodeficiency virus type 1-infected individuals: the relative roles of drift and selection. *J Virol.* 2000 (14):6262-6268.
- Mascolini M, Wensing AM, Boucher CA. HIV resistance assay results and their effect on therapeutic decisions. *AIDS.* 2001 Jan 5;15(1):124-6.
- Monique Nijhuis, Steven Deeks, Charles Boucher - Implications of antiviral resistance on viral fitness. *Current Opinion in Infectious Diseases*, 2001, 14:23-28.
- The EuroGuidelines Group for HIV Resistance. Clinical and laboratory guidelines for the use of HIV-1 drug resistance testing as part of treatment management: recommendations for the European setting. *AIDS* (2001) 15(3) p. 309-320.
- Joost W.J. van Esser, Hubert G.M. Niesters, Steven F.T. Thijsen, Ellen Meijer, Albert D.M.E. Osterhaus, Katja C. Wolthers, Charles A.B. Boucher, Jan Willem Gratama, Leo M. Budel, Bronno van der Holt, Anton M. van Loon, Bob Löwenberg, Leo F. Verdonck and Jan J. Cornelissen. Molecular quantification of viral load in plasma allows for fast and accurate prediction of response to therapy of Epstein-Barr virus-associated lymphoproliferative disease after allogeneic stem cell transplantation. *British Journal of Haematology* (2001), 113, 814-821.
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- Wensing AM, Reedijk M, Richter C, Boucher CA, Borleffs JC. Replacing ritonavir by nelfinavir or nelfinavir/saquinavir as part of highly active antiretroviral therapy leads to an improvement of triglyceride levels. *AIDS.* 2001 Nov 9;15(16):2191-3
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van Rensburg EJ, Wensing AM, van de Vijver DA, Boucher CA, Camacho R, Vandamme AM. An automated genotyping system for analysis of HIV-1 and other microbial sequences. *Bioinformatics*. 2005 Aug 2;

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- van Maarseveen NM, Huigen MC, de Jong D, Smits AM, Boucher CA, Nijhuis M. A novel real-time PCR assay to determine relative replication capacity for HIV-1 protease variants and/or reverse transcriptase variants. *J Virol Methods*. 2006 May;133(2):185-94.
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- Baxter JD, Schapiro JM, Boucher CA, Kohlbrenner VM, Hall DB, Scherer JR, Mayers DL. Genotypic changes in human immunodeficiency virus type 1 protease associated with reduced susceptibility and virologic response to the protease inhibitor tipranavir. *J Virol*. 2006 Nov; 80(21):10794-801. 2006
- Prevention of mother to child transmission of multi-drug resistant HIV-1 using maternal therapy with both enfuvirtide and tipranavir. Annemarie MJ Wensing, Charles AB Boucher, Marjo van Kasteren, Pieter J van Dijken, Sybil P Geelen and Job R Juttman AIDS. 2006 Jun 26;20(10):1465-1467
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- van Maarseveen NM, Wensing AM, de Jong D, Taconis M, Borleffs JC, Boucher CA,

Nijhuis M. Persistence of HIV-1 variants with multiple protease inhibitor (PI)-resistance mutations in the absence of PI therapy can be explained by compensatory fixation. *J Infect Dis.* 2007 Feb1;195(3):399-409. Epub 2006 Dec 29.

Name

Jan J. Cornelissen

CV

- 1991 – 1993 Hematologist, Member of the Staff of the Department of Hematology, University Hospital Utrecht
- 1994 – current Hematologist, Member of the Staff of the Department of Hematology, Erasmus MC/Daniel den Hoed Cancer Center,
- Head of hematopoietic stem cell transplantation program
- 1999 Sabbatical leave, Fred Hutchinson's Cancer Research Center, Seattle, WA, USA
- 1993-1994 Chairman of the Committee on Cytotoxic Drugs, University Hospital Utrecht
- 1994-1998 Member of the Committee on Hospital Drugs, Daniel den Hoed Cancer Center, Rotterdam
- 1995-1998 Member of the Staff Board, Daniel den Hoed Cancer Center, Rotterdam
- 2000- current Boardmember Dutch Society of Hematology

Selected Publications

1. Cornelissen JJ, Carston M, Kollman C, King R, Dekker AW, Löwenberg B, Anasetti C. Unrelated marrow transplantation for adult patients with poor-risk acute lymphoblastic leukemia: storing graft versus leukemia effect and risk factors determining outcome. *Blood* 2001;97(6): 1572-1577. (IF: 9.631)
2. Van Esser JWJ, Van der Holt B, Meijer E, Niesters HGM, Trenschele R, Thijsen SFT, Van Loon AM, Frassoni F, Bacigalupo A, Schaefer UW, Osterhaus ADME, Gratama JW, Löwenberg B, Verdonck LF, Cornelissen JJ. Epstein-Barr virus (EBV) reactivation is a frequent event after allogeneic stem cell transplantation (SCT) and quantitatively predicts EBV-lymphoproliferative disease following T-cell-depleted SCT. *Blood* 2001;98: 972-978. (IF: 9.631).
3. Van Esser JWJ, Niesters HG, Van der Holt B, Meijer E, Osterhaus AD, Gratama JW, Verdonck LF, Löwenberg B, Cornelissen JJ. Prevention of Epstein-Barr virus lymphoproliferative disease by molecular monitoring and preemptive rituximab in high-risk patients after allogeneic stem cell transplantation. *Blood* 2002;99: 4364-4369. (IF: 9.631)
4. O'Brien SG, Guilhot F, Larson RA, Gathmann I, Baccarani M, Cervantes F, Cornelissen JJ, Fischer Th, Hochhaus A, Hughes T, Lechner K, Nielsen JL, Rousselot Ph, Reiffers J, Saglio G, Shepherd J, Simonsson B, Gratwohl A, Goldman JM, Kantarjian H, Taylor K, Verhoef G, Bolton AE, Capdeville R, Druker BJ. Interferon and low-dose Cytarabine compared with Imatinib for newly diagnosed chronic-phase chronic myeloid leukemia. *N Engl J Med* 2003;348: 994-1004. (IF: 31.736).
5. Broers AE, Posthumus-van Sluijs SJ, Spits H, Van der Holt B, Löwenberg B, Braakman E, Cornelissen JJ. Interleukin-7 improves T-cell recovery after experimental T-cell-depleted bone marrow transplantation in T-cell-deficient mice by strong expansion of recent thymic emigrants. *Blood* 2003; 102: 1534-1540 (IF: 9.631).

Current Research Grant Support

NKB project EMCR 2002/2694, EMC 03-01-41-03-01

Cytokine accelerated T-cell recovery after allogeneic stem cell transplantation: experimental studies in mice with an emphasis on IL-7.

Projectleaders: Jan J Cornelissen, Eric Braakman and Hergen Spits.

Landsteiner Stichting voor Bloedtransfusie Research (LBSR) nr. 0103, EMC 03-01-43-03-01

Improving T-cell recovery after allogeneic stem cell transplantation by IL-7 and restoration of thymic function.

Projectleaders: Jan Cornelissen, Hergen Spits.

Landsteiner Stichting voor Bloedtransfusie Research (LSBR) nr 0221, EMC 03-01-43-03-01

"Dendritic cell-based induction of donor alloantigen-specific tolerance in allogeneic stem cell transplantation"

Projectleaders: Eric Braakman, Jan Cornelissen and Pieter Leenen

Name

Tom Cupedo

CV

My research is focused on the development of human lymphoid organs (lymph nodes and thymus) with the ultimate goal of using this knowledge to disrupt lymph node-like infiltrates during auto-immunity and regenerate thymic function after stem cell transplantation.

01.01.2006 – present Group leader, Dept. Hematology, ErasmusMC Rotterdam, the Netherlands
01.04.2003 – 31.12.2006 Postdoctoral research associate, Dept. Cell Biology and Histology, AMC Amsterdam, the Netherlands
01.11.1998 – 01.02.2003 PhD student. Dept. Molecular Cell Biology and Immunology, VU Medical Center Amsterdam, the Netherlands

Selected Publications

N. Legrand, T. Cupedo, A.U. van Lent, M.J. Ebeli, K. Weijer, T. Hanke and H. Spits
Transient accumulation of human mature thymocytes and regulatory T cells with CD28 superagonist in “human immune system” Rag2^{-/-}□_c^{-/-} mice
Blood 2006; 108: 238-245

W. Dontje*, R. Schotte*, T. Cupedo, M. Nagasawa, F. Scheren, R. Gimeno, H. Spits and B. Blom
DeltaLike1 induced Notch1 signalling regulates the human plasmacytoid dendritic cell versus T cell lineage decision through control of GATA-3 and Spi-B
Blood 2006; 107: 2446-2452. *equal contribution

T. Cupedo, M. Nagasawa, K. Weijer, B. Blom and H. Spits
Development and activation of CD4⁺CD25⁺ regulatory T cells in the human fetus
Eur. J. Immunol. 2005; 35: 383-390

T. Cupedo and R.E. Mebius
Cellular interactions in lymph node development
J. Immunol. 2005, 174(1): 21-5

T. Cupedo, W. Jansen, G. Kraal and R.E. Mebius
Induction of secondary and tertiary lymphoid structures in the skin
Immunity. 2004; 21(5): 655-67

T. Cupedo, F.E. Lund, V.N. Ngo, T.D. Randall, W. Jansen, M.J. Greuter, R. de Waal-Malefyt, G. Kraal, J.G. Cyster and R.E. Mebius
Initiation of cellular organization in lymph nodes is regulated by non-B cell-derived signals and is not dependent on CXC chemokine ligand 13
J. Immunol. 2004;173(8): 4889-96

T. Cupedo, M.F.R. Vondenhoff, E.J. Heeregrave, A.E. de Weerd, W. Jansen, D.G. Jackson, G. Kraal, and R.E. Mebius
Presumptive lymph node organizers are differentially represented in developing mesenteric and peripheral nodes
J. Immunol. 2004; 173(5): 2968-75

T. Cupedo and R.E. Mebius
Role of chemokines in the development of secondary and tertiary lymphoid tissues
Semin. Immunol. 2003;15(5): 243-8

T. Cupedo, G. Kraal and R.E. Mebius
The role of CD45⁺CD4⁺CD3⁻ cells in lymphoid organ development
Immunol. Rev. 2002 189: 41-50

R.E. Mebius, T. Miyamoto, J. Christensen, J. Domen, T. Cupedo, I. L. Weissman, and K. Akashi
The fetal liver counterpart of adult common lymphoid progenitors give rise to all lymphoid lineages, CD45⁺CD4⁺CD3⁻ cells, as well as macrophages

J. Immunol. 2001 166: 6593-6601

D. Kim, R.E. Mebius, J.D. MacMicking, T. Cupedo, Y. Castellanos, N. Kim, R. Josien, P.D. Rennert, and Y-W. Choi

Regulation of peripheral lymph node genesis by the TNF family member TRANCE

J. Exp. Med. 2000 192: 1467-1478

PhD Students

Currently, one PhD project is running in the lab:

E. Vroegindewij: Development of thymic regenerative therapy

Current Research Grant Support

Netherlands Organization for scientific research (ZON-MW) VENI Grant 916.66.0182005.

“Human lymphoid organogenesis”. Euro 200.000

Wijnand Pon stichting

Towards thymic regenerative therapy. (PhD position)

Current Research Topics

Our research is focused on understanding the normal development of human lymphoid organs, especially thymus (together with Prof. JJ Cornelissen) and lymph nodes, in order to use this knowledge to influence the function of these organs during disease.

1. Towards thymic regenerative therapy Stem cell transplantation is the preferred treatment for multiple hematological malignancies. While most hematological lineages recover within weeks after SCT, restoration T cell development can take up to 2 years, leaving patients severely immuno-compromised and susceptible to opportunistic infections. This lag in T cell development is due to severely diminished thymic function. Our research is aimed at understanding the molecular and cellular events that shape the thymus during human fetal development. By recapitulating this development in vitro, we will set the stage for thymic regenerative therapy, which should ideally combine SCT with a reactivation of thymic function in vivo.

2. Human lymph node development During several autoimmune disorders infiltrating lymphocytes are positioned in a highly organized fashion, resembling the architecture typically seen in lymph nodes. These so-called “tertiary lymphoid organs” are thought to be an active part of pathology, functioning to activate naïve auto-reactive lymphocytes and sustaining the aberrant inflammation by mechanisms similar to lymph nodes. Our work is focused on elucidating the cells and molecules involved in human lymph node development. Using this knowledge we will target autoimmune induced lymphoid organs in humanized animal models to disrupt the cellular organization in these structures and dampen the self-sustaining inflammation.

International Collaboration

C. Clare Blackburn, Stem Cell Institute, University of Edinburgh UK

Graham Anderson and Jorge Camano, University of Birmingham UK

Mark Coles, University of York UK

Shin-Ichi Nishikawa, RIKEN Research center for Developmental Biology, Kobe Japan

Takeshi Watanabe, RIKEN Research Center for Allergy and Immunology, Yokohama Japan

Hergen Spits, Genentech Inc, San Francisco USA

Name

Pieter A. van Doorn, Professor MD PhD

CV

Pieter van Doorn was born in 1959 in Utrecht. He studied Medicine at the Erasmus University Rotterdam, the Netherlands. Research for his PhD started in 1983 at the Department of Immunohematology, Leiden State University (Prof dr JJ van Rood). In 1985 he started his residency in Neurology at the Department of Neurology ErasmusMC. In 1990 he was registered as Neurologist and defended his thesis: 'Intravenous immunoglobulin in chronic inflammatory demyelinating polyneuropathy, a clinical and immunological study' (cum laude). Promotor Prof dr A Staal, co-promoters Prof dr M. Vermeulen en Prof dr A Brand. Since 1991 he is Staff Member of the Department of Neurology at ErasmusMC. Since 2003 he is Professor in Neuromuscular disorders, in specific immune-mediated disorders, in the Department of Neurology at Erasmus MC Rotterdam, The Netherlands.

His main research interests are immune-mediated polyneuropathies: Guillain-Barré syndrome and chronic inflammatory demyelinating polyneuropathies (CIDP); Pompe disease, a metabolic muscle disorder due to alpha-glucosidase deficiency, and the evaluation of assessment scales. He is involved in laboratory research concerning GBS preceding infections, anti-ganglioside antibody responses cross-reacting with peripheral nerve epitopes (molecular mimicry), hostfactors (SNP, immune response), pain and autonomic dysfunction in GBS, and the effect of intravenous immunoglobulin (IVIg) in GBS and CIDP. He has initiated and conducted randomized controlled trials (RCT) in GBS and CIDP. Besides conducting research, he is working as a clinical Neurologist and primary responsible for the neuromuscular branch at ErasmusMC. He is chairman of several boards including National guideline commissions on peripheral neuropathy and Guillain-Barré syndrome, and vice-chairman of the Inflammatory Neuropathy Consortium (INC).

Selected publications:

- Hughes RA, Donofrio P, Bril V, Dalakas MC, Deng C, Hanna K, Hartung HP, Latov N, Merkies IS, van Doorn PA: on behalf of the ICE Study Group. Intravenous immune globulin (10% caprylate-chromatography purified) for the treatment of chronic inflammatory demyelinating polyradiculoneuropathy (ICE study): a randomised placebo-controlled trial. **Lancet Neurol.** 2008; 7: 136-144.
- Hughes RAC, Swan AV, Raphaël JC, Annane D, van Koningsveld R, van Doorn PA. Immunotherapy for Guillain-Barré syndrome: a systematic review. **Brain** 2007; 130: 2245-57.
- Van Koningsveld R, Steyerberg E, Hughes RAC, Swan AV, van Doorn PA, Jacobs BC. A clinical prognostic scoring system for Guillain-Barré syndrome. **Lancet Neurol.** 2007;6:589-94.
- Geleijns K, Roos A, Houwing-Duistermaat JJ, Van Rijs W, Tio-Gillen AP, Laman JD, Van Doorn PA, Jacobs BC. Mannose-Binding Lectin Contributes to the Severity of Guillain-Barré Syndrome. **J Immunol.** 2006;177:4211-7.
- Van Doorn PA, Jacobs BC. Predicting the course of Guillain-Barré syndrome. **Lancet Neurol.** 2006;5:991-3.

- Ruts L, van Koningsveld R, van Doorn PA. Distinguishing acute-onset CIDP from Guillain-Barre syndrome with treatment related fluctuations. **Neurology**. 2005;65:138-40.
- Van Doorn PA. Treatment of Guillain-Barré syndrome and CIDP. **J Peripher Nerv Syst**. 2005;10:113-127
- Hagemans ML, Winkel LP, Van Doorn PA, Hop WJ, Loonen MC, Reuser AJ, Van der Ploeg AT. Clinical manifestation and natural course of late-onset Pompe's disease in 54 Dutch patients. **Brain**. 2005;128:671-7.
- Van Koningsveld R, Schmitz PI, Van der Meché FG, Visser LH, Meulstee J, Van Doorn PA; Dutch GBS study group. Effect of methylprednisolone when added to standard treatment with intravenous immunoglobulin for Guillain-Barré syndrome: randomised trial. **Lancet**. 2004;363:192-6.
- Winkel LP, Van den Hout JM, Kamphoven JH, Disseldorp JA, Remmerswaal M, Arts WF, Loonen MC, Vulto AG, Van Doorn PA, De Jong G, Hop W, Smit GP, Shapira SK, Boer MA, Van Diggelen OP, Reuser AJ, Van der Ploeg AT. Enzyme replacement therapy in late-onset Pompe's disease: a three-year follow-up. **Ann Neurol**. 2004;55:495-502.
- Garssen MP, Bussmann JB, Schmitz PI, Zandbergen A, Welter TG, Merkies IS, Stam HJ, Van Doorn PA. Physical training and fatigue, fitness, and quality of life in Guillain-Barré syndrome and CIDP. **Neurology**. 2004;63:2393-5.
- Merkies IS, Schmitz PI, Van der Meché FG, Samijn JP, Van Doorn PA. Psychometric evaluation of a new handicap scale in immune-mediated polyneuropathies. **Muscle Nerve** 2002;25:370-7.
- Ang CW, Laman JD, Willison HJ, Wagner ER, Endtz HP, De Klerk MA, Tio-Gillen AP, Van den Braak N, Jacobs BC, Van Doorn PA. Structure of Campylobacter jejuni lipopolysaccharides determines antiganglioside specificity and clinical features of Guillain-Barré and Miller Fisher patients. **Infect Immun** 2002;70:1202-8.
- Jacobs BC, Rothbarth PH, Van der Meché FGA, Herbrink P, Schmitz PIM, de Klerk MA, Van Doorn PA. The spectrum of antecedent infections in Guillain-Barré syndrome. A case-control study. **Neurology** 1998;51:1110-1115
- Van Doorn PA, Brand A, Strengers PFW, Meulstee J, Vermeulen M. High-dose intravenous immunoglobulin treatment in chronic inflammatory demyelinating polyneuropathy: a double-blind, placebo-controlled, crossover study. **Neurology** 1990;40:209-212
- Van Doorn PA, Brand A, Vermeulen M. Anti-neuroblastoma cell line antibodies in inflammatory demyelinating polyneuropathy. Inhibition in vitro in vivo bij IV immunoglobulin. **Neurology** 1988; 38:1592-1595

PhD Students

- C.P.W.G. Geleijns (2005). Immunogenetic polymorphisms in Guillain-Barré syndrome.
- M.P.J. Garssen (2005). *Treatment of Guillain-Barré syndrome; and causes and treatment of residual fatigue in GBS and CIDP.*
- B.C. Jacobs (1997). Antecedent infections and anti-ganglioside antibodies in Guillain-Barré syndrome. Their role in pathogenesis and heterogeneity. (cum laude) (co-promotor)
- C.W. Ang (2001). Molecular mimicry in the Guillain-Barré syndrome.(cum laude). (co-promotor)

- I.S.J. Merkies (2001). Evaluation of scales and measurement instruments in immune-mediated polyneuropathies. (cum laude). (co-promotor)
- R. van Koningsveld (2001). Epidemiology and clinical aspects of the Guillain-Barré syndrome. (co-promotor)

International Awards

2008 *GBS/CIDP Foundation International. Research grant. Skin biopsies in GBS*

Current Research Grant Support

- Janivo Foundation (Clinical variability, treatment and pain in Guillain-Barré syndrome). PhD student and technician.
- Janivo Foundation (Identification of GBS patients likely to develop severe pain and autonomic dysfunction). Research grant
- GBS/CIDP Foundation International. (Skin biopsies in GBS). Research grant.
- Prinses Beatrix Fonds. (Predicting and improving recovery in Guillain-Barré syndrome). BC Jacobs, EW Steyerberg and PA van Doorn. PhD student and RCT
- Baxter Medical. Comparing different branches of intravenous immunoglobulin in CIDP, and dose-finding study. PhD student and equipment.
- Revolving Fund ErasmusMC (Investigation into the natural course of late onset Pompe's disease and identification of patients eligible for enzyme replacement therapy) A.T. van der Ploeg en P.A. van Doorn
- Genzyme. Research in Pompe disease. AT van der Ploeg and PA van Doorn. Research grant.

Current research topics

- Guillain-Barré syndrome (GBS) and chronic inflammatory demyelinating polyneuropathy (CIDP): Preceding infections, anti-ganglioside antibodies, molecular mimicry, SNP, skin biopsies and relation with patient characteristics (severity, pain, autonomic dysfunction, fatigue and prognosis). Mechanisms of intravenous immunoglobulin (IVIg) and randomized clinical trials (RCT).
- Pompe disease. Patient characteristics, treatment with alfa-glucosidase, genetics.

International collaboration

Prof RAC Hughes, Kings Hospital London, UK

Dr N. Yuki, Dokkyo University, Tochigi, Japan

Prof H. Willison, Glasgow Biomedical Research Centre, Glasgow, Scotland

Prof DR Cornblath, Johns Hopkins University, Baltimore, USA

Name

Prof. Jacques J.M. van Dongen, M.D., Ph.D.

CV

Jacques J.M. van Dongen studied Medicine at the Erasmus University Rotterdam (Rotterdam, the Netherlands) and received his M.D. degree in 1981. From then on he worked in the field of immunology research, with special focus on human T- and B-cell differentiation as well as lymphoid malignancies and immunodeficiencies. Together with Herbert Hooijkaas, he initiated the immunodiagnostic laboratory of the Erasmus university Medical Center Rotterdam in 1985, which has developed into one of the leading centers for immunodiagnostics and translational research of lymphoproliferative diseases and immunodeficiencies in Europe. In 1990 he received his Ph.D. degree (thesis: "Human T-cell differentiation: Basic aspects and their clinical applications"). Since 1991 he has been full Professor of Immunology at the Erasmus MC/Erasmus University Rotterdam. His translational research focuses on molecular genetic processes during normal, malignant, and immunodeficient lymphoid differentiation and on the development and clinical evaluation of new immunodiagnostic methods in lymphoproliferative diseases and primary immunodeficiencies. He contributed to ~450 manuscripts, including ~340 international SCI publications (number of citations: ~9,500; H-factor: 55). He is/was coordinator of six European networks in the field of diagnostics in hemato-oncology.

Selected Publications

1. Van Dongen JJM, Langerak AW, Brüggemann M, Evans PA, Hummel M, Lavender L, Delabesse E, Davi F, Schuurin E, Garcia Sanz R, Van Krieken JHJM, Droese J, Gonzalez Diaz D, Bastard D, White H, Spaargaren M, Gonzáles M, Parreira A, Smith J, Morgan G, Kneba M, Macintyre EA. Design and standardization of PCR primers and protocols for detection of clonal immunoglobulin and T-cell receptor gene recombinations in suspect lymphoproliferations. Report of the BIOMED-2 Concerted Action BMH4-CT98-3936. *Leukemia* 2003;17:2257-2317.
2. Staal FJ, Weerkamp F, Baert MR, Van Den Burg CM, Van Noort M, De Haas EF, Van Dongen JJM. Wnt target genes identified by DNA microarrays in immature CD34(+) thymocytes regulate proliferation and cell adhesion. *J Immunol* 2004;172:1099-1108.
3. Szczepanski T, Van der Velden VHJ, Hoogeveen PG, De Bie M, Jacobs DC, Van Wering ER, Van Dongen JJM. Vd2-Ja gene rearrangements are frequent in precursor-B-acute lymphoblastic leukemia but rare in normal lymphoid cells. *Blood* 2004;103:3798-3804
4. Dik WA, Pike-Overzet K, Weerkamp F, de Ridder D, De Haas EF, Baert MR, Van der Spek P, Koster EE, Reinders MJ, Van Dongen JJM, Langerak AW, Staal FJT. New insights on human T cell development by quantitative T cell receptor gene rearrangement studies and gene expression profiling. *J Exp Med* 2005;201:1715-1723.
5. Van Zelm MC, Van der Burg M, De Ridder D, Barendregt BH, De Haas EF, Reinders MJ, Lankester AC, Revesz T, Staal FJ, Van Dongen JJM. Ig gene rearrangement steps are initiated in early human precursor B cell subsets and correlate with specific transcription factor expression. *J Immunol* 2005;175:5912-5922.
6. Van der Burg M, Van Veelen LR, Verkaik NS, Wiegant WW, Hartwig NG, Barendregt BH, Brugmans L, Raams A, Jaspers NG, Zdzienicka MZ, Van Dongen JJM, Van Gent DC. A new type of radiosensitive T-B-NK+ severe combined immunodeficiency caused by a LIG4 mutation. *J Clin Invest* 2006;116:137-145.
7. Weerkamp F, Baert MR, Naber BA, Koster EE, De Haas EF, Atkuri KR, Van Dongen JJM, Herzenberg LA, Staal FJT. Wnt signaling in the thymus is regulated by differential

- expression of intracellular signaling molecules. Proc Natl Acad Sci U S A. 2006;103:3322-3326.
8. Van Zelm MC, Reisli I, Van der Burg M, Castano D, Van Noesel CJ, Van Tol MJ, Woellner C, Grimbacher B, Patino PJ, Van Dongen JJM, Franco JL. An antibody-deficiency syndrome due to mutations in the CD19 gene. N Engl J Med 2006;354:1901-1912.
 9. Van Zelm MC, Szczepanski T, Van der Burg M, Van Dongen JJM. Replication history of B lymphocytes reveals homeostatic proliferation and extensive antigen-induced B cell expansion. J Exp Med 2007;204:645-655.
 10. Dik WA, Nadel B, Przybylski GK, Asnafi V, Grabarczyk P, Navarro JM, Verhaaf B, Schmidt CA, Macintyre EA, Van Dongen JJM, Langerak AW. Different chromosomal breakpoints impact the level of LMO2 expression in T-ALL. Blood 2007;110:388-392.

PhD Students

J.G. Noordzij (Jeroen)

Genotypic and phenotypic aspects of primary immunodeficiency diseases of the lymphoid system
Erasmus University Rotterdam (Dept. of Immunology), Rotterdam, 19 June 2002

M. van der Burg (Mirjam)

Molecular processes during human B-cell differentiation
Erasmus University Rotterdam (Dept. of Immunology), Rotterdam, 19 June 2002

T. Szczepanski (Tomasz)

Detection of minimal residual disease in acute lymphoblastic leukemia (cum laude)
Erasmus University Rotterdam (Dept. of Immunology), Rotterdam, 13 November 2002

F. Weerkamp (Floor)

Molecular regulation of early T-cell development in the thymus
Erasmus University Rotterdam (Dept. of Immunology), Rotterdam, 30 november 2005

N. Boeckx (Nancy)

Molecular and flow cytometric diagnostics for evaluation of therapy efficacy in myeloid leukemias
Erasmus University Rotterdam (Dept. of Immunology), Rotterdam, 22 maart 2006

Y. Sandberg (Yorick)

Basic and clinical aspects of the T-cell receptor in mature T-cell malignancies
Erasmus University Rotterdam (Dept. of Immunology), Rotterdam, 13 juni 2007

M.C. van Zelm (Menno)

B-cell development and primary antibody deficiencies (cum laude)
Erasmus University Rotterdam (Dept. of Immunology), Rotterdam, 20 juni 2007

K.Pike-Overzet (Karin)

Gene Therapy for RAG-deficient Severe Combined Immunodeficiency
Erasmus University Rotterdam (Dept. of Immunology), Rotterdam, 21 november 2007

T.C. Luis (Tiago)

Notch: Wnt interactions in hematopoiesis
Erasmus University Rotterdam (Dept. of Immunology), Rotterdam

N.S.D. Larmonie (Nicole)

Being in the wrong place at the wrong time? Unravelling the formation of TCR-associated translocations leading to T-ALL

Erasmus University Rotterdam (Dept. of Immunology), Rotterdam

(International) Awards

- Sept. 2001 : Botkin Award, St. Petersburg, Russia
Nov. 2002 : Leukaemia Research Fund, Annual Guest Lecture 2002, London, GB
Dec. 2002 : Katelyn Pasley Memorial Lecture (as Visiting Professor), University of Rochester Medical Center, Rochester, NY
Dec. 2006 : Medal "Friend of the Child Health Centre" of Children's Memorial Health Institute, Warsaw, Poland

Current Research Grant Support

1. Title : Transcription factors and their role in V(D)J recombination processes in normal and malignant T-cell differentiation.
Projectleaders : A.W. Langerak (PI) and J.J.M. van Dongen (PI)
Grant supplier : Dutch Cancer Society/Koningin Wilhelmina Fonds
Grant Application EMCR 002-27072.
2. Title : Identification of DNA double-strand break repair genes that are important for maintaining chromosomal stability and ionizing radiation resistance.
Projectleaders : D.C. van Gent (PI), M.Z. Zdzienicka, and J.J.M. van Dongen
Grant supplier : Dutch Cancer Society/Koningin Wilhelmina Fonds
Grant Application EMCR 002-27343.
3. Title : Search for new genetic defects in primary antibody deficiencies: approach via Affymetrix DNA-microarray analysis and in vitro function tests.
Projectleaders : R. de Groot and J.J.M. van Dongen (PI)
Grant supplier : Sophia Foundation for Medical Research (SSWO)
Grant Application 349 (17540564).
4. Title : Molecular diagnosis of leukemias and lymphomas through clinical genomics.
Projectleaders : F.J.T. Staal, J.J.M. van Dongen, and H.J.H.M. Claassen
Grant supplier : NWO-STIGON
Grant Application for start-up company DYNOMICS5.
5. Title : European Study Group on MRD detection in acute lymphoblastic leukemia (ESG-MRD-ALL).
Projectleader : J.J.M. van Dongen (PI)
Grant supplier : Leukaemia Research Fund (GB)
Grant Application for five European meetings 6.
6. Title : European LeukemiaNet: Strengthen and develop scientific and technological excellence in research and therapy of leukemia (CML, AML, ALL, CLL, MDS, MDS, CMPD) by integration in the leading national leukemia networks and their interdisciplinary partner groups in Europe.

- Projectleaders : R. Hehlmann (coordinator) and many co-applicants, o.a. J.J.M.van Dongen
- Grant supplier : European Commission, Directorate General XII Framework 6 Program (FP6) Network of Excellence (NOE) LSHC-CT-2004-5032167.
7. Title : MRD-ALL10 diagnostiek
- Projectleader : J.J.M. van Dongen
- Grant supplier : Nederlandse zorgverzekeraars via SKION8.
8. Title : Gene Therapy of Primary Immunodeficiencies
- Projectleaders : G. Wagemaker, F.J.T. Staal, J.J.M. van Dongen, R. de Groot
- Grant supplier : NWO Zon MW 431-00-0169.
9. Title : Unraveling of aberrant Ig/TCR recombination events in NBS patients for early diagnosis of hematological malignancies and improved patient care.
- Projectleader : K.H. Chrzanowska (CMHI, Warsaw, PL). Part of project by Immunology: A.W. Langerak and J.J.M. van Dongen
- Grant supplier : Ministry of Science and Higher Education (Poland)10.
10. Title : Novel diagnostics in "Common variable immunodeficiency" (CVID)
- Projectleader : M. van der Burg, J.J.M. van Dongen, P.M. van Hagen, N.G. Hartwig
- Grant supplier : M. van Hagen / Pharmaceut (Octopharma)11.
11. Title : Zorgvernieuwing voor primaire immunodeficiënties door snellere en doelmatigere diagnostiek.
- Projectleaders : J.J.M. van Dongen, M. van der Burg, N.G. Hartwig, R. de Groot, J. Wladimiroff, D. Halley
- Grant supplier : Zorgverzekeraars12.
12. Title : Can multi-color flowcytometric immunophenotyping replace PCR-based detection of minimal residual disease in childhood acute lymphoblastic leukemia?
- Projectleaders : V.H.J. van der Velden, R. Pieters, J.J.M. van Dongen
- Grant supplier : Dutch Cancer Society/Koningin Wilhelmina Fonds Grant application EMCR 2005-3428:13.
13. Title : Flow cytometry for fast and sensitive diagnosis and follow-up of haematological malignancies (EuroFlow).
- Projectleader : J.J.M. van Dongen
- Grant supplier : European Commission, Directorate General XII Framework 6 Program (FP6); Specific Targeted Research Project (STREP) LSHB-CT-2006-018708

Current Research Topics

Normal, malignant, and immunodeficient lymphoid differentiation.

International Collaboration

- Coordinator of BIOMED-2 Concerted Action (EU-DGXII grant: BMH4-CT98-3936): "PCR-based clonality studies for early diagnosis of lymphoproliferative disorders: technology development, international standardization and diagnostic evaluation" (1998-2001; 3.5 years): 47 laboratories in 7 European countries (NL, BE, ES, PT, GB, DE, FR)

- Co-coordinator and network leader of Netherlands/Belgium in Europe against Cancer (EAC) study (EU-DGV SANCO grant: S12.129294 (99 CYF2-016): "European coordinated implementation of a new molecular strategy for prevention of clinical relapse in leukemia via a training and quality control program" (1999-2002; 3 years): 25 laboratories in 11 European countries (FR, NL, BE, ES, PT, IT, DE, AT, GB, SE, and DK).
- Coordinator of MRD Task Force of International BFM Study Group (1999-up to now): 6 laboratories in 4 European countries (NL, DE, AT, IT).
- Coordinator of Study Group on pre-BMT studies in childhood ALL, supported by Leukaemia Research Fund (2000-2002; 3 years): 7 laboratories in 5 European countries (NL, DE, GB, DK, CZ).
- Coordinator of the European Study Group on MRD detection in ALL (ESG-MRD-ALL), supported by Leukaemia Research Fund (2001 – up to now): 32 laboratories in 17 European countries (NL, DE, UK, FR, IT, AT, CZ, BE, ES, DK, SE, CH, PT, FI).
- Chairman of EuroFlow Consortium "Flow cytometry for fast and sensitive diagnosis and follow-up of haematological malignancies" (EC grant: LSHB-CT-2006-018708): 10 institutes in 8 European countries (NL, ES, PT, DE, FR, UK, CZ, PL).

Name

Hubert P. Endtz, MD PhD

CV

Hubert Endtz received his medical degree from the University of Leiden (1981). He received postdoctoral training at Curacao (Royal Dutch Navy, Netherlands Antilles), Cairo (US Naval Medical Research Unit, Egypt), Paris (Institut Pasteur, France) and Edmonton (University of Alberta, Canada). He did a PhD thesis at the University of Leiden (1993). He joined the Department of Medical Microbiology & Infectious Diseases at Erasmus University Medical Center in Rotterdam in 1990, and was appointed as deputy chairman in 1995. His research focuses on (1) the pathogenesis of bacterial diarrhea and postinfectious complications, in particular *Campylobacter* infections and the Guillain-Barré syndrome and (2) the epidemiology of antimicrobial resistance and use.

Selected Publications

- Godschalk, PCR, Heikema AE, Gilbert M, Komagamine T, Ang CW, Glerum J, Brochu D, Li J, Yuki N, Jacobs BC, van Belkum A, Endtz HP. The crucial role of *Campylobacter jejuni* genes in antiganglioside antibody induction in Guillain Barré syndrome. *J Clin Invest* 2004;114:1659-1665
- van Belkum A, van Den Braak N, Godschalk P, Ang W, Jacobs B, Gilbert M, Wakarchuk W, Verbrugh H, Endtz H, 2001. A *Campylobacter jejuni* gene associated with immune-mediated neuropathy. *Nat Med* 7: 752-3.
- Gilbert M, Godschalk PCR, Karwaki MF, Ang CW, van Belkum A, Li J, Wakarchuk WW, Endtz HP. Evidence for acquisition of the lipooligosaccharide biosynthesis locus in *Campylobacter jejuni* GB11, a strain isolated from a patient with Guillain-Barré syndrome, by horizontal exchange. *Infect Imm* 2004; 72: 1162-1165.
- Filius PM, Gyssens IC, Kershof IM, Roovers PJE, Ott A, Vulto, Verbrugh HA, Endtz HP. Colonization and resistance dynamics of Gram-negative bacteria during and after hospitalization. *Antimicrob Agents Chemother* 2005;49:2879-2886.
- Endtz HP, van West J, Godschalk PCR, de Haan L, Halabi Y, van den Braak N, Kestýüs BI, Leyde E, Ott A, Verkooyen R, Price LJ, Woodward DL, Rodgers FG, Ang CW, van Koningsveld R, van Belkum A, Gerstenbluth I. Risk factors associated with *Campylobacter jejuni* infections in Curacao, Netherlands Antilles. *J Clin Microbiol* 2003; 41: 5588-5592.
- Choo-Smith LP, Maquelin K, van Vreeswijk T, Bruining HA, Puppels GJ, Thi NA, Kirschner C, Naumann D, Ami D, Villa AM, Orsini F, Doglia SM, Lamfarraj H, Sockalingum GD, Manfait M, Allouch P, Endtz HP, 2001. Investigating microbial (micro)colony heterogeneity by vibrational spectroscopy. *Appl Environ Microbiol* 67: 1461-9.
- van Belkum A, Goessens W, van der Schee C, Lemmens-de Toorn N, Vos MC, Cornelissen J, Lugtenburg E, de Marie S, Verbrugh HA, Lowenberg B, Endtz HP, 2001. Outbreaks of ciprofloxacin-resistant enterobacteriaceae containing multiple resistance-associated integrons in a hematology department. *Emerg Infect Dis* 7: 862-71
- van Belkum A, Goessens W, van der Schee C, Lemmens-de Toorn N, Vos MC, Cornelissen J, Lugtenburg E, de Marie S, Verbrugh HA, Lowenberg B, Endtz HP, 2001. Outbreaks of ciprofloxacin-resistant enterobacteriaceae containing multiple resistance-associated integrons in a hematology department. *Emerg Infect Dis* 7: 862-71
- Endtz HP, Ang CW, van Den Braak N, Duim B, Rigter A, Price LJ, Woodward DL, Rodgers FG, Johnson WM, Wagenaar JA, Jacobs BC, Verbrugh HA, van Belkum A, 2000. Molecular

characterization of *Campylobacter jejuni* from patients with Guillain-Barré and Miller Fisher syndromes. *J Clin Microbiol* 38: 2297-301.

- Endtz HP, Ruijs GJ, van Klingeren B, Jansen WH, van der Reyden T, Mouton RP, 1991. Quinolone resistance in campylobacter isolated from man and poultry following the introduction of fluoroquinolones in veterinary medicine. *J Antimicrob Chemother* 27: 199-208

PhD Students

- C.W. Ang, 2001: Molecular mimicry in the Guillain-Barré syndrome
- N. van den Braak, 2001: Glycopeptide resistant enterococci in the Netherlands
- K. Maquelin, 2002: Confocal RAMAN Microspectroscopy
- M.S.Ibelings, 2005: Nosocomial intensive care infections
- M.Filius, 2005: Antimicrobial use and resistance in hospitalized patients
- P.C.R. Godschalk, 2007: Genetics of *C.jejuni* and the pathogenesis of Guillain-Barré syndrome

Current Research Grant Support

Human Science Frontier program/EU

STW/NWO

MDL Stichting

Erasmus MC grant

Current Research Topics

1. the pathogenesis of bacterial diarrhea and postinfectious complications, in particular *Campylobacter* infections and the Guillain-Barré syndrome.
2. the epidemiology of antimicrobial resistance and use.

International Collaboration

Institute of Biological Sciences, National Research Council Canada

Dokkyo University School of Medicine, Japan

International Center for Diarrheal Disease Research, Bangladesh

Name

Ron A.M. Fouchier, Ph.D.

CV

Ron Fouchier received a PhD in Medicine from the University of Amsterdam in 1995, for his studies on molecular determinants of HIV-1 phenotype variability at the Department of Clinical Viro-immunology, Sanquin Research. He was a post-doctoral fellow at the Howard Hughes Medical Institute, University of Pennsylvania School of Medicine in Philadelphia, from 1995-1998, where he studied the function of the HIV-1 Vif protein, and nuclear transport of HIV-1 pre-integration complexes. He subsequently joined the Department of Virology at Erasmus MC to start a new group studying the molecular biology of respiratory viruses, in particular influenza A virus. Ron Fouchier is a member of the "Jonge Akademie" of the KNAW.

Selected Publications

- Influenza B virus in seals. A.D.M.E. Osterhaus, G.F. Rimmelzwaan, B.E.E. Martina, T.M. Bestebroer and R.A.M. Fouchier. *Science* 288:1051-1053 (2000).
- A newly discovered human pneumovirus associated with respiratory disease in young children. B.G. van den Hoogen, J.C. de Jong, J. Groen, R. de Groot, R.A.M. Fouchier and A.D.M.E. Osterhaus. *Nature Medicine* 7:719-724 (2001).
- Aetiology: Koch's postulates fulfilled for SARS virus. R.A.M. Fouchier, T. Kuiken, M. Schutten, G. Van Amerongen, G.J.J. Van Doornum, B.G. Van Den Hoogen, M. Peiris, W. Lim, K. Stohr and A.D.M.E. Osterhaus. *Nature* 423:240 (2003).
- Avian influenza A (H7N7) virus associated with human conjunctivitis and a fatal case of acute respiratory distress syndrome. R.A.M. Fouchier, P.M. Schneeberger, F.W. Rozendaal, J.M. Broekman, S.A.G. Kemink, V. Munster, T. Kuiken, G.F. Rimmelzwaan, M. Schutten, G.J.J. van Doornum, G. Koch, A. Bosman, M. Koopmans and A.D.M.E. Osterhaus. *P.N.A.S.* 101:1356-61 (2004).
- Pegylated interferon- α protects type 1 pneumocytes against SARS coronavirus infection in macaques. B.L. Haagmans, T. Kuiken, B.E.E. Martina, R.A.M. Fouchier, G.F. Rimmelzwaan, G. van Amerongen, D. van Riel, T. de Jong, S. Itamura, K.H. Chan, M. Tashiro and A.D.M.E. Osterhaus. *Nature Medicine* 10:290-4 (2004)
- A previously undescribed coronavirus associated with respiratory disease in humans. R.A.M. Fouchier, N.G. Hartwig, T.M. Bestebroer, B. Niemeyer, J.C. de Jong, J.H. Simon, and A.D.M.E. Osterhaus. *P.N.A.S.* 101:6212-6 (2004).
- Mapping the antigenic and genetic evolution of influenza virus. D.J. Smith, A.S. Lapedes, J.C. de Jong, T.M. Bestebroer, G.F. Rimmelzwaan, A.D.M.E. Osterhaus and R.A.M. Fouchier. *Science* 305:371-376 (2004).
- Avian H5N1 influenza in cats. T. Kuiken, G.F. Rimmelzwaan, D. van Riel, G. van Amerongen, M. Baars, R.A.M. Fouchier, A.D.M.E. Osterhaus. *Science*. 306:241. (2004).
- Global patterns of influenza A virus in wild birds. B. Olsen, V.J. Munster, A. Wallensten, J. Waldenström, A.D.M.E. Osterhaus, R.A.M. Fouchier. *Science*, 312:384-8 (2006).
- Multiple introductions of H5N1 in Nigeria. M.F. Ducatez, C.M. Ollinger, A.A. Owoade, S. De Landtsheer, W. Ammerlaan, H.G.M. Niesters, A.D.M.E. Osterhaus, R.A.M. Fouchier and C.P. Muller. *Nature* 442:37 (2006).

PhD Students

- B.G. van den Hoogen. Human metapneumovirus; discovery, characterisation and associated disease (February 2004)
- E. de Wit. Molecular determinants of influenza A virus replication and pathogenesis (December 2006)
- V.J. Munster. Ecology, Evolution and pathogenesis of avian influenza viruses (December 2006)
- S. Herfst. Human metapneumovirus (in progress)
- M. de Graag. Human metapneumovirus (in progress)
- J. Keawcharoen. Influenza A virus (in progress)

(International) Awards

- Fellow of the Royal Dutch Academy of Arts and Sciences (K.N.A.W.) ('00-'05)
- Recipient of the James H. Nakano citation for outstanding scientific paper in 2003 (Science 300:1394-9, 2003) awarded by NCID/CDC, USA (this paper was also nominated for the Charles C. Shepard Science Award).
- Recipient of the 2006 Heine-Medin award of the European Society for Clinical Virology.

Current Research Grant Support

- Erasmus MC
- The Dutch Ministry of Agriculture (L.N.V.)
- MedImmune Inc./ViroNovative B.V.
- ZonMw/WOTRO Research Centre Program
- EU framework VI program RiviGene
- EU framework VI program NewFluBird
- NWO-ALW International Polar Year program Birdhealth
- Fonds Economische Structuurversterking, NL
- National Institutes of Health, USA

Current Research Topics

As a KNAW fellow, Fouchier started studies on influenza virus zoonoses and pathogenicity. Recent achievements of his team include the identification and characterization of several "new" viruses; the human metapneumovirus (hMPV), a human coronavirus (hCoV-NL), the SARS coronavirus (SARS-CoV), and a new influenza A virus subtype (H16). Currently, his research is focused on the evolution and molecular biology of respiratory viruses in humans and animals, with special emphasis on influenza virus zoonoses and pandemics, and hMPV.

International Collaboration

WHO Working Group on Influenza Research at the Human/Animal Interface

WHO global vaccine strain selection program

OIE/FAO OFFLU network of expertise on avian influenza

Dr. D. Smith, Zoology, Cambridge University, UK

Dr. A. Lapedes, Theoretical Biology, Los Alamos National Laboratory, USA

Dr. T. Jones, Dept. Tecnologia, Universidad de Pompeu Fabra, Barcelona, Spain

Dr. P. Palese, Mount Sinai School of Medicine, NY, USA

Dr. D. Perez, University of Maryland, USA

Dr. S. Salzberg, TIGR, USA

Dr. D. Suarez & Dr. D. Swayne, Southeast Poultry Research Labs, Atlanta, USA

Dr. E. Holmes & Dr. B. Grenfell, Penn State University, USA
Dr. I. Brown & Dr. J. Banks, Veterinary Laboratory Agencies, Weybridge, UK
Dr. T. Harder, Friedrich-Loeffler-Institut, Insel Riems, Germany
Dr. B. Olsen, Ottenby Bird Observatory, Kalmar, Sweden
Numerous individual ornithologists and ornithology organisations

Name

Teun van Gelder, MD, PhD

CV

Dr. T. van Gelder, MD PhD (Teun) received his medical degree from the Erasmus University in Rotterdam (1987) and subsequently trained as an internist in the Erasmus Medical Center in Rotterdam. He then further specialized in nephrology, and did a PhD thesis on the use of anti-interleukin-2 monoclonal antibodies in clinical kidney and heart transplantation.

In 1998 and 1999 he spent a post-doctoral fellowship in Transplantation Immunology at Stanford University in the US. After returning to the Netherlands he also obtained a full certification as an internist-clinical pharmacologist.

Since 2002 he is heading the clinical pharmacology unit of the Hospital Pharmacy at the Erasmus MC. In 1998 he was appointed associate professor of

Clinical Pharmacology. He has positions in both the department of internal medicine, and in the hospital pharmacy.

Dr van Gelder is involved in studies of immunosuppressive drugs in solid organ transplantation. His research focuses on therapeutic drug monitoring, pharmacokinetics and pharmacogenetics.

Selected Publications

1. Burlingham WJ, Grailer AP, Heisey DM, Claas FHJ, Norman D, Mohanakumar T, Brennan DC, Fijter de H, Van Gelder T, Pirsch JD, Sollinger HW, Bean MA. The effect of tolerance to noninherited maternal HLA antigens on the survival of renal transplants from sibling donors. *N Engl J Med* 1998;339:1657-1664.
2. Van Gelder T, Hilbrands LB, Vanrenterghem Y, Weimar W, De Fijter JW, Squifflet JP, Hene RJ, Verpooten GA, Navarro MT, Hale MD, Nicholls AJ. A randomized double-blind, multicenter plasma concentration controlled study of the safety and efficacy of oral mycophenolate mofetil for the prevention of acute rejection after kidney transplantation. *Transplantation* 1999;68:261-266.
3. Van Gelder T, Klupp J, Barten MB, Christians U, Morris RE. Comparison of the effects of tacrolimus and cyclosporine on the pharmacokinetics of mycophenolic acid. *Ther Drug Monitor* 2001;23:119-128.
4. Smak Gregoor PJH, Sévaux RGL de, Ligtenberg G, Hoitsma AJ, Hené RJ, Weimar W, Hilbrands LB, Van Gelder T. Withdrawal of cyclosporine or prednisone six months after kidney transplantation in patients on triple drug therapy: a randomized, prospective, multicenter study. *J Am Soc Nephrol* 2002; 13: 1365-1373
5. Barten MJ, Van Gelder T, Gummert JF, Boeke K, Shorthouse R, Billingham ME, Morris RE. Pharmacodynamics of mycophenolate mofetil after heart transplantation: New mechanisms of action and correlations with histologic severity of graft rejection. *Am J Transpl* 2002;2:719-732.
6. Hesselink DA, Van Schaik RHN, Van der Heiden IP, Van der Werf M, Smak Gregoor PJH, Lindemans J, Weimar W, Van Gelder T. Genetic polymorphisms of the CYP3A4, CYP3A5 and MDR-1 genes and pharmacokinetics of the calcineurin inhibitors cyclosporine and tacrolimus. *Clin Pharm Ther* 2003;74:245-254.
7. Hesselink DA, Van Gelder T, Van Schaik RHN, Balk AHMM, Van der Heiden IP, Van Dam T, Van der Werf M, Weimar W, Mathot RAA. Population pharmacokinetics of cyclosporine in kidney and heart transplant recipients and the influence of ethnicity and genetic polymorphisms in the MDR-1, CYP3A4, and CYP3A5 genes. *Clin Pharmacol Ther* 2004;76:545-556.
8. Hesselink DA, Van Hest RM, Mathot RAA, Bonthuis F, Weimar W, De Bruin RWF, Van RAA, Van Gelder T. Cyclosporine interacts with mycophenolate mofetil by inhibiting the multidrug resistance-associated protein 2. *Am J Transpl* 2005;5:987-994.

9. Hesselink DA, Van Gelder T. Genetic and non-genetic determinants of between-patient variability in the pharmacokinetics of mycophenolic acid. Clin Pharm Ther 2005;78:317-321.
10. Van Hest RM, Mathôt RAA, Pescovitz MD, Gordon R, Mamelok RD, Van Gelder T. Explaining variability in mycophenolic acid (MPA) exposure to optimize mycophenolate mofetil dosing: a population pharmacokinetic meta-analysis of MPA in renal transplant recipients. J Am Soc Nephrol 2006;17:871-880.

PhD Students

Dr. Peter Smak Gregoor, internist-nephrologist
"Mycophenolate mofetil in kidney transplantation."
May 23, 2001 (co-promotor)

Drs. Dennis A. Hesselink, MD
"Pharmacokinetic and pharmacogenetic studies in solid organ transplant recipients treated with calcineurin inhibitors."
expected : May 2007 (co-promotor)

Drs. Reinier van Hest, PharmD
"Explaining within- and between-patient variability in the pharmacokinetics of mycophenolate mofetil in renal transplant patients."
expected : January 24, 2007 (co-promotor)

Drs. Madelon van Agteren, internist-nephrologist
"Immunosuppressive therapy after renal transplantation : the impact of polymorphisms in genes involved in PK/PD."
expected : 2008 (co-promotor)

Drs. Heleen van der Sijs, hospital pharmacist
"Implementation of electronic drug prescription and drug safety."
expected : 2008 (co-promotor)

Drs. Ferdi Sombogaard, pharmacist
"How to best monitor mycophenolate mofetil therapy: MPA concentrations or IMPDH activity?"
expected : 2009 (co-promotor)

Drs. Monique Bijl, pharmacist
"Pharmacological and clinical implications of CYP2D6 polymorphism in the Rotterdam Study."
expected : 2009 (co-promotor)

Drs. Brenda de Winter, pharmacist
"Population pharmacokinetic studies in mycophenolate mofetil treated renal transplant patients."
expected : 2009 (co-promotor)

(International) Awards

- 1994 Nephrology Award (Dutch Society for Nephrology)
1996 Jon J. van Rood Award (Dutch Transplantation Society)
1997 Young Investigator Award (European Society Heart Lung Transplantation)
1998 International Young Investigator Award (American Society Transplant Physicians)
2000 International Young Investigator Award (American Society of Transplantation)

2005 Outstanding Speaker Award (American Association for Clinical Chemistry)

Current Research Grant Support

Current research projects are supported by Roche Pharmaceuticals, NUTS-OHRA, Revolving Fund, JANIVO Foundation.

Current Research Topics

Immunosuppressive drug therapy, therapeutic drug monitoring, pharmacokinetics, pharmacogenetics, pharmacodynamics, medication safety

International Collaboration

Strong collaborations exist with:

Department of Clinical Chemistry, Georg August University - Göttingen, Germany (professor Michael Oellerich)

Analytical Unit, St George's Medical School, London, UK (professor David Holt)

Renal Transplant Unit, University Charite, Berlin, Germany (Dr Klemens Budde)

Roche Center for Medical Genomics, Basel, Switzerland (professor Klaus Lindpaintner)

Name

Luc Ben Stefan Gelinck

CV

Born 30 april 1970, Nijmegen.

1988 - 1993 Medicine, University Leiden; Doctoral in 1993

1993 - 1996 Clerkships Medicine, University Leiden; MD in 1996

Selected publications

- Visser H, Gelinck LBS, Hazes JMW, Breedveld FC. Diagnostic significance of Rheumatoid Factor testing in Rheumatoid Arthritis. *Arthritis & Rheumatism*, Vol. 36: S100; 1993. (Abstract)
- Visser H, Gelinck LBS, Kampfraath AH, Hazes JMW, Breedveld FC. Diagnostic significance of Rheumatoid Factor testing in Rheumatoid Arthritis. *Annals of the Rheumatic Diseases*, Vol. 55: 157-161; 1996.
- Gelinck LBS, van Steenberghe JE, van Dissel JT. 'Severe acute respiratory syndrome' (SARS): epidemiologie, kliniek, diagnostiek en preventie. *Nederlands Tijdschrift voor Geneeskunde* 2003; 147 (30): 1449-54.
- Gelinck LBS, Spaan WJM, van den Broek PJ. SARS (severe acute respiratory syndrome) – voorkómen kan beter. *Tijdschrift voor Hygiëne en Infectiepreventie* 2003; 22 (5): 132-135.
- Gelinck LBS, Beersma MFC, Visser LG, Van Dissel JT. West Nile virus in The Netherlands. Letter. *British Medical Journal (Monthly Dutch edition)* 2003; 18 (9): 66.
- Verduyn Lunel FM, Voss A, Kuijper EJ, Gelinck LBS, Hoogerbrugge PM, Liem KL, Kullberg BJ, Verweij PE. Detection of the Candida antigen mannan in cerebrospinal fluid specimens from patients suspected of having Candida meningitis. *J Clin Microbiol* 2004 Feb;42(2):867-70.
- Van Dam AP, Pruijm MT, Harinck BI, Gelinck LBS, Kuijper EJ. Pneumonia involving *Aspergillus* and *Rhizopus* spp. after a near-drowning incident with subsequent *Nocardia cyriacigeorgici* and *N. farcinica* coinfection as a late complication. *Eur J Clin Microbiol Infect Dis* 2005; 24: 61-4.
- Gelinck LBS, Claas EC, Kroon FP. The risk of adefovir monotherapy in human immunodeficiency virus (HIV) and hepatitis B virus (HBV) co-infected patients. *J Hepatol*. 2005 Aug;43(2):360-1.
- Brüggemann RJM, Kauffmann RH, Gelinck LBS, Wolterbeek R, Le Bruin PPH, Touw DJ. Switching A Twice-daily Regime of 200 mg Nevirapine to a Once Daily Regime of 400mg, Has no Additional Hepatotoxic Effect in the Therapy of HIV-infected Patients. Abstract no. 718: ICAAC2007 Chicago.
- De Boer MG, Bruijnesteijn van Coppenraet LE, Gaasbeek A, Berger SP, Gelinck LBS, van Houwelingen HC, van den Broek P, Kuijper EJ, Kroon FP, Vandenbroucke JP. An outbreak of *Pneumocystis jiroveci* pneumonia with 1 predominant genotype among renal transplant recipients: interhuman transmission or a common environmental source? *Clin Infect Dis*. 2007; 44: 1143-9.
- Van der Ploeg V, Gelinck LBS, Jonkers IJAM, Mourer JS, Van Dam AP. Backpain and BLNAR: recrudescence of vertebral osteomyelitis due to beta-lactamase low-level ampicillin-resistant *Haemophilus influenzae* after prolonged amoxicillin treatment. *Submitted*.
- Lopriore E, Rozendaal L, Bökenkamp R, Boelen CCA, Gelinck LBS, Walther FJ. Dizygotic twins with dilated cardiomyopathy and complete heart block born to an HIV-infected mother treated with highly active antiretroviral therapy. *AIDS*. 2007 Nov 30;21(18):2564-5.

- Gelinck LBS, Van der Bijl AE, Beyer WEP, Visser LG, T.W.J. Huizinga TWJ, Van Hogezaand RA, Rimmelzwaan GF, Kroon FP. The effect of anti-tumor necrosis factor alpha treatment on the antibody response to influenza vaccination. *Ann Rheum Dis.* 2007 Oct 26; [Epub ahead of print].
- Gelinck LBS, Van der Bijl AE, Visser LG, Huizinga TWJ, Van Hogezaand RA, Rijkers GT, Kroon FP. Synergistic immunosuppressive effect of anti-TNF combined with methotrexate on antibody response to the 23 valent pneumococcal polysaccharide vaccine. *Submitted.*
- Gelinck LBS, Teng YKO, Rimmelzwaan GF, Van den Bemt BJF, Kroon FP, Van Laar JM. Poor serological responses upon influenza vaccination in patients with rheumatoid arthritis treated with rituximab. *Ann Rheum Dis.* 2007; 66: 1402-3.
- Gelinck LBS, Visser LG, Rimmelzwaan GF, Kroon FP. Dose sparing intracutaneous influenza vaccination in HIV infected patients is immunogenic and well tolerated. Abstract 475. CROI 2007 Los Angeles.

Name

Monique M. Gerrits

CV

Monique Gerrits studied Molecular Biology and Medical Microbiology at the Hogeschool of Utrecht, the Netherlands (1992-1996). After receiving her degree she worked at the Department of Medical Microbiology of the Vrije Universiteit, Amsterdam. In 2001, she moved to the Department of Gastroenterology and Hepatology of the Erasmus MC in Rotterdam, where she performed her Ph.D study (2002-2004) on Molecular mechanisms of antibiotic resistance in *Helicobacter pylori*. During her Ph.D she visited the Department of Pharmacology and Gastroenterology of the São Francisco University in Bragança Paulista, Brazil (2003). After her Ph.D study she continued her research at the Department of Gastroenterology and Hepatology of the Erasmus MC in Rotterdam, focussing on carcinogenesis of the colon. In September 2006, she became staff member at the Department of Gastroenterology and Hepatology of the Erasmus MC in Rotterdam, the Netherlands.

Selected Publications

1. Godoy, AP, Reis, F, Ferraz, L, Gerrits, MM, Mendonca, S, Kusters, JG, Ottoboni, L, Ribeiro, ML, Pedrazzoli, J, Jr. Differentially expressed genes in response to amoxicillin in *Helicobacter pylori* analyzed by RNA arbitrarily primed PCR. FEMS Immunol Med Microbiol. Accepted, Nov 27, 2006.
2. Gerrits, MM, van Vliet, AH, Kuipers, EJ, Kusters, JG. Helicobacter pylori and antimicrobial resistance: molecular mechanisms and clinical implications. Lancet Infect Dis 2006;6:699-709.
3. Gerrits, MM, Godoy, AP, Kuipers, EJ, Ribeiro, ML, Stoof, J, Mendonca, S, van Vliet, AH, Pedrazzoli, J, Jr., Kusters, JG. Multiple mutations in or adjacent to the conserved penicillin-binding protein motifs of the penicillin-binding protein 1A confer amoxicillin resistance to *Helicobacter pylori*. Helicobacter 2006;11:181-7.
4. Glocker, E, Berning, M, Gerrits, MM, Kusters, JG, Kist, M. Real-time PCR screening for 16S rRNA mutations associated with resistance to tetracycline in *Helicobacter pylori*. Antimicrob Agents Chemother 2005;49:3166-70.
5. Gerrits, MM, van der Wouden, EJ, Bax, DA, van Zwet, AA, van Vliet, AH, de Jong, A, Kusters, JG, Thijs, JC, Kuipers, EJ. Role of the rdxA and frxA genes in oxygen-dependent metronidazole resistance of *Helicobacter pylori*. J Med Microbiol 2004;53:1123-8.
6. Ribeiro, ML, Gerrits, MM, Benvengo, YH, Berning, M, Godoy, AP, Kuipers, EJ, Mendonca, S, van Vliet, AH, Pedrazzoli, J, Jr., Kusters, JG. Detection of high-level tetracycline resistance in clinical isolates of *Helicobacter pylori* using PCR-RFLP. FEMS Immunol Med Microbiol 2004;40:57-61.
7. Gerrits, MM, Berning, M, Van Vliet, AH, Kuipers, EJ, Kusters, JG. Effects of 16S rRNA gene mutations on tetracycline resistance in *Helicobacter pylori*. Antimicrob Agents Chemother 2003;47:2984-6.
8. Gerrits, MM, de Zoete, MR, Arents, NL, Kuipers, EJ, Kusters, JG. 16S rRNA mutation-mediated tetracycline resistance in *Helicobacter pylori*. Antimicrob Agents Chemother 2002;46:2996-3000.
9. Gerrits, MM, Schuijffel, D, van Zwet, AA, Kuipers, EJ, Vandenbroucke-Grauls, CM, Kusters, JG. Alterations in penicillin-binding protein 1A confer resistance to beta-lactam antibiotics in *Helicobacter pylori*. Antimicrob Agents Chemother 2002;46:2229-33.
10. Kuipers, EJ, Israel, DA, Kusters, JG, Gerrits, MM, Weel, J, van Der Ende, A, van Der Hulst, RW, Wirth, HP, Hook-Nikanne, J, Thompson, SA, Blaser, MJ. Quasispecies development

of *Helicobacter pylori* observed in paired isolates obtained years apart from the same host. *J Infect Dis* 2000;181:273-82.

PhD Students

Min Chen (defence second half 2008)

(International) Awards

Winner Young Scientists Award, best poster presentation, session genetics, 5th International workshop on pathogenesis and host response in *Helicobacter* infections, Helsingør, Denmark, 2002.

Best oral presentation, session drug resistance and novel treatments, 17th International workshop of the European *Helicobacter* study group, Vienna, Austria, 2004.

Current Research Grant Support

Research grant received from Erasmus MC Section Doelmatigheid & Zorg 2006. Applicants: M.M. Gerrits, J.G. Kusters, P. Siersema, C.J. van der Woude, E.W. Steyerberg, H. van Dekken, E.J. Kuipers

Current Research Topics

Detection of prognostic parameters in colon epithelium that can predict if malignancy will develop. Screening of high-risk patients (e.g. history of polyps or inflammatory bowel disease, family history of colorectal cancer) using biomarker-based flowcytometry.

Characterization of pathways that initiate and/or maintain colorectal cancer-related neoplastic progression.

Antibiotic resistance in *Helicobacter pylori*.

International Collaboration

Brazil: Prof. J. Pedrazzoli and Prof. M. Ribeiro (Braganca Paulista) on characterization of molecular mechanisms of antibiotic resistance in *H. pylori*.

Germany: Prof. M. Kist (Freiburg) on molecular detection of antibiotic resistance in *H. pylori*.

United States: Dr. S. Phadnis (Milwaukee) on detection of penicillin-binding protein.

Canada: Dr. G. Cooper-Lesins and Dr. S. Veldhuyzen van Zanten (Halifax) on detection of antibiotic resistance in *H. pylori*.

Name

W. Goessens

CV

Studied biology at the State University of Utrecht from 1974-1980. Started in may 1980 as a PhD student at the Dept. of Clinical Microbiology and Antimicrobial Therapy of the Erasmus University of Rotterdam. This experimental phase was finished in December 1985 followed by a PhD degree in 1986. Switched in januari 1986 to a post-doc position at the Biochemistry Department of the State University of Leiden. During this post-doc period a short-term fellowship was followed at the Julius-Maximilian University of Würzburg, at the dept. of Prof. Roland Benz working on conductivity changes of black lipids upon exposure to MS2 lysis protein.

Since 1988 senior staff member at the Dept. of Clinical Microbiology and Infectious Diseases of the ErasmusMC Rotterdam. Since 2001 registered as Medical Microbiologist by Stichting Medisch Biologisch Wetenschappelijk Onderzoek.

Since 2000 active member of the Dutch Committee on guidelines for susceptibility testing.

Selected Publications

In-vitro activity of Trovafloxacin against *Bacteroides fragilis* in mixed culture with either *Escherichia coli* or a vancomycin resistant strain of *Enterococcus faecium* using an anaerobic time kill technique.

Lorna E.T. Stearne, Clarissa Kooi, Wil H.F. Goessens, Irma A.J.M. Bakker-Woudenberg and Inge C. Gyssens.

Antimicrobial Agents and Chemotherapy, 2001, 45:243-251.

In-vivo efficacy of Trovafloxacin against *Bacteroides fragilis* in mixed infection with either *Escherichia coli* or a Vancomycin-resistant strain of *Enterococcus faecium* in an established abscess murine model.

Lorna E.T. Stearne, Inge C. Gyssens,, Wil H.F. Goessens, Johan W. Mouton, Wim J.G. Oyen, Jos van der Meer and Henri A. Verbrugh.

Antimicrobial Agents and Chemotherapy, 2001, 45: 1394-1401.

Rapid emergence of ciprofloxacin-resistant Enterobacteriaceae containing multiple gentamicin resistance-associated integrons in a Dutch Hospital.

A. van Belkum, W.H.F. Goessens, C. van der Schee, N. Lemmens-den Toom, M.C. Vos, J. Cornelissen, E. Lugtenburg, S. de Marie, H. Verbrugh, B. Löwenberg and H.P. Endtz.

Emerging Infectious Diseases, 2001, 7: 862-871.

Phylogenetic background and virulence profiles of fluoroquinolone-resistant clinical *Escherichia coli* isolates from the Netherlands.

James R. Johnson, Cindy van der Schee, Michael A. Kuskowski, Wil Goessens and Alex van Belkum.

Journal of Infectious Diseases 2002, 186: 1852-1856

Patterns of resistance associated with integrons, the extended-spectrum β -lactamase SHV-5 gene, and a multidrug efflux pump of *Klebsiella pneumoniae* causing a nosocomial outbreak.

P. Gruteke, W.H.F. Goessens, J. van Gils, Paul Peerbooms, N. Lemmens-den Toom, M. van Santen-Verheuveel, A. van Belkum and H.A. Verbrugh.

Journal of Clinical Microbiology, 2003, 41: 1161-1166.

Comparative study of the effects of ceftizoxime, piperacillin, and piperacillin/tazobactam concentrations on antibacterial activity and selection of antibiotic-resistant mutants of *Enterobacter cloacae* and *Bacteroides fragilis* In vitro and In vivo in mixed-infection abscesses.

L. E.T. Stearne, D. van Boxtel, N. Lemmens, W.H.F. Goessens, J.W. Mouton and I.C. Gyssens. Antimicrobial Agents and Chemotherapy, 2004, 48:1688-1698.

Effect of treatment duration on Pharmacokinetic/pharmacodynamic indices correlating with therapeutic efficacy of ceftazidime in experimental *Klebsiella pneumoniae* lung infection.

I.A.J.M. Bakker-Woudenberg, M.T. ten Kate, W.H.F. Goessens and J.W. Mouton Antimicrobial agents and Chemotherapy, 2006, 50:2929-2925

Role of ceftazidime dose regimen on the selection of resistant *Enterobacter cloacae* in the intestinal flora of rats treated for an experimental pulmonary infection

W.H.F. Goessens, J.W. Mouton, M.T. ten Kate, S. Voermans, A.J. Bijl, J. Laurijssens, A. Ott and A.J.M. Bakker-Woudenberg

Journal of Antimicrobial Chemotherapy, 2007, 59:507-516

PhD Students

Juliette Severin: Inventarisation and characterization of multi-resistant *E. coli* and *Klebsiella pneumoniae* in the community and hospital population of Surabaya (Indonesia)

(International) Awards

Astra-Zeneca/ESCMID award. Unrestricted research grant 2005 for research in the field of antibiotic resistance awarded to I.A.J.M. Bakker-Woudenberg, W.H.F. Goessens and J.W. Mouton. Emergence of beta-lactam resistance in gram-negative bacteria during therapy: factors important to the emergence of resistance, mechanisms of resistance and prevention

Current Research Grant Support

Pharmaceutical industry

Current Research Topics

- Determination and characterization of factors involved in multi-resistance of *K. pneumoniae*
- Influence of Pharmaco-kinetics and dynamics on in-vivo resistance selection of gram-negative rods
- Characterization of the bactericidal effect of β -lactams on *Staphylococcus aureus* isolates

Name

Prof.dr R. de Groot

CV

Ronald de Groot (1948) studied medicine in Rotterdam (MD, 1975), followed by a residency in Gynecology/Obstetrics and Surgery as a preparation for a 2½ year period as Senior Medical Officer in Zonkwa Hospital, Nigeria. He subsequently did his pediatric training in Rotterdam (1979-1983), became chief resident (1983-1985) followed by a research fellowship (1985-1988) in pediatric infectious diseases in the University of Washington, Seattle, USA. In 1988 he returned to the Erasmus University in Rotterdam and became in 1998 head of the training program and Professor in Pediatric Infectious Diseases and Immunology. On May 1st, 2005 he was nominated as head of the Department of Paediatrics of the University Medical Centre Nijmegen.

His research activities cover several themes including the study of respiratory tract infections, the molecular pathogenesis of infections by *S. pneumoniae*, *Neisseria meningitidis* and HIV and clinical and translational research in children with immunodeficiencies.

Selected Publications

- Menges T., Hermans P.W.M., Little S.G., Welters I., Langefeld T., Böning O., Engel J., Sluijter M., de Groot R., Hempelmann G. The plasminogen-activator inhibitor-1 4G/5G promoter polymorphism and prognosis of severely injured patients. *Lancet* 2001;357:1096-1097.
- V.d. Hoogen B.G., de Jong J.C., Groen J., Kuiken T., de Groot R., Fouchier R.A.M., Osterhaus A.D.M.E. A newly discovered human pneumovirus isolated from young children with respiratory tract disease. *Nature Med.* 2001;7:6:1-6.
- Van Rossum A.M.C., Scherpbier H.J. van Lochem E.G., Pakker N.G., Slieker W.A.T., Wolthers K.C., Roos M.T.L., Kuijpers J.H.S.A.M., Hooijkaas H., Hartwig N.G., Geelen S.P.M., Wolfs T.F.W., Lange J.M.A., Miedema F., de Groot R., for the Dutch study group for children with HIV infections. Therapeutic immune reconstitution in HIV-1 infected children is independent of their age and pretreatment immune status. *AIDS* 2001;15:2267-75.
- Van Rossum A.M.C., Fraaij P.L.A., de Groot R. Efficacy of highly active antiretroviral therapy in HIV-1 infected children. *Lancet Infect. Dis.* 2002;2:93-102.
- Noordzij J.G., Verkaik N.S., van Veelen L.R., de Bruin-Versteeg S., Vossen J.M.J.J., Weemaes C.M.R., de Groot R., Zdzienicka M.Z., van Gent D.C., van Dongen J.J.M. Radiosensitive SCID patients with Artemis gene mutations show a complete B-cell differentiation arrest at the pre-BCR checkpoint in bone marrow. *Blood* 2003;101:1446-52
- Veenhoven R., Bogaert D., Uiterwaal C., Brouwer C., Kiezebrink H., Bruin J., Hermans P.W.M., de Groot R., Kuis W., Rijkers G., Schilder A., Sanders L. Effect of conjugate pneumococcal vaccine followed by polysaccharide pneumococcal vaccine on recurrent acute otitis media: a randomised study. *Lancet* 2003; 361:2189-95
- Emonts, M., de Groot R., Hermans W.P.M. Host genetic determinants of *Neisseria meningitidis* infections". *Lancet Infect. Dis.* 2003;3:565-77
- Bogaert D., van Belkum A., Sluijter M., Luijendijk A., de Groot R., Rümke H.C., Verbrugh H.A., Hermans P.W.M. Colonisation by *Streptococcus pneumoniae* and *Staphylococcus aureus* in healthy children. *Lancet* 2004;363:1871-2
- Bogaert D., de Groot R., Hermans P.W.M. *Streptococcus pneumoniae* colonisation: the key to pneumococcal disease. *Lancet Infect. Dis.* 2004; 4:144-54
- Burger D.M., Verweel G., Rakhmanina N., Verwey-van Wissen C.P.W.G.M., La Porte C.J.L., Bergshoeff A.S., Lyall H., Hartwig N.G., Green H., Soldin S., Gibb D.M., de Groot R. Age-

dependent pharmacokinetics of lamivudine in HIV-infected children. Clin. Pharmacol. Ther. 2007;81(4):517-20.

PhD Students

- Dr. M.C.J. Kneyber. Ph.D. thesis entitled "Respiratory syncytial virus infections in infancy: epidemiological and clinical aspects". February 16, 2000. Promotor: R. de Groot. Copromotor: H.A. Moll.
- Dr. K. Overweg. Ph.D. thesis entitled "Streptococcus pneumoniae: molecular epidemiological aspects and the identification of virulence factors". September 8, 2000. Promotor: R. de Groot. Copromotor: P.W.M. Hermans.
- Dr. E.D. de Kleijn. Ph.D. thesis entitled "Meningococcal infections: enhanced understanding of pathogenesis leading to novel approaches in therapy and prevention". January 10, 2001. Promotor: R. de Groot. Copromotor: J.A. Hazelzet.
- Dr. A.M.C. van Rossum. Ph.D. thesis (cum laude) entitled "Challenges in the treatment of HIV-1 infected children with highly active antiretroviral therapy". April 3, 2002. Promotor: R. de Groot. Dr. van Rossum received the Research Award of the Erasmus University Rotterdam and the young investigator award of the Paediatric Association of the Netherlands (2002).
- Dr. J. Noordzij. Ph.D. thesis entitled: "Molecular immunology of primary immunodeficiencies". June 19, 2002 Promotores: J.J.M. van Dongen and R. de Groot.
- Dr. S.E. Bleeker. Ph.D. thesis entitled: "Children with fever without apparent source: diagnosis and dilemmas". September 11, 2002 Promotores: R. de Groot and D.E. Grobbee. Copromotores: H.A. Moll and K.G.M. Moons.
- Dr. E. Rietveld. Ph.D. thesis entitled: "Severe respiratory syncytial virus (RSV) infections in young children: risk assesment and prevention". December 10, 2003. Promotor: R. de Groot. Copromotores: Dr. H.A. Moll and Dr. E.W. Steyerberg.
- Dr. A.S. Bergshoeff. Ph.D. thesis entitled: "Exploring the clinical pharmacology of antiretroviral agents in HIV-1 infected children". April 26, 2004. Promotores: R. de Groot and Y.A. Hekster. Copromotor Dr. D.M. Burger. (University Medical Center Nijmegen).
- Dr. D. Bogaert. Ph.D. thesis (cum laude) entitled: "Host-pathogen interactions during Streptococcus pneumoniae colonization and infection". June 2, 2004. Promotor: R. de Groot. Copromotor P.W.M. Hermans.
- Dr. C.L. Vermont. Ph.D. thesis entitled "Laboratory predictors of meningococcal diseases and vaccination in children". September 1, 2004. Promotor: R. de Groot. Copromotor: G.P.J.M. van Dobbelsteen (RIVM).
- Dr. P. L.A. Fraaij. Ph.D. thesis entitled "Clinical care and management of HIV-1 infected children". January 26, 2005. Promotor: R. de Groot.
- Dr. M.C. van Zelm (cum laude). Ph.D thesis entitled "B-cell development and primary antibody deficiencies". June 20, 2007. Promotores: J.J.M. van Dongen and R. de Groot. Compromotor: M. van der Burg. ErasmusMC Rotterdam
- Dr. A.A.E.M. van Alfen-van der Velden. Ph.D.thesis entitled "Changes in cerebral oxygenation and hemodynamics during clinical interventions in newborn infants". December 13, 2007. Promotor: R. de Groot. Compromotor: Dr. K.D. Liem.
- Drs. G.I.J.G. Rours. Chlamydia trachomatis infections in pregnancy and infancy. Collaboration with H.A. Verbrugh and R.P. Verkooijen (Department of Medical Microbiology and Infectious Diseases). Ph.D. thesis scheduled in 2008.
- Drs. M. Emonts. Genetic polymorphisms in immune response genes in infectious diseases and autoimmune diseases. This study was supported by a Revolving Fund Top Down grant

of the Erasmus MC. Collaboration with J. Laman (Department of Immunology) and P.W.M. Hermans. Ph.D. thesis scheduled in 2008.

- Drs. W.T. Hendriksen. Identification of signal networks regulating the expression of virulence genes in *Streptococcus pneumoniae*. Collaboration with P.W.M. Hermans. Ph.D. thesis scheduled in 2008.
- Drs. G. Verweel. The art of HAART; Various aspects of treatment in paediatric HIV. Collaboration with N.G. Hartwig (Department of Infectious Diseases, Erasmus MC). Ph.D. thesis scheduled in 2008.
- Drs. V. Hira. Development of specific monoclonal antibodies for the prevention of nosocomial infections caused by coagulase-negative staphylococci (CNS) in neonates. Collaboration with P.W.M. Hermans. Ph.D. thesis scheduled in 2008.
- Drs. S. Banus. Host genetics of *Bordetella pertussis* and the variable response to pertussis vaccination. Collaboration with T. Kimman RIVM Bilthoven. Ph.D. thesis scheduled in 2008.
- Drs. L. v.d. Meer-Kapelle. Vroegdiagnostiek en pathofysiologische mechanismen van neonatale infecties. Collaboration with P. Herbrink (Delft). Ph.D. thesis scheduled in 2008.
- Drs. J. van Kampen. Development and application of a sensitive high throughput method for quantification of intracellular NRTI-triphosphates. Aids Fund. Collaboration with Dr. T. Luiders (Neuro-oncology, Erasmus MC). Ph.D. thesis scheduled in 2008
- Drs. L. Duijts. Immune system and respiratory tract infections. (Part of the Generation R study). Collaboration with Dr. H.A. Moll. Ph. D. thesis scheduled in 2008.
- Drs. J.A.M. Labout. Dragerschap en luchtweginfecties. (Part of the Generation R study). Collaboration with Dr. H.A. Moll. Ph.D. thesis scheduled in 2008.
- Drs. W.P. de Boode. Klinische implementatie en evaluatie van hartminuutvolumemeting bij neonaten met persisterende pulmonale hypertensie behandeld met veno-arteriële ECMO. Ph.D. thesis scheduled in 2009.
- Drs. L.C. Gerrits. Cerebral oxygenation and hemodynamics during extracorporeal membrane oxygenation. Collaborator with Dr. K.D. Liem, Dr. A.F.J. van Heijst. Ph.D. thesis scheduled in 2010.

Current Research Grant Support

Project Development and application of genomic array footprinting in *Streptococcus pneumoniae*, a high-throughput technology for genome-wide identification and analysis of essential genes in bacteria

Sponsor IOP Genomics (Senter)

Period 2004-2007

Project Genomics of host-respiratory virus interactions. Towards novel intervention strategies (VIRGO project)

Sponsor BISK (Senter)

Period 2005-2008

Project Pneumococcal vaccine development

Sponsor Sanofi-Pasteur

Period 2005-2007

Project Novel prevention and treatment possibilities for Otitis Media through the comprehensive identification of antigenic proteins

Sponsor European Commission

Period 2006-2009

Project Pediatric HIV in Tanzania
Sponsor PRIOR
Period 2006-2010

Project Pneumococcal vaccine development
Sponsor Mucosis
Period 2007

Current Research Topics

Different topics in the fields of pediatric immunology and infectious diseases:

- Clinical, immunological and molecular aspects of childhood sepsis, meningitis, respiratory tract infections, HIV/AIDS and neonatal infections
- Microbial pathogenesis and genetics of infections by and host response against *Streptococcus pneumoniae* and *Neisseria meningitidis*
- Molecular and clinical aspects of immunodeficiencies
- Vaccine studies

International Collaboration

Prof. Mike Levin, S. Mary's Hospital, London, UK

Prof. Andrew Cant, Newcastle, UK

Prof. Andy Pollard, Oxford, UK

Prof. Jeff Weiser, Philadelphia, USA

Prof. Arnold L. Smith, University of Washington, Seattle, USA

Prof. Keith English, Memphis, USA

Name

P.M. van Hagen

CV

P. Martin van Hagen received his medical degree in 1987. Began his training in "Internal Medicine" in 1988 at the Erasmus MC Rotterdam and was registered in 1993. In 1999 registered as Immunologist. In 2000 he was appointed head of section "Clinical Immunology" of the dept. Internal Medicine. Erasmus MC Rotterdam.

In 2005 became staff member of the Eye Hospital Rotterdam. Special areas of research are immuno-endocrinology, immune deficiency diseases, and clinical and basic aspects of autoimmune eye diseases.

Selected Publications

- Bokum AM, Hofland LJ, Hagen PM. Somatostatin and somatostatin receptors in the immune system. *Eur Cytokine Netw.* 2000 Apr;11(2):161-176.
- Van Hagen PM, Baarsma GS, Mooy CM, Ercoskan EM, ter Averst E, Hofland LJ, Lamberts SW, Hofland LJ, Kuijpers RW. Somatostatin and somatostatin receptors in retinal diseases. *Eur J Endocrinol.* 2000 Oct;143(S1):S043-S051.
- Dalm VA., van Hagen PM, van Koetsveld P.M., Langerak Aw, van der Iely AJ, Lamberts S.W.J., Hofland LJ. "Cortistatin rather than somatostatin as a potential endogenous ligand for somatostatin receptors in the human immune system." *J Clin Endocrinol Metab* 2003 Jan;88: 270-6.
- Hofland LJ, Capello A, Krenning EP, de Jong M, van Hagen PM. Induction of apoptosis with hybrids of Arg-Gly-Asp molecules and peptides and antimetabolic effects of hybrids of cytostatic drugs and peptides. *J Nucl Med.* 2005 Jan;46
- J AM van Laar, T Missotten, P LA van Daele, A Jamnitski, G S Baarsma, and P M van Hagen. Adalimumab; a new modality for Behçet's disease? *Ann Rheum Dis*, Nov 2006.

PhD Students

- A. ten Bokum. Somatostatin receptors in the immune system and immune-mediated disease. Erasmusmc University Rotterdam. 1999
- V. Dalm. Somatostatin receptors and their ligands in the human immune system. Erasmus University Rotterdam. October 1, 2003
- T Missotten. The action of somatostatin analogues in uveitis. ongoing
- G Driessen: Identification of B-cell differentiation/maturation defects in Common Variable Immunodeficiency (CVID). ongoing

Current Research Grant Support

- 2006: Cortistatin and somatostatins in thymus development.
- 2003-2006: An open label trial of anti-TNF α chimeric monoclonal antibody (infliximab) in the treatment of endogenous uveitis or vasculitis unresponsive to standard therapy
- 2006-2008: A Double Blind, Randomized, Placebo Controlled Trial of Anti-TNF α Chimeric Monoclonal Antibody Infliximab, Remicade® in Exudative Age Related Macular Degeneration
- 2005: Identification of B-cell differentiation/maturation defects in Common Variable Immunodeficiency (CVID).
- Development of new peptides for diagnostic and therapeutic purposes. In cooperation with prof. dr. S. Achilefus (Washington University St. Louis)

Current Research Topics

Special areas of research are immuno-endocrinology, immune deficiency diseases, and clinical and basic aspects of autoimmune eye diseases.

International Collaboration

Prof. dr. S. Achilefus, Washington University St. Louis, USA

Prof Rajata Rajatanavin, Mahidol University, Bangkok

Prof K Engelmann, University of Hamburg, Germany

Prof E Ghigo, University of Turin, Italy

Dr M Culler, Ipsen, Milford USA

Name

Dr. N.G. Hartwig

CV

Dr. Nico Hartwig has had his medical training at the University of Amsterdam. After graduation he performed his PhD thesis at the University of Leiden. Topic of his thesis was disturbances of normal developmental processes due to intrauterine infections, especially Parvovirus B19. He started his training in Pediatrics in 1991 at the Sophia Children's Hospital Rotterdam, followed by a training in pediatric infectious diseases under supervision of Prof. Dr. R. de Groot. After 5 years working as medical staff, he became head of the subdivision infectious diseases and immunology in 2005. From a clinical perspective main topics are HIV-AIDS, primary immunodeficiencies and complicated infections in children. He is intensively involved in the educational programs of the ErasmusMC at all levels from preclinical students to postgraduates. Together with Dr. C. Vink, molecular biologist at the laboratory of pediatrics, a research project on clinical, epidemiological and molecular aspects of infections with Mycoplasma pneumonia was started in 2006.

PhD Students

J. van Kampen
V. Hira
G. Verweel
M. Emonts
G.J.A. Driessen

Current Research Grant Support

ESPID fellowship (awardee M. v.d. Flier)
Erasmus MC fellowship (awardee A.M.C. van Rossum)
Revolving Fund (awardee J. van Kampen)

Current Research Topics

Mycoplasma pneumoniae
HIV/AIDS
Primary immunodeficiencies

International Collaboration

A. Cant	New Castle
H. Lyall	London
P. Crocker	Dundee
E. Bernatowska	Warschau
D. Kowalczyk	Krakau
J.S. Jensen	Copenhagen
E. Jacobs	Dresden
R. Dumke	Dresden

Name

John P. Hays

CV

John Hays is a postdoctoral scientist (wetenschappelijke onderzoeker) in the Department of Medical Microbiology and Infectious Diseases, Erasmus MC.

He made a permanent move to the Netherlands in 2000 and was awarded a Dutch PhD from the Erasmus MC in March 2006.

Previously, he studied for a BSc in Biology with Food Science and Technology and an MSc in Biomedical Sciences in the UK, as well as spending 5 years in the routine microbiology, virology and serology laboratories of the Queen's Medical Centre, Nottingham, UK.

He was also awarded a PhD in virology from Leicester University in 1996 and spent 2 years at the Central Public Health Laboratory (CPHL), Colindale, London on a GlaxoWellcome funded project.

He is currently the principal investigator and manager of 2 European Union funded projects, and has been the principal investigator for a SOPHIA stichting grant that was completed in 2005. He supervises 2 PhD students, whose research involves investigations of virulence genes of the bacterium *Moraxella catarrhalis* and the epidemiology of mobile genetic elements associated with bacterial antibiotic resistance.

He has also successfully completed the Staatsexamen Nederlands als Tweede Taal (NT2) course.

Selected Publications

- van Pelt E, van Belkum A, Hays JP. 2008. Principles and Technical Aspects of PCR Amplification. Springer Science + Business Media B.V. ISBN 978-4020-6240-7.
- Hays JP. "The Genus *Moraxella*." 2005. Ch.3.3.38, pp958 – 987. In "The Prokaryotes" 3rded., Vol. 6: Proteobacteria: Gamma Subclass. Dworkin, Martin, Falkow, S.; Rosenberg, E.; Schleifer, K-H; Stackebrandt, E. (Eds.). Springer-Verlag, New York. ISBN: 978-0-387-25496-8
- van Belkum A, Duim B, Hays JP (eds). 2003. Experimental Approaches For Assessing Genetic Diversity Among Microbial Pathogens. Ponsen & Looijen BV. Wageningen. ISBN 90-9016462-6
- Khan, M. A., van der Wal, M., Farrell, D. J., Cossins, L., van Belkum, A., Alaidan, A., Hays, J. P. Analysis of VanA vancomycin-resistant *Enterococcus faecium* isolates from Saudi Arabian hospitals reveals the presence of clonal cluster 17 and two new Tn1546 lineage types. 2008. J Antimicrob. Chemother. In Press.
- Suzanne J.C. Verhaegh, André Streefland, Joy K. Dewnarain, David J. Farrell, Alex van Belkum, John P. Hays. Age-related genotypic and phenotypic differences in *Moraxella catarrhalis* isolates from children and adults presenting with respiratory disease in 2001 - 2002. 2008. Microbiology. 154(4): 1178 – 1184.
- John P. Hays, Roy Gorkink, Guus Simons, Justine K. Peeters, Kim Eadie, Cees M. Verduin, Henri Verbrugh, Alex van Belkum. 2007. High-throughput amplification fragment length polymorphism (htAFLP) analysis identifies genetic lineage markers but not complement phenotype-specific markers in *Moraxella catarrhalis*. Clin. Microbiol. Infect. 13(1): 55-62.
- John P. Hays, Saskia van Selm, Theo Hoogenboezem, Silvia Estevão, Kimberly Eadie, Peter van Veelen, Jan Tommassen, Alex van Belkum, Peter W. M. Hermans. 2005. The identification and characterization of a novel outer membrane protein (OMP J) of *Moraxella catarrhalis* that exists in two major forms. J. Bacteriol. 187(23): 7977-7984.

- John P. Hays, Alewijn Ott, Cees M. Verduin, Alex van Belkum, S. Kuipers. *Moraxella catarrhalis* only a weak activator of the mannose binding lectin pathway of complement activation. FEMS Microbiology Letters 249 (2005): 207-209.
- Hays JP, Kimberly Eadie, Cees M. Verduin, Henri Verbrugh and Alex van Belkum. A novel plasmid (pEMCJH03) isolated from *Moraxella catarrhalis* possibly useful as a cloning and expression vector within this species. Plasmid. 53 (2005):263-268.
- Hays JP, Eadie K, Veenhoven R, Verduin CM, Verbrugh H, van Belkum A. 2004. Pneumococcal vaccination does not affect the genetic diversity of *Moraxella catarrhalis* isolates in children. Eur. J. Clin. Microbiol. Infect. Dis. Oct; 23(10): 801-3.
- Hays JP, Eadie K, Verduin CM, Hazelzet J, Verbrugh H, van Belkum A. 2003. Changes in genetic types and population dynamics of *Moraxella catarrhalis* in hospitalized children are not associated with an exacerbation of existing disease. J. Med. Microbiol. Sep;52: 815-20
- Hays JP, van der Schee C, Loogman A, Eadie K, Verduin C, Faden H, Verbrugh H, van Belkum 2003. Total genome polymorphism and low frequency of intra-genomic variation in the *uspA1* and *uspA2* genes of *Moraxella catarrhalis* in otitis prone and non-prone children up to 2 years of age. Consequences for vaccine design? Vaccine. 7;21: 1118-24

PhD Students

- S. Verhaegh. (2007 –). Studies into virulence traits and putative vaccine candidates of the bacterium *Moraxella catarrhalis*
- M. Khan (2007 –). Mobile genetic elements associated with bacterial antibiotic resistance.

International Awards

European Union FP6 project (consortium) - Novel prevention and treatment possibilities for otitis media through the comprehensive identification of antigenic proteins €355.000,-

Current Research Topics

Putative vaccine candidates and virulence traits of the bacterium *Moraxella catarrhalis*

Epidemiological investigations into antibiotic resistance-carrying mobile genetic elements in bacteria

Name

Prof.Dr. J.M.W. Hazes, MD PhD

CV

In 2000 Professor Hazes has been appointed head of a new department of rheumatology of the Erasmus Medical Centre at Rotterdam. She has a broad experience in clinical and epidemiological research in rheumatology, with a special interest in prediction of onset and outcome of inflammatory arthropathies. In addition she extended her interest to osteoarthritis in the population. She also plays an active role in "The Bone And Joint Decade 2000 – 2010" with a specific interest in the monitoring of the burden of disease of musculoskeletal conditions. She supervised 12 PhD theses in the past and 6 theses presently.

Name:	Hazes, J. Mieke
Born	19th July 1955
Working address	Erasmus University Medical Center, Dep of Rheumatology, P.O.-Box 2040, 3000 CA Rotterdam, The Netherlands
	Tel: +31 10 4634602 Fax: +31 10 4635688 E: j.hazes@erasmusmc.nl
	<i>Education, Professional training</i>
1973	Secondary education, Gymnasium, Leiden
1980	Medical qualification University Leiden, MD
1988	Specialist registration in rheumatology, Rheumatology
1990	Doctorate, Leiden University
	Thesis: Conception, contraception in rheumatoid arthritis, Reproductive variables studied in the relation to genetic susceptibility
1994	Ph.D. registration in epidemiology
2001	Professor of Rheumatology Erasmus University Rotterdam
	<i>Previous and present positions</i>
1977 – 1977	Student fellow Department of Anaesthesiology, University Hospital Leiden
1980 – 1981	Residency in Occupational Medicine
1981 – 1986	Residencies in Internal Medicine and Rheumatology, Leiden.
1986 – 1988	Assistant Professor Rheumatology, University Hospital Leiden
1988 – 1995	Medical Head of a specialist Rheumatology Clinic "Solo Mio", Noordwijk, The Netherlands
1989 – 1990	Visiting Epidemiologist; Arthritis and Rheumatism Council Epidemiology Research Unit, Manchester University, U.K.
1995 – 1996	Associate Professor in Rheumatology, special interest rehabilitation and clinical epidemiology
1996 – 2000	Head of the Out-Patient Department and Deputy Head of Department of Rheumatology, Leiden University Hospital
2000 -	Professor in Rheumatology and Head of the Department of Rheumatology, University Medical Centre Rotterdam
	<i>Scientific organisations and others:</i>
1985 – present	Member of the Dutch Society for Rheumatology
1998 – present	Member of the British Society of Rheumatology

1990 – present	Member of the Dutch Society of Epidemiology
1991 – present	Member of the Dutch Society for Rheumatoid Surgery (NERASS)
1993 – present	Member of the American College of Rheumatology
1997 – present	Member of the Dutch Society of Medical Specialists
	Advisory Boards
1995 – 2003	Member of the Editorial Board of the Annals of Rheumatic Diseases
1996 – 2000	Scientific committee of the Dutch Society for Rheumatoid Surgery
1997 – 2004	Advisory committees of 2 scientific programs of the Dutch health care research council (ZON MW)
1998 – present	Member of the International Steering Committee of “The Bone and Joint Decade 2000 – 2010”
1999 – present	Member of the International “Bone and Joint Monitor Project Health needs assessment of musculoskeletal conditions”
1998 – 2000	Member of the Medical-Ethical Committee of the Leiden University Medical Centre
1999 – 2005	Chair of the Dutch National Action Network of the Bone and Joint Decade
1999 – 2002	Executive secretary of the Dutch society of Rheumatology
2002 - present	<i>Member of the advisory board for medical research of the Royal Netherlands Academy of Science</i>
2002-2003	Member of the Revolving Fund Committee Erasmus MC
2002- 2004	Member of the Erasmus MC fund for translational research (Breedtestrategie)
2003- 2006	Chair of the Erasmus MC Fund for care ad cost-effectiveness research
2004 – 2006	Chair of the Erasmus MC research integrity committee
2004 – 2006	Member of the board of the Dutch Society for Rheumatology, PR-officer.
2005 – 2006	Member of the Medical Research Advice Committee Erasmus MC (Mrace)
2006 - present	Chair of the Medical Research Advice Committee Erasmus MC (Mrace)
2006 - present	Member of the Supervisory Board Stichting BoOg

Publications in peer review journals since 2003:

- Tjhuis GJ, Zwinderman AH, Hazes JMW, Breedveld FC, Vliet Vlieland TPM. The two year follow-up of a randomised controlled trial of a clinical nurse specialist intervention, inpatient and day patient team care in rheumatoid arthritis. J Adv Nurs. 2003;41:34-43.
- Van den Hout WB, Tjhuis GJ, Hazes JMW, Breedveld FC, Vliet Vlieland TPM. Cost-effectiveness and cost-utility analysis of multidisciplinary care in patients with rheumatoid arthritis: A randomised comparison of clinical nurse specialist care, inpatient team care and day patient team care. Ann Rheum Dis 2003;62:308-15.
- Voskuyl AE, Hazes JMW, Zwinderman AH, Paleolog EM, van der Meer FJ, Daha MR, Breedveld FC. Diagnostic strategy for the assessment of rheumatoid vasculitis. Ann Rheum Dis 2003;62:407-413

- Tijhuis GJ, Kooiman CG, Zwinderman AH, Hazes JMW, Breedveld FC, Vliet Vlieland TPM. Validation of a Novel satisfaction questionnaire for patients with rheumatoid arthritis receiving outpatient clinical nurse specialist care, inpatient care, or day patient team care. *Arthritis Rheum (Arthritis Care & Research)* 2003;49:193-200.
- Hazes JMW. Determinants of physical function in rheumatoid arthritis: association with the disease process. *Rheumatology* 2003; 42 (Suppl 2):17-22.
- Munneke M, De Jong Z, Zwinderman AH, Jansen A, Runday HK, Peter WFH, Boonman DCG, Van den Ende HM, Vliet Vlieland TPM, Hazes JMW. Adherence and satisfaction of rheumatoid arthritis patients with a long-term intensive dynamic exercise program (RAPIT-program). *Arthritis Rheum (Arthritis Care & Research)* 2003;49 (5):665-72.
- Picavet HSJ, Hazes JMW. The prevalence of self-reported musculoskeletal diseases is high. *Ann Rheum Dis* 2003;62:644-651.
- De Jong Z, Munneke M, Zwinderman AH, Kroon HM, Jansen A, Runday KH, van Schaardenburg D, Dijkmans BAC, Van den Ende CHM, Breedveld FC, Vliet Vlieland TPM, Hazes JMW. Is a long-term high intensity exercise programme effective and safe in patients with rheumatoid arthritis? Results of a randomised controlled trial. *Arthritis Rheum* 2003;48(9), 2415-2424.
- De Jonge R, Brouwer R, Smit M, De Frankrijker-Merkesteijn M, Dolhain RJEM, Hazes JMW, Van Toorenbergen A, Lindemans J. Automated counting of white blood cells in synovial fluid. *Rheumatology* 2004;43:170-173.
- Van Aken J, Lard LR, LeCessie S, Hazes JMW, Breedveld FC, Huizinga TWJ. Radiological outcome after four years of early versus delayed treatment strategy in patients with recent-onset rheumatoid arthritis. *Ann Rheum Dis* 2004;63(3):274-279.
- Munneke M, de Jong Z, Zwinderman AH, Runday HK, van den Ende CHM, Vliet Vlieland TPM, Hazes JMW. High intensity exercise or conventional exercise for patients with rheumatoid arthritis? Outcome expectations of patients, rheumatologists and physiotherapists. *Ann Rheum Dis* 2004; 63(7):804-808.
- De Jong Z, Munneke M, Jansen LM, Runday KH, Schaardenbure D van, Brand R, Van den Ende CHM, Zuijderduin WM, Hazes JMW. Differences between participants and non-participants in an exercise trial for adults with rheumatoid arthritis. *Arthritis Rheum (Arthritis Care & Research)* 2004;51(4):593-600.
- Lodder MC, de Jong Z, Kostense PJ, Molenaar ESTH, Staal K, Voskuyl AE, Hazes JMW, Dijkmans BAC, Lems WF. Bone mineral density in patients with rheumatoid arthritis: Relation between disease severity and low bone mineral density". *Annals Rheum Dis* 2004;63(12):1576-1580.
- Reijman M, Hazes JMW, Koes BW, Verhagen AP, Bierma-Zeinstra SMA. Validity, reliability and applicability of six definitions of hip osteoarthritis used in epidemiological and clinical studies: a systematic appraisal. *Ann Rheum Dis* 2004;63(3):226-232.
- De Jong Z, Munneke M, Lems WF, Zwinderman AH, Kroon HM, Pauwels EKJ, Jansen, An, Runday KH, Dijkmans BAC, Breedveld FC, Vliet Vlieland TPM, Hazes JMW. Slowing of bone loss in patients with rheumatoid arthritis by long term intensity exercise. Results of a randomized controlled trial. *Arthritis Rheum* 2004;50(4):1066-1076
- De Jong Z, Munneke M, Zwinderman AH, Kroon HM, Runday KH, Lems WL, Dijkmans BAC, Breedveld FC, Vliet Vlieland TPM, Hazes JMW, Huizinga TWJ. Long-term high-intensity exercise and damage of small joints in rheumatoid arthritis. *Annals Rheum Dis* 2004;63:1399-1405.
- Reijman M, Hazes JMW, Pols HAP, Bernsen RMD, Koes BW, Bierma-Zeistra BMA. Validity and reliability of 3 definition of hip osteoarthritis. *Annals Rheum Dis* 2004;63 ;1427-1433.

- Reijman M, Hazes JMW, Bierma-Zeinstra BMA, Koes BW, Christgau S, Christiaansen C, Pols HAP. A New marker for osteoarthritis: cross-sectional and longitudinal approach. *Arthritis Rheum* 2004;50(8):2471-2478.
- Jansen LM, van der Horst-Bruinsma IE, van Schaardenburg D, Lard LR, Hazes JM, Huizinga TW, Dijkmans BA. Comparison of the baseline disease activity of early oligo- and polyarthritis in sequents years. *Clin Exp Reum* 2004(22(4):447-52.
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- Dahaghin S, Bierma-Zeinstra SM, Hazes JMW, Koes BW. Clinical burden of radiographic hand osteoarthritis: A systematic appraisal. *Arthritis Rheum*. 2006 Jul 27;55(4):636-647.

- Kroot EJA, Hazes JMW, Colin EM, Dolhain RJEM. Poncet's disease: reactive arthritis accompanying tuberculosis. Two cases reports and a review of the literature. *Rheumatology* 2006, 1 of 6.
- Reijman M, Pols HA, Bergink AP, Hazes JM, Belo JN, Lieveense AM, Bierma-Zeinstra SM. Body mass index associated with onset and progression of osteoarthritis of the knee but not of the hip. The Rotterdam Study. *Ann Rheum Dis*. 2006 Jul 12.
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- Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Allaart CF, Zeben van D, Kerstens PJ, Hazes JM, Zwinderman AH, Peeters AJ, de Jonge-Bok JM, Mallee C, Beus de WM, Sonnaville PB, Ewals JA, Breedveld FC, Dijkmans BA. Comparison of treatment strategies in early rheumatoid arthritis: a randomized trial. *Ann Intern Med*. 2007 Mar;20;146(6):406-15.
- Geuskens GA, Burdorf A, Hazes JM. Consequences of rheumatoid arthritis for performance of social roles—a literature review. *J Rheumatol*. 2007 Jun;34(6):1248-60.
- Escorpizo R, Bombardier C, Boonen A, Hazes JM, Lacaille D, Strand V, Beaton D. Worker productivity outcome measures in arthritis. *J Rheumatol*. 2007 Jun;34(6):1372-80.
- Kirwan JR, Minnock P, Adebajo A, Bresnihan B, Choy E, de Wit M, Hazes JM, Richards P, Saag K, Suarez-Almazor M, Wells G, Hewlett S. Patient Perspective: Fatigue as a Recommended Patient Centered Outcome Measure in Rheumatoid Arthritis. *J. Rheumatol*. 2007 May;34(5):1174-7.
- de Jong Z, Munneke M, Vilim V, Zwinderman AH, Kroon HM, Runday HK, Lems WF, Dijkmans BAC, Breedveld FC, Vliet Vlieland TPM, Hazes JMW, de Groot J. Value of serum cartilage oligomeric matrix protein (COMP) as a prognostic marker of large joint damage in rheumatoid arthritis. Data from the RAPIT study. *Rheumatology* (accepted)
- van de Geijn FE, Dolhain RJ, van Rijs W, Hazes JM, de Groot CJ. Mannose-binding lectin genotypes and pre-eclampsia: a case-control study. *Hum Immunol*. 2007 Nov;68(11):888-93.

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- Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Allaart CF, van Zeben D, Kerstens PJ, Hazes JM, Zwinderman AH, Roday HK, Han KH, Westedt ML, Gerards AH, van Groenendael JH, Lems WF, van Krugten MV, Breedveld FC, Dijkmans BA. Clinical and radiographic outcomes of four different treatment strategies in patients with early rheumatoid arthritis (the Best study): A randomized, controlled trial. *Arthritis Rheum*. 2008 Feb;58(2 Suppl):S126-35.
- de Jong Z, Munneke M, Vilim V, Zwinderman AH, Kroon HM, Roday HK, Lems WF, Dijkmans BA, Breedveld FC, Vlieland TP, Hazes JM, Degroot J. Value of serum cartilage oligomeric matrix protein as a prognostic marker of large-joint damage in rheumatoid arthritis—data from the RAPIT study. *Rheumatology (Oxford)*. 2008 Apr 9; [Epub ahead of print].

Name

Jaap J. van Hellemond, PhD

CV

Jaap van Hellemond, born in 1969, received his Masters degree in Medical biology (1993) and his PhD, on the anaerobic energy metabolism of parasites (1997, with honours) at the Utrecht University, The Netherlands. As a postdoctoral fellow of the Wellcome Trust, he studied 'cell cycle control in trypanosomes' at the Glasgow University (1998-1999), subsequently 'signal transduction during development' at the Netherlands Inst.for Developmental Biology. From 2000 untill 2007 he was assistant professor in Biochemistry of Parasites at the Fac. Veterinary Medicine, Utrecht University, The Netherlands. From 2007 onwards he is associate professor in parasitology at the dept. Medical Microbiology and Infectious Diseases and part-time also based in the Rotterdam Harbour Hospital and Institute for Tropical Diseases.

Selected publications

- van Hellemond, J.J., Hoek, A., Wichgers Schreur, P., Chupin, V., Özdirekcan, S., Geysen, D., van Grinsven, K.W.A., Koets, A., Van den Bossche, P., Geerts, S. and Tielens, A.G.M. (2007) The energy metabolism of bloodstream form *Trypanosoma theileri*. *Euk. Cell* 6, 1693-1696.
- Wu, Y.P., Lenting, P.J., Tielens, A.G.M., de Groot, P.G. and van Hellemond, J.J. (2007) Differential platelet adhesion to distinct life-cycle stages of the parasitic helminth *Schistosoma mansoni*. *J. Thrombosis Haemostasis* 5, 2146-2148.
- Sprong, H., Suchanek, M., van Dijk, J., van Remoortere, A., S.M., Klumperman, Avram, D., van der Linden, J., Leusden, J.H.W., van Hellemond, J.J. and Thiele, C. (2006) Aberrant receptor-mediated endocytosis of *Schistosoma mansoni* glycoproteins on host lipoproteins. *PLOS Medicine* 3, e253.
- van Hellemond, J.J., Bakker, B.M. and Tielens, A.G.M. (2005) The energy metabolism and its compartmentation in *Trypanosoma brucei*. *Adv. Microbial Physiol.* 50, 199-226.
- van Balkom, B.W.M., van Gestel, R.A., Brouwers, J.F.H.M., Krijgsveld, J., Tielens, A.G.M., Heck, A.J.R. and van Hellemond, J.J. (2005) Mass spectrometric analysis of the *Schistosoma mansoni* tegumental sub-proteome. *J. Proteome Res.* 4, 958-966.
- Boxma, B., de Graaf, R.M., van der Staay, G.W.M., van Alen, T.A., Ricard, G., Gabaldón, T., van Hoek, A.H.A.M., Moon-van der Staay, S.Y., Koopman, W.J.H., van Hellemond, J.J., Tielens, A.G.M., Friedrich, T., Veenhuis, M., Huynen, M.A., and Hackstein, J.H.P. (2005) An anaerobic mitochondrion that produces hydrogen. *Nature* 434, 74-79.
- Van Hellemond, J.J., Opperdoes, F.R. and Tielens, A.G.M. (1998) Trypanosomatidae produce acetate via a mitochondrial acetate:succinate CoA-transferase. *Proc. Natl. Acad. Sci. U.S.A.* 95, 3036-3041.

PhD students

- Susanne .W.H. van Weelden
 - Bioenergetics of parasitic protozoa, thesis 2005
- Kim Retra
 - Immune-modulating lipids of *Schistosoma mansoni*, thesis 2007
- Anita van der Klei

- Expression and synthesis of rhodoquinone, thesis 2009
- Koen W.A. van Grinsven
 - Anaerobic energy metabolism of parasites, thesis 2009
- Saskia de Walick
 - Outer-surface of *Schistosoma mansoni* and immune modulation, thesis 2011

(International) awards

- Junior teacher of the year, Faculty Veterinary Medicine, Utrecht University (2005)
- Merial Award for Parasitology (2000)
- Travelling research fellow Wellcome Trust (1998-1999)
- Young Scientist Award of the European Federation for Parasitology (1996)

Research support

- 'Proteomics of outer-surface of schistosomes', Neth. Inst. Vet. Sciences (2004)
- 'Stimuleringssubsidie' High Potential program, Utrecht University (2004)
- EMBO-fellowship and Wellcome Trust Traveling Research fellowship on "Cell cycle control in the protozoan parasite *Trypanosoma brucei*". (1998)

Current research topics

His research is focused on (1) the host-parasite interaction of schistosomes in order to identify novel factors involved in modulation of the host immune system or haemostasis of the host, (2) the identification of unique and essential processes in parasites (e.g. energy metabolism) in order to identify targets for therapeutic intervention, and (3) the development of novel methods for detection of parasitic infections.

(International) collaboration

Prof.dr. M. Yazdanbakhsh (Leiden University, The Netherlands):

Host-parasite interaction and immunology of schistosomal infections.

Dr. H. Sprong (Nat. Inst. Public Health, Bilthoven, The Netherlands)

Schistosomal surface glycoproteins and their effect on host lipoprotein metabolism.

Dr. C.H. Hokke and Prof.dr. A. Deelder (Leiden University, The Netherlands):

Identification of host lectins binding to schistosomal glycoconjugates.

Prof.dr. C. Grevelding (University Giessen, Giessen, Germany):

RNA-interference and genetic manipulation of schistosomes.

Prof.dr. W. Martin (Heinrich-Heine University, Düsseldorf, Germany):

Evolution of energy generating organelles.

Prof.dr. F.R. Opperdoes and Prof.dr. P. Michels (Christian de Duve Inst., Brussels, Belgium):

The metabolism of parasitic protozoa.

Name

Rudi Hendriks

CV

Rudi Hendriks studied Biology at the University of Utrecht and did his PhD studies on X chromosome inactivation patterns in human X-linked immunodeficiency diseases in the Department of Immunohaematology at the Leiden University Medical Center (Prof. J.J. van Rood). After a post-doctoral training in the Genetics Laboratory of the University of Oxford, where he studied genetic aspects of X chromosome inactivation, he started his own line of research within the lab of Frank Grosveld at the Department of Cell Biology and Genetics of the Erasmus MC Rotterdam. His research focuses on the molecular biology of the developmental program of B and T lymphocytes, in relation to immunodeficiency diseases and leukemia. In 1999 he moved his group to the Department of Immunology at the Erasmus MC. The current research aims comprise the characterization of signal transduction pathways and lymphoid-specific transcription factors that implement cell fate decisions at specific checkpoints, controlled by antigen receptors and their immature forms.

Selected Publications

- Dingjan, G.M., Middendorp, S., Dahlenborg, K., Maas, A., Grosveld, F. and Hendriks, R.W. (2001) Bruton's tyrosine kinase regulates the activation of gene rearrangements at the lambda light chain locus in precursor B cells in the mouse. *J. Exp. Med.* **193**:1169-1178.
- Nawijn, M.C., Ferreira, R., Dingjan, G.M., Kahre, O., Drabek, D., Karis, A., Grosveld, F. and Hendriks, R.W. (2001) Enforced expression of GATA-3 during T cell development inhibits maturation of CD8 single positive cells and induces thymic lymphoma in transgenic mice. *J. Immunol.* **167**:715-723.
- Kersseboom, R., Middendorp, S., Dingjan, G.M., Dahlenborg, K., Reth, M., Jumaa, H., and Hendriks, R.W. (2003). Bruton's tyrosine kinase cooperates with the B-cell linker protein SLP-65 as a tumor suppressor in pre-B cells. *J. Exp. Med.* **198**: 91-98.
- Jumaa, H., Hendriks, R.W. and Reth, M. (2005). B cell signaling and tumorigenesis. *Annual Rev. Immunol.* **23**:415-45.
- Middendorp, S., Zijlstra, A.E.J., Kersseboom, R., Dingjan, G.M., Jumaa, H. and Hendriks, R.W. (2005). Tumor suppressor function of Bruton's tyrosine kinase is independent of its catalytic activity. *Blood* **105**:259-265.

Ph.D. Students

- M. de Weers, *Molecular analyses of Bruton's tyrosine kinase*, Leiden University, 29th November 1995
- Maas, *Studies on the function of Bruton's tyrosine kinase in B cell development*, EUR, Rotterdam, 16th December 1998
- M. Nawijn, *Regulation of cell-fate decisions in T lymphocyte differentiation*, EUR, Rotterdam, 6th December 2000
- S. Middendorp, *Btk at the pre-BCR checkpoint (cum laude)*, EUR, Rotterdam, 19th May 2004
- R. Kersseboom, start November 2001 (MD/Ph.D. program)
- J. P van Hamburg, start December 2002
- V. Ta, start September 2005 (MD/Ph.D. program)
- Ribeiro de Almeida, start November 2005

Current research support

- 2001 KWF Project Grant “Functional Analysis of Transcription Factor GATA-3 in T cell malignancies”
- 2004 Association International Cancer Research (AICR) Grant “Tumour suppressor function of the signaling molecules Btk and SLP-65 in pre-B cells”
- 2005 KWF Project Grant “Molecular Mechanism of malignant transformation of precursor B cells in SLP-65-deficient leukaemia”
- 2005 FCT Portugal Grant “Role of CTCF transcription factor in B and T lymphocyte development”
- 2005 NWO-Mozaiek Grant “The Role of the V(D)J recombinase system in the development of pre-B cell leukemia”

Name

Peter W.M. Hermans, PhD

CV

1988-1992: Research fellow (PhD student). Unit Molecular Microbiology (Dr. J.D.A. van Embden), National Institute of Public Health and the Environment, Bilthoven, The Netherlands. Research subject: Molecular epidemiology and diagnosis of tuberculosis. PhD thesis (February 1992): Repeated DNA sequences of *Mycobacterium tuberculosis*: molecular characterization and application in diagnosis and epidemiology of tuberculosis. Prof.dr. W.P.M. Hoekstra (promotor); University of Utrecht, The Netherlands.

1992-1993: Senior scientist of the Armauer Hansen Research Institute (development of a tuberculosis research unit) and associate professor of the Addis Ababa University, Addis Ababa, Ethiopia. Research subject: Molecular epidemiology and immunology of tuberculosis.

1993-2000: University lecturer (UD), senior scientist and chairman of the Laboratory of Pediatrics (development of a molecular biology research unit), department of Pediatrics, Erasmus University Rotterdam, The Netherlands. Research subject: Bacterial infectious diseases: molecular epidemiology, molecular pathogenesis and host genetics.

2000-2005: Associate professor (UHD), senior scientist and head of the Laboratory of Pediatrics, department of Pediatrics, Erasmus University Medical Centre Rotterdam, The Netherlands. Research subject: Bacterial infectious diseases: molecular epidemiology, molecular pathogenesis and host genetics.

2001-2006: Director Research and Development Bacterial Vaccines, Vaxinostics Ltd., Erasmus University Medical Centre Rotterdam, The Netherlands.

2005-present: Associate professor (UHD) and head of the Laboratory of Pediatric Infectious Diseases, department of Pediatrics, cluster CUKZ, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands.

Selected Publications

- Hendriksen, W.T., H.J. Bootsma, S. Estevão, T. Hoogenboezem, A. de Jong, R. de Groot, O.P. Kuipers, and P.W.M. Hermans. 2007. CodY of *Streptococcus pneumoniae*: link between nutritional gene regulation and virulence. *J. Bacteriol.* 2007 Nov 16; [Epub ahead of print].
- Bootsma, H.J., M. Egmont-Petersen, and P.W.M. Hermans. 2007. Analysis of the in vitro transcriptional response of human pharyngeal epithelial cells to adherent *Streptococcus pneumoniae*: evidence for a distinct response to encapsulated strains. *Infect. Immun.* 75:5489-5499.
- Burghout, P.J., H.J. Bootsma, T.G. Kloosterman, J.J.E. Bijlsma, C.E. de Jongh, O.P. Kuipers, and P.W.M. Hermans. 2007. In search for genes essential for pneumococcal transformation: the RadA DNA repair protein plays a role in genomic recombination of donor DNA. *J. Bacteriol.* 189:6540-6550.
- Emonts, M., S.P. Wiertsema, R.H. Veenhoven, J.J. Houwing-Duistermaat, V. Walraven, R. de Groot, P.W.M. Hermans, and E.A.M. Sanders. 2007. The PAI1 4G/5G plasminogen activator inhibitor-1 genotype is associated with frequent recurrence of acute otitis media. *Pediatrics* 120:e317-e323.
- Bijlsma, J.J.E., P.J. Burghout, T.G. Kloosterman, H.J. Bootsma, A. de Jong, P.W.M. Hermans, and O.P. Kuipers. 2007. Development of Genomic Array Footprinting for the identification of conditionally essential genes in *Streptococcus pneumoniae*. *Appl. Environ. Microbiol.* 73:1514-1524.

- Hendriksen, W.T., N. Silva, H.J. Bootsma, C.E. Blue, G.K. Paterson, A.R. Kerr, A. de Jong, O.P. Kuipers, P.W.M. Hermans, and T.J. Mitchell. 2007. Regulation of gene expression in *Streptococcus pneumoniae* by response regulator 09 is strain-dependent. *J. Bacteriol.* 189:1382-1389.
- Kloosterman, T.G., W.T. Hendriksen, J.J.E. Bijlsma, H.J. Bootsma, S.A. van Hijum, J. Kok, P.W.M. Hermans, and O.P. Kuipers. 2006. Regulation of glutamine and glutamate metabolism by GlnR and GlnA in *Streptococcus pneumoniae*. *J. Biol. Chem.* 281:25097-25109.
- Hermans, P.W.M., P.V. Adrian, C. Albert, S.C. Estevão, T. Hoogenboezem, I.H.T. Luijendijk, T. Kamphausen, and S. Hammerschmidt. 2006. The streptococcal lipoprotein rotamase A (SlrA) is a functional peptidyl-prolyl isomerase involved in pneumococcal colonisation. *J. Biol. Chem.* 281:968-976.
- Hays, J.P., S. van Selm, T. Hoogenboezem, S.C. Estevão, K. Eadie, P. van Veelen, J. Tommassen, A. van Belkum, and P.W.M. Hermans. 2005. Identification and characterization of a novel outer membrane protein (OMP J) of *Moraxella catarrhalis* that exists in two major forms. *J. Bacteriol.* 187:7977-7984.
- Bogaert, D., A. van Belkum, M. Sluijter, A. Luijendijk, R. de Groot, H.C. Rümke, H.A. Verbrugh, and P.W.M. Hermans. 2004. Colonisation by *Streptococcus pneumoniae* and *Staphylococcus aureus* in healthy children. *Lancet* 363:1871-1872.

PhD Students

- K. Overweg (2000)
- D. Bogaert (2004)
- J. Hays (2006)
- M. Emonts (2008)
- W. Hendriksen (2008)
- V. Hira (2008)
- J. Labout (2008)
- K. Brand (2009)
- K. Stol (2009)
- L. Cron (2009)
- M. Bart (2010)
- Olivera (2010)
- M. Maes (2010)

Current Research Grant Support

Project Development and application of genomic array footprinting in *Streptococcus pneumoniae*, a high-throughput technology for genome-wide identification and analysis of essential genes in bacteria

Sponsor IOP Genomics (Senter)

Period 2004-2008\

Budget € 650,000,-

Project Genomics of host-respiratory virus interactions. Towards novel intervention strategies (VIRGO project)

Sponsor BISK (Senter)

Period 2005-2008

Budget € 440.000,-

Project	Human monoclonals development against pneumococcal infections
Sponsor	IQ Corporation
Period	2005-2008
Budget	€ 120.000,-
Project	Novel prevention and treatment possibilities for Otitis Media through the comprehensive identification of antigenic proteins
Sponsor	European Commission
Period	2006-2009
Budget	€ 375.000,-
Project	Pneumococcal carriage and infection in Venezuela
Sponsor	Central University of Venezuela
Period	2006-2010
Budget	€ 150.000,-
Project	Pediatric HIV in Tanzania
Sponsor	PRIOR
Period	2006-2010
Budget	€ 100.000,-
Project	Genomics and evolution of Bordetella pertussis
Sponsor	RIVM, Bilthoven
Period	2007-2010
Budget	€ 321.000,-
Project	Improving management and outcomes of patients admitted to hospital with community-acquired pneumonia in Indonesia
Sponsor	KNAW
Period	2007-2009
Budget	€ 50.000,-
Project	Pneumococcal carriage and infection in Ghana
Sponsor	Ghanaian-Dutch Research Program
Period	2007-2009
Budget	€ 100.000,-
Project	Pneumococcal mucosal vaccine development
Sponsor	PATH
Period	2008-2009
Budget	€ 225.000,-

Current Research Topics

The research line on Pediatric Infectious Diseases and Immunology within the Department of Pediatrics of the Radboud University Nijmegen Medical Centre originates from the Division of Pediatric Infectious Diseases and Immunology (Dr. P.W.M. Hermans, Prof.dr. R. de Groot, and Dr. A. Warris). The division considers as one of her core priorities the organization of top clinical and top reference care for children with serious and complicated (pediatric) infectious diseases, immune deficiencies, immune-mediated diseases and HIV/AIDS. The translational research of the

group is performed within the Laboratory of Pediatric Infectious Diseases (head: Dr. P.W.M. Hermans). Within the Laboratory of Pediatric Infectious Diseases the pathogenesis, immunology and epidemiology of pediatric infectious diseases are the central research themes. In close collaboration with various laboratories and medical departments within Radboud University Nijmegen Medical Centre, the Laboratory of Pediatric Infectious Diseases aims to improve the molecular and clinical understanding of the biology of infectious diseases. In collaboration with various renowned researchers in the field of microbial pathogenesis, we seek to study the molecular interaction between host and microorganism. Our work searches for the development of tools to diagnose, treat and prevent infectious diseases. Hence, our work contributes to the medical care of children suffering from life-threatening infections.

International Collaboration

Prof.dr. S. Hammerschmidt (Germany)

Prof.dr. T. Mitchell (UK)

Prof.dr. P. Andrew (UK)

Dr. D. Rozen (UK)

Prof.dr. J.-P. Claverys (France)

Prof.dr. D. Morrison (USA)

Prof.dr. J. Weiser (USA)

Dr. A. Meinke (Austria)

Prof.dr. A. Kungl (Austria)

Dr. B. Henriques-Normark (Sweden)

Dr. B. Albiger (Sweden)

Prof.dr. J. van Eldere (Belgium)

Dr. R. Sa Leao (Portugal)

Dr. J. de Waard (Venezuela)

Name

Rogier Quintus Hintzen

CV

Date of birth: February 16, 1963

1999: Neurologist

1995: Registration as Immunologist (SMBWO).

1994: PhD thesis: "CD27:Marker and Mediator of T-cell activation. Studies in healthy individuals and MS patients" Promotors: Prof. J.C. Koetsier and Prof. L.A. Aarden (*cum laude*), combined at University of Amsterdam (UVA) and Free University Amsterdam, The Netherlands.

1990: M.D. University of Leiden, The Netherlands.

1999: until now: Staff neurologist-CNS inflammation, Dept of Neurology. Active in daily patient care, research, teaching and management. Head MS Center ErasMS.

1997: Clinical training in MS and Neuro-oncology, Free University Hospital, Amsterdam

1997: Postdoctoral fellow: clinical and neuro-immunological aspects of MS and HAM/TSP at dept of Neurology, University of British Columbia, Vancouver, Canada (prof. D. Paty and prof. J. Oger).

1994: Resident in Neurology, Dept of Neurology, Leiden Academic Hospital (prof. R. Roos).

1990: Ph.D. study at Dept of Clinical (Viro-)Immunology, Central Laboratory of the Netherlands Red Cross Blood Transfusion Service (CLB), at University of Amsterdam (UVA) and dept. of Neurology, Free University Hospital Amsterdam. Defense of thesis at latter University.

1989: Research project at the Central Laboratory of the Netherlands Red Cross Blood Transfusion Service (CLB), Amsterdam: T-cell activation and cytokines in Multiple Sclerosis.

1987: Research student, Albert Einstein College of Medicine in New York, Dept. of Neuropathology (Prof. C.S. Raine) "Oligodendrocyte proliferation and remyelination in chronic relapsing autoimmune encephalomyelitis".

1984: Until 1988: Coördinator transplantation office, Eurotransplant Foundation Leiden (supervisor: prof. J. van Rood)

Teaching activities

Within Erasmus MC:

Regular medical student programme Erasmus MC, Neurology and Neurosciences

Coördinator Keuzeonderwijs en Keuzeonderzoek

Coördinator neurology-pathology teaching sessions

Teaching courses for residents in Neurology, Rehabilitation Medicine and Ophtalmology

Teaching courses NIHES, Erasmus Neuroscience

Initiator (together with Frank van Vliet) of a novel Molecular Medicine *Post-doctoral* course

Jan/feb 2005: "Immunity in the central nervous system".

Initiator (together with Frank van Vliet) of a novel Molecular Medicine *keuzeonderwijs* course

Jan/feb 2005: "Immunity in the central nervous system".

Supervision and teaching of PhD students, medical and biology students

Outside Erasmus MC:

Teaching courses European School of Neuroimmunology

Teaching courses for regional and national specialist nurses in Neurology

Production of questions for board exams at national level (neurologists) and international level (European School for Neuroimmunology)

Invited seminars for neurologists, both regional and national

Invited seminars at international meetings and upon invitation in centers for Neurology and (Neuro-)Immunology

Several educational activities to lay public in the field of immunology, neuroimmunology and neurology.

(International) Awards

2001 Price for best study at ECTRIMS meeting (The annual European MS Meeting), Dublin Sept 2001 for a prospective study on infections and relapses.

2003 Clinical fellowship NWO (The Netherlands organisation for science research)

Current research projects

Participation in several MS treatment trials, including Rotterdam Bone marrow Transplantation trial, experimental trials with anti-VLA4 monoclonal antibody, Interferon beta, fumaric acid, and FTY.

Main activity has been the initiation of the Rotterdam MS centre ErasMS, including composition of both research and business plans, development of a multidisciplinary research group on neuroinflammation, as well as the daily management of research, money and personnel. The centre aims to catalyse translational research on inflammatory diseases of the central nervous system. ErasMS also serves as one of the two national MS expertise centres (together with VUMC) and has three pillars: 1. a multidisciplinary collaborative research consortium including the departments of Neurology, Genetic Epidemiology, Immunology, Virology, together with the proteomics and genomics facilities, 2. the MS outpatient clinic for patient care (Neurology) including two MS research nurses and 3. training of AIO's, postdocs, clinical residents, medical students, increasingly within the context of Molecular Medicine and partly NIHES. In addition, ErasMS plays an important national and international role in the training of MS specialist nurses. Current daily function of RQH: head of management team. External advisor is Prof. G. Ebers-Oxford. An International Audit Committee in 2004 and 2006 has given excellent notes for the collaborative research programme.

Dutch bank for cerebrospinal fluid and associated clinical research. Role: project leader with Prof. D. Swaab and Prof. C.H. Polman

Ganymed (founded by Nobelprize winner Prof. R. Zinkernagel) on virus discovery and detection of autoimmune specificity in brain inflammation.

Collaboration with ViroNovative (Prof. Dr. A. Osterhaus) on virus discovery in viral encephalitis and CNS demyelination.

Genome screen of multiplex MS families in a Dutch genetic isolate (GRIP). Role: project leader with Prof. C. Van Duijn.

Collaboration with Rotterdam Eye Hospital on diagnostic and prognostic factors in ophtalmological inflammation (initiator and project leader).

Neurotrophic growth factors as markers for disease course in MS (initiator and project leader).

FLAIR study; industry trial on new clinical scales in MS. Role: principle investigator

Antegren study, pivotal industry trial on new drug: anti-VLA4 monoclonal antibody. Role: principle investigator, extension phase.

1900 study, effect of fumaric acid on MS relapses. Role: principle investigator.

Project leader within Postdoctoral School Molecular Medicine (CNS neuroimmunology)

Name

Bart C. Jacobs

CV

Dr Bart C. Jacobs studied Medicine and Philosophy at the Erasmus University in Rotterdam. In 1997 he graduated *cum laude* as a PhD on the role of infections, molecular mimicry and anti-ganglioside antibodies in the pathogenesis of the Guillain-Barré syndrome and completed his training as an Immunologist. That year he started his residency in Neurology and since 2003 he is working as a staff consultant at the department of Neurology, Erasmus MC. He is a general neurologist but has a special interest in patients with immune-mediated neuromuscular diseases. He also has an appointment at the department of Immunology at the Erasmus MC where he supervises the research on the pathogenesis of post-infectious and immune-mediated polyneuropathies including the Guillain-Barré syndrome. He is a member of the education committee of the Molecular Medicine research school.

Selected Publications

- van Doorn PA, Jacobs BC. Predicting the course of Guillain-Barré syndrome. *Lancet Neurol* 2006;5:992-994
- Geleijns K, Roos A, Houwing-Duistermaat JJ, van Rijs W, Tio-Gillen AP, Laman JD, van Doorn PA, Jacobs BC. Mannose-binding lectin contributes to the severity of Guillain-Barré syndrome. *J Immunol* 2006;177:4211
- Kuijff ML, van Doorn PA, Tio-Gillen AP, Geleijns K, Hooijkaas H, Hop WC, Jacobs BC. Diagnostic value of anti-GM1 ganglioside serology and validation of the INCAT-ELISA. *J Neurol Sci* 2005;239:37-44
- Geleijns K, Laman JD, van Rijs W, Tio-Gillen AP, Hintzen RQ, van Doorn PA, Jacobs BC. Fas polymorphisms are associated with the presence of anti-ganglioside antibodies in Guillain-Barré syndrome. *J Neuroimmunol* 2005;161:183-189
- Godschalk PCR, Heikema AP, Gilbert M, Komagamine T, Ang CW, Glerum J, Brochu D, Li J, Yuki N, Jacobs BC, van Belkum A, Endtz HPh. The crucial role of *Campylobacter jejuni* genes in autoimmune antibody induction. *J Clin Invest* 2004;114:1659
- Ang CW, Jacobs BC, Laman JD. The Guillain-Barré syndrome: a thure case of molecular mimicry. *Trends in Immunol* 2004;25:61
- Jacobs BC, O'Hanlon GM, Bullens RWM, Veitch J, Plomp JJ, Willison HJ. Immunoglobulins inhibit pathophysiological effects of anti-GQ1b positive sera at motor nerve terminals through inhibition of antibody binding. *Brain* 2003;126:2220-2229
- Jacobs BC, Bullens RW, O'Hanlon GM, Ang CW, Willison HJ, Plomp JJ. Detection and prevalence of alpha-latrotoxin-like effects of serum from patients with Guillain-Barré syndrome. *Muscle Nerve* 2002;25:549-558
- Ang CW, Laman JD, Willison HJ, Wagner ER, Endtz HPh, de Klerk MA, Tio-Gillen AP, van den Braak N, Jacobs BC, van Doorn PA. Structure of *Campylobacter jejuni* lipopolysaccharide determines anti-ganglioside specificity and clinical features of Guillain-Barré and Miller Fisher patients. *Infection Immun* 2002;70:1202-1208
- Ang CW, Koga M, Jacobs BC, Yuki N, van der Meché FG, van Doorn PA. Differential immune response to gangliosides in Guillain-Barré syndrome patients from Japan and The Netherlands. *J Neuroimmunol* 2001;121:83-87.

PhD Students

- Dr. K. Geleijns: 'Genetic polymorphisms in the pathogenesis of the Guillain-Barré syndrome', promotion date May 18th 2005
- Drs. M.L. Kuijf: 'Post-infectious cellular immune response causing GBS', promotion date June 2008
- Drs. F. Zitman: 'Neurotoxic effects of anti-ganglioside antibodies', promotion date March 2009

(International) Awards

2004 laureate European Neurological Society

Current Research Grant Support

- Clinical fellowship, NWO, 2003-2009
- 'Working mechanism of intravenous immunoglobulins in GBS and CIDP' Prinses Beatrix Fonds, co-applicant, 2005-2009
- 'Pathophysiological actions of anti-ganglioside antibodies at the motor nerve terminal' Erasmus MC Grant, 2006-2010
- 'Cellular mechanism driving the antibody response to *Campylobacter jejuni* causing the Guillain-Barré syndrome'

Current Research Topics

The research focuses on the diagnosis, pathogens and treatment of patients with immune mediated polyneuropathies, including the Guillain-Barré syndrome. The current research topics are:

- Development of new diagnostic markers for immune mediated polyneuropathies.
- The role of antecedent infections, molecular mimicry and anti-ganglioside antibodies in the pathogenesis.
- Cellular mechanism driving the antibody response to *Campylobacter jejuni* causing the Guillain-Barré syndrome.
- The role of gene polymorphisms in the susceptibility and severity of immune mediated polyneuropathies.
- The working mechanism of intravenous immunoglobulins in patients with immune mediated polyneuropathies.

International Collaboration

Prof.Dr. Richard Hughes, Department of Clinical Neurosciences, Guy's Hospital and St Thomas' School of Medicine, London, UK

Prof.dr. Hugh Willison, Institute of Neurosciences, Southern General Hospital, Glasgow, Scotland, UK

Dr. Nobuhiro Yuki, Department of Neurology, Dokkyo University School of Medicine, Tochigi, Japan

Name

Henricus Leonardus Antonius Janssen

CV

Professor in Hepatology
Section Liver Diseases & Liver Transplantation
Department of Gastroenterology and Hepatology
Erasmus MC, University Medical Center Rotterdam
The Netherlands

2001 to date Consultant in Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam (prof. EJ Kuipers, MD)

2002 to date Head of Clinical Research Bureau, Dept. Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam

2005 to date Head of Liver Unit, Dept. Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam

Selected Publications

Darwish Murad S, Valla DC, Groen de PC, Zeitoun G, Hopmans JC, Haagsma EZ, Hoek van B, Hansen B, Rosendaal FR, Janssen HLA. Determinants of survival and the effect of portosystemic shunting in patients with Budd-Chiari syndrome. *Hepatology* 2004;39:500-508 (IF 9.8).

Zonneveld van M, Niesters HG, Honkoop P, Darwish Murad S, de Man RA, Schalm SW, Janssen HLA. Long-term follow-up of alpha-interferon treatment in chronic hepatitis B. *Hepatology* 2004;39:800-804 (IF 9.8).

Molen van der RG, Sprengers D, Binda R, Jong de EC, Niesters HG, Kusters JG, Kwekkeboom J, Janssen HLA. Functional impairment of myeloid and plasmacytoid dendritic cells of patients with chronic hepatitis B. *Hepatology* 2004;40:738-746 (IF 9.8).

Janssen HLA, Zonneveld van M, Senturk H, Zeuzem S, Akarca U, Cakaloglu Y, Simon K, So Man Kit T, Gerken G, Man de RA, Niesters HG, Zondervan P, Schalm SW. Pegylated interferon α -2b alone or in combination with lamivudine for HBeAg-positive chronic hepatitis B: a randomised trial. *Lancet* 2005;365:123-129 (IF 23.8).

Stoop JN, Molen van der RG, Laan van der LJW, Kuipers EJ, Schalm SW, Kusters JG, Janssen HLA. Regulatory T cells contribute to the impaired immune response in patients with chronic hepatitis B virus infection. *Hepatology* 2005;41:771-778 (IF 9.8).

Janssen HLA, Lau GK. Chronic hepatitis B: HBeAg seroconversion after pegylated interferon and nucleos(t)ide analogs. *Hepatology* 2005;42(6):1459-60 (IF 9.8).

Janssen HLA, Leebeek FWG. JAK2 mutation: the best diagnostic tool for myeloproliferative disease in splanchnic vein thrombosis? *Hepatology* 2006;44:1391-1393 (Editorial; IF 9.8).

Janssen HLA. Combination therapy for chronic hepatitis B: A one-two knockout punch, or a swing and a miss? *Gastroenterology* 2006;130:614-15. (IF 12.3).

Buster EHCJ, Hansen BE, Buti M, Delwaide J, Niederau C, Michielsen PP, Flisiak R, Zondervan PE, Schalm SW, Janssen HLA. Peginterferon alpha-2b is safe and effective in HBeAg positive chronic hepatitis B patients with advanced fibrosis. *Hepatology* 2007, in press (IF 9.8)

Veldt BJ, Heathcote EJ, Wedemeyer H, Reichen J, Hofmann WP, Zeuzem S, Manns M, Hansen BE, Schalm SW, Janssen HLA. Sustained virological response leads to an improved clinical outcome in patients with hepatitis C and advanced fibrosis. *Annals of Internal Medicine* 2007, in press (IF 13.3).

PhD Students

- TJ Tang, MD. Intrahepatic T-cell response in hepatitis B virus eradication.
2000 - 2004
- M van Zonneveld, MD. Combination therapy of alpha-interferon and lamivudine for chronic hepatitis B.
2001 – 2005
- D Sprengers, MD. Immune response and immune modulation in chronic hepatitis B virus infection
2001 – 2006
- HJ Flink, MD. Pegylated interferon alfa in HBeAg-positive chronic hepatitis B.
2003 – 2006
- BJ Veldt, MD. Decision analysis to determine treatment outcome in chronic hepatitis C
2002 to date
- S Darwish Murad, MD. Prognostic factors and therapeutic interventions in vascular liver disease
2002 to date
- JN Stoop, MSc. The function of regulatory T-cells in hepatitis B virus tolerance and chronicity
2003 to date
- WF Leemans, MD. Viral suppression and HBV resistance during antiviral therapy for chronic hepatitis B virus infection
2003 to date
- ML op den Brouw, MSc. Molecular interaction and signal transduction between hepatitis B virus and dendritic cells
2004 to date
- MJ ter Borg, MD. Viral kinetics during alpha-interferon therapy for chronic hepatitis B.
2004 to date
- G Bezemer, MD. Quality of life and toxicity during antiviral therapy in chronic hepatitis C
2004 to date
- JJ Gutteling, MSc. Quality of life assessment in chronic liver disease
2004 to date
- VMCW Spaander, MD. Prognostication and therapy of gastrointestinal bleeding in portal vein thrombosis
2005 to date
- EHCJ Buster, MD. Immune modifying treatment in chronic HBV infection.
2005 to date

- M Claassen, MD. Intrahepatic T cell immunology in chronic viral hepatitis C. 2005 to date
- JJ Kuiper, MD. Terlipressin therapy in complications of portal hypertension. 2005 to date
- JF Bergmann, MD. Modifications of interferon alpha therapy in chronic hepatitis C. 2005 to date
- EEM Kuiper, MD. Long-term prognosis in cholestatic liver disease. 2006 to date
- ETTL Tjwa, MD. Innate immune reactivity and natural killer cell function in chronic hepatitis B. 2006 to date.
- L van Laar, MSc. Molecular mechanisms regulating human dendritic cell development and survival. 2006 to date
- JGP Reijnders, MD. Resistance in antiviral therapy for chronic hepatitis B. 2006 to date
- J Hoekstra, MD. Etiological factors in hepatic and portal vein thrombosis. 2006 to date
- BE Hansen, MSc. Mathematic models to predict viral kinetics in chronic hepatitis B and C. 2006 to date
- P Taimr, MD. Contrast enriched ultrasound for detection of focal liver lesions. 2006 to date
- C. Verveer, MD. Elastographic measurement of liver fibrosis in chronic viral hepatitis. 2006 to date
- Qiuwei Pan, MSc. Gene therapy as prevention of hepatitis C reinfection in liver grafts. 2006 to date
- Bisheng Liu, MSc. Interaction between dendritic cells and T-cells in chronic hepatitis C. 2007 to date
- Vincent Rijckborst, MD. Immune modulation in HBeAg-negative chronic hepatitis B. 2007 to date

(International) Awards

- 2003 Hepatology research award Netherlands Society Gastroenterology Elected as Rising Star in Gastroenterology & Hepatology by the Association of the National European and Mediterranean Societies of Gastroenterology (ASNEMGE)
- 2004 Altana award for best presentation during meeting of Dutch Society of Hepatology

Current Research Grant Support

2006 Sponsorship for a randomized controlled trial. "Subcutaneous continuous infusion of interferon Alfacon-1 and ribavirin in hepatitis C genotype 1 nonresponders (SCIN-C study)" (Medtronic, USA; 1.4 million Euro).

2006 Innate immunity in antiviral therapy with telbivudine, peg-interferon and combination therapy (Novartis, Switzerland; 320,000 Euro)

2006 Long-term follow up of pegylated interferon alfa 2a and ribavirin combination therapy in chronic HBeAg-negative chronic hepatitis B (Roche, Switzerland; 240,000 Euro)

2006 Mechanism of response of pegylated interferon and ribavirin in chronic hepatitis C (CIRES study) (Schering Plough, USA; 180,000 Euro)

2007 High dose versus standard dose ribavirin in combination with peginterferon alfa-2a for chronic hepatitis C (VIRID study; Roche, Switzerland; 960,000 Euro)

2007 Sustained response after entecavir or peginterferon alfa 2b in HBeAg positive chronic hepatitis B: a retrospective analysis (Bristol-Myers Squibb, USA; 50,000 Euro)

Current Research Topics

- Viral Hepatitis
- Vascular Liver Disease

International Collaboration

1999 to date. The Global Hepatitis B Intervention Group (HBV 99-01 study) (12 National and 33 International Hospitals)

2001 to date. European Group for the Study of Hepatic Vascular Diseases (En VIE; Founding member)

2003 to date. The Kirin Hepatitis B Intervention Study.

2004 to date. The European Hepatitis B Intervention Group (PARC study)

Name

Dirk Jan Kok, PhD

CV

Dirk Jan Kok, (Dik) studied Chemistry at the Leiden University, with specialisations in Biochemistry, Physical Chemistry, Immunology and Informational Sciences. After finishing his study in 1983 he started as research assistant at the Department of Endocrinology of the Leiden University Medical Center. In 1991 he received his PhD (Cum laude) on the thesis "The role of crystallization processes in calcium oxalate urolithiasis. In 1991 he helped setting up the Stone Clinic of the Oschner Medical Foundation in New Orleans. From 1991 to 1995 he was the recipient of a NWO-NATO and a KNAW fellowship. During this time he performed research at respectively the LUMC, the University of Texas Medical Center at Dallas, The Oschner Medical Foundation in New Orleans, the University of Florida at Gainesville and the Inselspital in Bern. In 1995 he started, with an Erasmus Fellowship, as Assistant Professor Pediatric Urology at the Department of Urology of the ErasmusMC. He has been responsible for setting up and conducting research programs in the area of Pediatric Urology. The main research themes are "the obstructed bladder", "renal involvement in urolithiasis" and "urinary tract infection". In this period he has functioned also as president of the 9th European Urolithiasis Symposium, Rotterdam 2001, member of the advisory board of the Euro-lithiasis Society. Dr. Kok is reviewer for Urology, Urological research, Clinica Chimica Acta, Kidney International and other international medical journals and grant proposal consultant for the oxalosis and hyperoxaluria foundation, the National Research Foundations of Hong Kong and of South Africa, the Alton Ochsner Medical Foundation, the Allehengny Singer Hospital and the University of Maastricht. He was recipient of multiple research prizes.

Selected Publications

- Daha MR, Kok DJ, van ES LA. Regulation of the C3-nephritic factor stabilized C3/C5 convertase of complement by purified human erythrocyte C3b receptor. *Clin Exp Immun* 1982; 50: 209
- Kok DJ, Papapoulos SE, Bijvoet OLM. Excessive crystal agglomeration with low citrate excretion in recurrent stone formers. *The Lancet* 1986;i : 1056__1058.
- Kok DJ, Khan SR. Calcium oxalate Nephrolithiasis, a free or fixed particle disease. *Kidney Int*, 1994; 46: 847-854.
- R. de Water, C. Noordermeer, A.B. Houtsmuller, D.J. Kok, H. Nizze, F.H. Schröder. The role of macrophages in Nephrolithiasis in rats: An analysis of the renal interstitium. *Am J Kidney Dis* 2000; 36: 615-625.
- Salahuddin S, Hsu YS, Buchholz NP, Dieleman JP, Gyssens IC, Kok DJ. Is Indinavir crystalluria an indicator for indinavir stone formation? *AIDS* 2001; 15: 1079-1080
- Mathoera RB, Kok DJ, Verduin K, Nijman RJM. Pathological and therapeutical significance of cellular invasion by *Proteus Mirabilis* in an enterocystoplasty infection stone model. *Infect Immun* 2002; 70: 7022-7032.
- de Jong BWD, Bakker Schut TC, Maquelin K, van der Kwast TH, Bangma CH, Kok DJ, Puppels GJ. Discrimination between non-tumor bladder tissue and tumor by Raman spectroscopy. *Anal Chem* 2006, in press
- Hess B, Kok DJ. Nucleation, Growth and aggregation of stone forming crystals.
- In: *Kidney stones: Medical and surgical management*. Coe FL, Favus M, Pak CYC, Parks J and Preminger G. (eds.) Lippincott-Raven. Philadelphia. 1996; Chapter 1; 3-32. ISBN 0-7817-0263-1

- Kok DJ. Inhibitors of calcium oxalate crystallization.in: Calcium oxalate in biological systems. Editor Khan SR, CRC press of Boca Raton, FI USA. 1995, chapter 2, pp 23-36.
- EUROLITHIASIS. editors: DJ Kok, HC Romijn, PCMS Verhagen, CF Verkoelen. Shaker Verlag, Maastricht 2001. ISBN 90-423-0171-6

PhD students (past 6 years)

R.B. Mathoera. Stone formation in the infected pediatric enterocystoplasty. Erasmus University Rotterdam, May 21, 2003

K.P. Wolffenbuttel. Functional changes in the obstructed bladder. In progress.

B.W. D. de Jong. Analysis of urinary tract structure. The value of immune histochemistry and Raman Spectroscopy. In progress

Current Research support (PI)

Bacterial populations in the urinary tract, SUWO.

Pharmaceutical intervention studies in the obstructed bladder, Dutch Kidney Foundation.

Diagnosis of urinary tract infection using urine protein profiling, Dutch Kidney Foundation.

Name

Marion Koopmans, professor DVM PhD
Born september 21 1956

Laboratory Address

Laboratory for Infectious Diseases and Screening (LIS)
Center for Infectious Diseases
National Institute for Public Health and the Environment (RIVM)
Antoni van Leeuwenhoeklaan 9
3720BA Bilthoven, The Netherlands
Tel: (31) 30.2743515/3945; 31.6.52098601
Fax: (31) 30.2744418
Marion.koopmans@rivm.nl

Education

1974: Gymnasium B, Collegium Marianum, Venlo, The Netherlands
1976: Graduated cum laude, Candidate's degree in Veterinary Medicine, Utrecht State University
1979: Graduated with honors, Doctoral degree in Veterinary Medicine, Utrecht State University
1983: Graduated with honors, Doctor of Veterinary Medicine, Utrecht State University
1990: Ph.D., Department of Infectious Diseases and Immunology, Virology Division, Veterinary Faculty, Utrecht State University. Dissertation title: "Diagnosis and epidemiology of torovirus infections in cattle"
1997: Registration as veterinary microbiologists, KNMvD
1981: Training in Tropical Veterinary Medicine in Gujarat, India.
1988: Training course "Introduction to modern epidemiology", Veterinary Faculty, Utrecht University
1991: Training course: "Molecular biological techniques", CDC, Atlanta, USA
1992: Training course: "Advanced Immunology", CDC, Atlanta, USA
1994: Training course: "Project Management", RIVM, Bilthoven
1995-1996: Training course: "Research Management", MOC, Bunnik
1997: Training course: "Molecular phylogeny", University of Antwerp.
2000: Training course: "Handling risks in food industry. Part II.
2003-2004: Development of management skills, Van de Boomen Management Coaching.
2005: Course "Advanced infectious Diseases epidemiology and mathematical modeling". Imperial College, London, UK.

Professional experience

April 2006-
September 2004- Professor of Public health Virology, Erasmus MC, Rotterdam
Deputy Laboratory Director, Diagnostic Laboratory for Infectious Diseases
Jan 2002- Chief of Virology, Diagnostic Lab for Infectious Diseases, (RIVM)
March 1994-Dec 2001 Scenior scientist in charge of enteric virus programme at the National Institute of Public Health, The Netherlands
May and October 1996: WHO temporary advisor for workshops on rotavirus in London, UK, and Geneva, Switzerland.

June 1992- Dec 1994	Visiting scientist at the Viral Exanthems and Herpesvirus Branch, Centers for Disease control, Atlanta, GA, USA
Dec 1992-May 1993	Consultant on HCMV detection methods for Photonic Sensor Syst, Inc, Atlanta, GA.
Jan 1991-May 1992	Visiting fellow at the Viral Gastroenteritis Unit, Centers for Disease Control, Atlanta, Georgia, USA
1990:	Associate Investigator, Department of Infectious Diseases and Immunology, Veterinary Faculty, Utrecht State University
1983-1989:	Faculty member of the Department of Large Animal Medicine, Veterinary Faculty, Utrecht State University Ph.D. research at the Department of Infectious Diseases and Immunology, Virology Division, Veterinary Faculty, Utrecht State University
1983:	Locum tenens at several small and large animal practices
1978:	Veterinary assistant, National Dairy Development Board, Anand, Gujarat, India

Other activities

- Member of the selection committee for the Beijerinck award, National Academy of Sciences
- Chair of the Study Group Caliciviridae of the International Committee for Taxonomy of Viruses (since 1999)
- Vice president of the European Society for Clinical Virology since 2006
- Section Editor for The Journal of Clinical Virology
- Editor for Virus Research
- Member of EU Network forum, with co-ordinators of 19 Europe-wide surveillance projects.
- Organizer of the 2nd International Calicivirus Conference, Dijon, 2004
- Scientific advisor to WHO Food Safety office
- Member of the Board of Eijkman Graduate School 1 and 2, U.M.C.U., 2006
- Reviewer for various infectious disease journals

Patents and awards

- HHS invention award, 1993. J.G. Dobbins, M.P. Koopmans, J.A. Stewart, and P.E. Pellett. Diagnostic diaper for identifying congenital infection with CMV and other pathogens.1993.
- S.S. Monroe, R.I. Glass, M.P.G. Koopmans and B. Jiang. Nucleic acids encoding human astrovirus serotype 2 and uses thereof. 1997.
- RIVM, Department for Infectious Diseases: Topscientist award per 1-5-1998.
- Wollinsky award for the best publication in Clinical Infectious Diseases, 2002.
- W.R.O. Goslingprijs, Nederlandse Vereniging voor Infectieziekten, 2004.

Grants

- NIH grant U19 CI000404-01 for project 'Avian influenza CRC-studies at the human-animal interface', CDC 2006 - 2009.
- EU grant DG Sanco, June 2004. Prevention of emerging (food-borne) enteric viral infections: diagnosis, viability testing, networking and epidemiology providing tools to prevent emergence of enteric viruses (DIVINE).
- EU 6th framework research grant. Providing tools to prevent emergence of enteric viruses (EVENT)

- Asthma fonds project: Immune modulation by early infections; the role of gastrointestinal infections and intestinal microflora in relation to development of atopic eczema and wheezing in infants 2 years of age. Projectleider Universiteit van Maastricht, ism CLB. Juni 2004.
- EPASTAR grant: Estimating microbial risk from drinking water: Integrating direct estimates of risk from epidemiology with indirect estimates of risk from disease transmission models. Augustus 2004. Projectleader Joseph Eisenberg, Emory University, Atlanta, USA.
- NWO Program grant. Programma Verantwoorde Voeding, November 2000. Molecular detection and viability screening of non-cultivable food-borne viruses.
- EU RTD grant: Rapid detection of transnational foodborne viral infections and elucidation of transmission routes through molecular tracing and development of a common database. 5th framework programme, quality of life. February 2000.
- ZON: Control and prevention of viral diarrhoea outbreaks through calicivirus vaccination. November 1999.
- PAD: Ontwikkeling van humane darmepitheelcel kweeksystemen voor vermeerdering van enteropathogene virussen. 1998-2000, extended August 2000.
- Sophia stichting: Identification of the NSP4 receptor inducing diarrhea. October 1998. Principal Investigator Dr. S. Einerhand, EUR.
- MLDS: Identificatie van receptoren voor symptomatische rotavirus-infectie. 1998. Principal Investigator Dr. S. Einerhand.
- RIVM: The hygiene hypothesis: relation between infection and allergy. Toponderzoekersproject, October 1998.
- Beatrix fonds: Immuniteit tegen poliovirus in transgene muizen. 1997-2000. Principal Investigator Dr. T. Kimman
- NIH grant YO2-A1-90002-02 for work at viral gastroenteritis unit, CDC 1990-1991.

Selected Publications

1. M. Koopmans, J. Vinjé, M. de Wit, W. van der Poel, and Y. van Duynhoven. Molecular epidemiology of Caliciviruses in The Netherlands. *J. Infect. Dis.* 2000;181:S262-269.
2. Green, J., Vinjé, J., Gallimore, C., Koopmans, M., Hale, A., and Brown, D. Capsid protein diversity among small round structured viruses. *Virus genes.*2000;20:227-236.
3. Buisman, A., Sonsma, J., Kimman, T., and Koopmans, M. Mucosal and systemic immunity to poliovirus in mice transgenic for the poliovirus receptor. *J Infect Dis.* 2000 Mar;181(3):815-23.
4. Mounts, A.W., Ando, T.A., Koopmans, M., Bresee, J.S., Inouye, S., Noel, J., and Glass, R.I. Cold weather seasonality of gastroenteritis associated with Norwalk-like viruses. *J Infect Dis.* 2000;181:S284-87.
5. Poel, W. van der, Vinjé, J., van der Heide, R., Herrera, M., Vivo, A., and Koopmans, M. Presence of Norwalk-like caliciviruses in faeces of farm animals. *Emerging Infectious Disease Journal* 2000;6:1-7.
6. Wit, M. de, Koopmans, M., Blij, J.F. van der, Duynhoven, Y. van. Hospital admissions for rotavirus in the Netherlands. *Clin Infect Dis.* 2000; 3: 698-704.
7. Van Kraaij, M.G.J., Dekker, A.W., Verdonck, L.F., van Loon, A.M., Vinjé, J., Koopmans, M., and Rozenberg-Arska, M. Infectious gastro-enteritis in adult allogeneic and autologous bone marrow transplant recipients. *Bone Marrow Transplantation* 2000;26:299-303.
8. De Wit, M., Koopmans, M., Kortbeek, L., van Leeuwen, N., Bartelds, A., and van Duynhoven, Y. Gastroenteritis in sentinel practices in The Netherlands. *Emerging infectious diseases Journal* 2001;7:82-90.

9. Widdowson, M., Doornum, G., van der Poel, W., de Boer, A., Mahdi, U., Koopmans, M. Protracted nosocomial outbreak of diarrhoea in neonates caused by newly emerging group A rotavirus genotype P[6]G9. *Lancet*, 2000;356(9236):1161-2
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Name

Thijs Kuiken, professor DVM PHD

CV

I obtained a degree as doctor in veterinary medicine from Utrecht University in 1988, and a Ph.D. degree from the University of Saskatchewan, Canada, in 1998, where I studied Newcastle disease virus in cormorants. I received my qualification as Diplomate of the American College of Veterinary Pathologists in 2002. I was a Research Associate in the Zoological Society of London, where I concentrated on viral diseases in stranded marine mammals. In 1999, I joined the Department of Virology at Erasmus MC, where I was appointed professor of comparative pathology in 2006. The central theme of my research is the comparative pathology of viral diseases, such as highly pathogenic H5N1 influenza, SARS, and human metapneumovirus infection.

Selected publications

- van Riel,D., Munster,V.J., de Wit,E., Rimmelzwaan,G.F., Fouchier,R.A., Osterhaus,A.D., and Kuiken,T. (2007): Human and Avian Influenza Viruses Target Different Cells in the Lower Respiratory Tract of Humans and Other Mammals. *Am.J.Pathol.*, 171:1-9.
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- Kuiken,T., Holmes,E.C., McCauley,J., Rimmelzwaan,G.F., Williams,C.S., and Grenfell,B.T. (2006): Host species barriers to influenza virus infections. *Science*, 312:394-397.
- Rimmelzwaan,G., van Riel,D., Baars,M., Bestebroer,T.M., van Amerongen,G., Fouchier,R.A.M., Osterhaus,A.D.M.E., and Kuiken,T. (2006): Influenza A virus (H5N1) infection in cats causes systemic disease with potential novel routes of virus spread within and between hosts. *Am.J.Pathol.*, 168:176-183.
- van Riel,D., Munster,V.J., de Wit,E., Rimmelzwaan,G.F., Fouchier,R.A.M., Osterhaus,A.D.M.E., and Kuiken,T. (2006): H5N1 virus attachment to lower respiratory tract. *Science*, 311:399
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- Kuiken,T., van den Hoogen,B.G., van Riel,D.A., Laman,J.D., van Amerongen,G., Sprong,L., Fouchier,R.A., and Osterhaus,A.D. (2004): Experimental human metapneumovirus infection

of cynomolgus macaques (*Macaca fascicularis*) results in virus replication in ciliated epithelial cells and pneumocytes with associated lesions throughout the respiratory tract. *Am.J.Pathol.*, 164:1893-1900.

- Fouchier,R.A., Kuiken,T., Schutten,M., van Amerongen,G., van Doornum,G.J., van den Hoogen,B.G., Peiris,M., Lim,W., Stohr,K., and Osterhaus,A.D. (2003): Aetiology: Koch's postulates fulfilled for SARS virus. *Nature*, 423:240
- Kuiken,T., Rimmelzwaan,G.F., van Amerongen,G., and Osterhaus,A.D. (2003): Pathology of human influenza A (H5N1) virus disease in cynomolgus macaques (*Macaca fascicularis*). *Vet.Pathol.*, 40:304-310.
- Kuiken,T., Fouchier,R.A., Rimmelzwaan,G.F., and Osterhaus,A. (2003): Emerging viral infections in a rapidly changing world. *Curr.Opin.Biotechnol.*, 14:641-646.
- Kuiken,T., Fouchier,R.A., Schutten,M., Rimmelzwaan,G.F., van Amerongen,G., van Riel,D., Laman,J.D., de Jong,T., van Doornum,G., Lim,W., Ling,A.E., Chan,P.K., Tam,J.S., Zambon,M.C., Gopal,R., Drosten,C., van der,W.S., Escriou,N., Manuguerra,J.C., Stohr,K., Peiris,J.S., and Osterhaus,A.D. (2003): Newly discovered coronavirus as the primary cause of severe acute respiratory syndrome. *Lancet*, 362:263-270.
- Martina,B.E., Haagmans,B.L., Kuiken,T., Fouchier,R.A., Rimmelzwaan,G.F., van Amerongen,G., Peiris,J.S., Lim,W., and Osterhaus,A.D. (2003): Virology: SARS virus infection of cats and ferrets. *Nature*, 425:915
- Jensen,T., van de,B.M., Dietz,H.H., Andersen,T.H., Hammer,A.S., Kuiken,T., and Osterhaus,A. (2002): Another phocine distemper outbreak in Europe. *Science*, 297:209
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- van den Hoogen,B.G., de Jong,J.C., Groen,J., Kuiken,T., de Groot,R., Fouchier,R.A.M., and Osterhaus,A.D.M.E. (2001): A newly discovered human pneumovirus isolated from young children with respiratory disease. *Nat.Med.*, 7:719-724.

Ph.D. students

- J.D.W. Philippa. Vaccination of non-domestic animals against emerging virus infections (2007)
- J.M. Rijks. Phocine distemper revisited. Multifactorial analysis of the 2002 phocine distemper virus epidemic in the Netherlands (2003 – present)
- J.M. van den Brand. Pathogenesis of SARS (2007- present)
- L.A. Reperant. *Epidemiology and pathogenesis of highly pathogenic avian influenza H5N1 virus in wildlife* (2007 – present)
- D. van Riel. Pathogenesis of influenza pneumonia (2008 – present)

Current Research Grant Support

- EU Grant (DISSECT)
- EU Grant (New-Flubird)
- VIRGO
- NIH Grant (CRISP)
- NIH Grant (SARS)
- FES (Impuls Veterinair Aviaire Influenza Onderzoek Nederland)

Current research topics

- Comparative pathology and pathogenesis of respiratory viral diseases
- Pathology of viral diseases in wildlife

International collaboration

- National Institutes of Health, Dr. J. Taubenberger
- Princeton University, Dr. A. Dobson
- U.S. Department of Agriculture, Dr. B. Rosenthal
- University of Cambridge, Dr. W. Amos
- University of Prince Edward Island, Dr. P.-Y. Daoust
- University of Saskatchewan, Dr. F.A. Leighton
- Pennsylvania State University, Dr. O. Bjornstad
- Ehime University, Dr. S. Tanabe
- University of North Carolina at Chapel Hill, Dr. R. Baric
- Washington University, Dr. M. Katze

Name

Ernst J. Kuipers

CV

Studied Medicine at the University of Groningen and trained in Internal Medicine and Gastroenterology between 1986 and 1994. He participated in the 1994 WHO meeting on H. pylori and gastric cancer. In 1995, he completed his thesis (cum laude) on the interrelation between H. pylori, chronic gastritis and gastric cancer, and was awarded the 1996 Dutch Gastrointestinal Research Award. He worked in 1995 - 1997 as research associate in the Division of Infectious Diseases at Vanderbilt University, Nashville, Tennessee, USA under Prof. M.J. Blaser. In 2000, he became Chair of the Department of Gastroenterology and Hepatology of the Erasmus MC. Since September 2006 he also chairs the Department of Internal Medicine. He is / has been a member of the editorial boards of APT, American Journal of Gastroenterology, Best Practice and Research in Gastroenterology, Digestion, Gastroenterology, Gut, World Journal of Gastroenterology, and the Cochrane group for upper gastrointestinal and pancreatic disorders, and as of 2008 handling editor of Gut. He is a member of the Dutch National Health Council, and President-elect of the Dutch Society of Gastroenterologists and the European Helicobacter Study Group. In 2006, he was awarded a fellowship of the American Gastroenterology Association.

Selected Publications

- Van Soest EM, Dieleman JP, Siersema PD, Sturkenboom MCJM, Kuipers EJ. Increasing incidence of Barrett's esophagus in the general population. *Gut* 2005; 54: 1062-6. IF 9.0
- Kuipers EJ. Proton pump inhibitors and gastric neoplasia. *Gut* 2006; 55: 1217-21. IF 9.0
- Malfertheiner P, Megraud F, O'Morain C, Bazzoli F, El-Omar E, Graham D, Hunt R, Rokkas T, Vakil N, Kuipers EJ. Current concepts in the management of Helicobacter pylori infection – the Maastricht III consensus report. *Gut* 2007; 56: 772-81. IF 9.0
- Kusters JG, van Vliet AHM, Kuipers EJ. Pathogenesis of Helicobacter pylori infection. *Clin Microbiol Rev* 2006; 19: 449-90
- Kuipers EJ. Can Helicobacter pylori eradication therapy be shortened to 4 days? *Nature Clin Gastro Hep* 2007; 4: 68-9.
- De Vries AC, Meijer GA, Looman CWN, Casparie MK, van Grieken NCT, Hansen BE, Kuipers EJ. Epidemiological trends of premalignant gastric lesions in the Netherlands; a long-term nationwide study. *Gut* 2007; ePub ahead of print. IF 9.0.
- Ramsoekh D, van Leerdam ME, Dekker E, Ouwendijk RTh, van Dekken H, Dinjens W, Kuipers EJ. Sporadic duodenal adenoma and the association with colorectal neoplasia, a case-control study. *Am J Gastroenterol* 2008; in press
- Kuipers EJ, Surawicz CM. Clinical update on Clostridium difficile. *Lancet* 2008; in press.

PhD Students

- Pim Sloots. Motility and endosonographic studies in patients with anorectal disorders, 2003.
- Janneke Weiss. Chromosomal instability in gastric cancer, 2003.
- Nicolette de Vries. Gene regulation and host adaptation in Helicobacter pylori, 2003.
- Nicole van Grieken. Morphological and chromosomal alterations during gastric carcinogenesis, 2003.
- Ramon de Jonge. Virulence mechanisms in Helicobacter pylori, 2004.
- Marjolein Homs. Palliation of dysphagia from esophageal cancer, 2004.

- Rachel West. Diagnosis and treatment of pelvic floor disorders in inflammatory bowel disease, 2004.
- Monique Gerrits. Mechanisms of antibiotic resistance in *Helicobacter pylori*, 2004
- Marleen van Nuenen. Intestinal microbiota and inflammatory bowel disease, 2005
- Mariska Hage. Barrett's esophagus: treatment aspects, 2005.
- Florian Ernst. Transcriptional regulation of the nickel and iron metabolism in *Helicobacter pylori*, 2005
- Dorine Bax. Barrett's esophagus: a molecular characterization, 2005
- Peter Mensink. The clinical impact of tonometry on the diagnosis and treatment of gastrointestinal ischemia, 2006
- Mark van Blankenstein. Some observations on the epidemiology of Barrett's oesophagus and adenocarcinoma of the oesophagus, 2006
- Han Otte. Exercise tonometry for the diagnosis of chronic intestinal ischemia, 2006
- Evelyn van Vliet. Staging investigations in patients with esophageal cancer: a critical re-appraisal, 2006
- Klaas van der Linde. Genetic polymorphisms in inflammatory bowel disease, 2006
- Jolanda van Dieren. Treatment of mucosal inflammatory disorders; new targets, new agents, new routes of administration. 2007
- Bas van Tuyl. Videocapsule endoscopy; fiction becoming fact. 2007
- Marion Kerkhof. Barrett's esophagus: improving surveillance strategies. 2007
- Els Verschuur. Nurse-led follow-up and palliative care of esophageal cancer patients. 2007
- Clara Belzer. Surviving the enterohepatic tract. Molecular mechanisms of stress adaptation in *Helicobacter hepaticus*. 2007

Current Research Grant Support

Current grants among others come from ZonMw and KWF, as well as from the Erasmus MRace programs and the MLDS, and focus among others on the etiology of Barrett's esophagus, gastric cancer, and colon cancer prevention.

Current Research Topics

The research focuses on the etiology, diagnosis and prevention of early neoplastic lesions of the gastrointestinal tract, including *H. pylori*-associated gastric cancer.

Name

Dr. Jaap Kwekkeboom

CV

Jaap Kwekkeboom (1959) graduated in Medical Biology at the University of Utrecht in 1984. He performed his PhD-study at the Gaubius Laboratory of the Netherlands Organization for Applied Research (TNO) in Leiden on the regulation of bile acid synthesis in cultured hepatocytes. In 1990 he obtained his PhD-degree from the University of Leiden. His postdoctoral training focused on *cellular immunology* (Department of Cell Biology and Histology, Academic Medical Centre, Amsterdam; 1990–1993), and *hematopoietic stem cell transplantation* (Sanquin/CLB research institute, Amsterdam; 1993-1996). In 1997 he became assistant professor at the Department of Internal Medicine II of the Erasmus MC-University Medical Center in Rotterdam, where he built up laboratory facilities for basic and translational *liver immunology research*. In 2000 he joined the newly formed Department of Gastroenterology and Hepatology of the Erasmus MC.

Selected Publications

Kwekkeboom J, Princen HM, van Voorthuizen EM, Kempen HJ: Bile acids exert negative feedback control on bile acid synthesis in cultured pig hepatocytes by suppression of cholesterol 7 alpha-hydroxylase activity. *Hepatology* 12(5):1209, 1990.

Kwekkeboom J, de Rijk D, Kasran A, Barcy S, de Groot C, de Boer M: Helper effector function of human T cells stimulated by anti-CD3 mAb can be enhanced by co-stimulatory signals and is partially dependent on CD40-CD40 ligand interaction. *Eur J Immunol* 24(3):508, 1994.

Kwekkeboom J, Buurman DE, Ploemacher RE, Baars JW, Loos HA, Slaper-Cortenbach IC: A nylon wool filter coated with human immunoglobulin for rapid depletion of monocytes and myeloid cells from peripheral blood stem cell transplants. *Exp Hematol* 26(5):400, 1998.

van Rijen MM, Kuijf ML, Metselaar HJ, Tilanus HW, Bouma GJ, de Weger RA, Jonker M, Kwekkeboom J: CD154 is expressed during treatment with calcineurin inhibitors after organ transplantation. *Transplantation* 73(10):1666, 2002.

de Reuver P, Pravica V, Hop W, Boor P, Metselaar HJ, Hutchinson IV, Tilanus HW, Kwekkeboom J: Recipient *ctla-4 +49 G/G* genotype is associated with reduced incidence of acute rejection after liver transplantation. *Am J Transplant* 3(12):1587, 2003.

Kwekkeboom J, Zondervan PE, Kuijpers MA, Tilanus HW, Metselaar HJ: Fine-needle aspiration cytology in the diagnosis of acute rejection after liver transplantation. *Br J Surg* 90(2):246, 2003.

van der Molen RG, Sprengers D, Binda RS, de Jong EC, Niesters HG, Kusters JG, Kwekkeboom J, Janssen HL: Functional impairment of myeloid and plasmacytoid dendritic cells of patients with chronic hepatitis B. *Hepatology* 40(3):738, 2004.

Kwekkeboom J, Tha-In T, Tra WM, Hop W, Boor PP, Mancham S, Zondervan PE, Vossen AC, Kusters JG, de Man RA, Metselaar HJ: Hepatitis B immunoglobulins inhibit dendritic cells and T cells and protect against acute rejection after liver transplantation.

Am J Transplant 5(10):2393, 2005.

Boor PP, Metselaar HJ, Mancham S, Tilanus HW, Kusters JG, Kwekkeboom J: Prednisolone suppresses the function and promotes apoptosis of plasmacytoid dendritic cells. Am J Transplant 6(10):2332, 2006.

Tapirdamaz O, Pravica V, Metselaar HJ, Hansen B, Moons L, van Meurs JB, Hutchinson IV, Shaw J, Agarwal K, Adams DH, Day CP, Kwekkeboom J: Polymorphisms in the T cell regulatory gene cytotoxic T lymphocyte antigen 4 influence the rate of acute rejection after liver transplantation. Gut 55(6):863, 2006.

PhD Students

Thjon Tang	2000 - 2003
Brenda Bosma	2004 - 2007
Tanya Tha-In	2005 - 2008
Patick Boor	2005 - 2009
Özlem Tapirdamaz	2007 - 2011

Current Research Grant Support

Erasmus MC Revolving Fund. Deficiency in antigen-presenting capacity of dendritic cells in hepatic lymph nodes causes persistence of HBV-infection (€ 68.000)

Gastrostart grant of the Netherlands Society for Gastroenterology. *Ex-vivo* modulation of dendritic cells for induction of liver transplant tolerance (€ 7.500)

Biotest Seralc Pharma research grants. Immunomodulation with IVIg in liver transplant recipients (total: €106.000)

NWO-Mozaiek (Tha-In, Kwekkeboom, Metselaar) IVIg: the solution for long-lasting allograft acceptance (€180.000)

NWO-Mozaiek (Tapirdamaz, Kwekkeboom, Metselaar) Development of an innovative sensitive assay to detect transplant tolerance (€180.000)

Foundation for Liver Research. Induction of tolerance with plasmacytoid dendritic cells (€ 36.000)

Innogenetics BV. Genetic polymorphisms in secreted- and signaling receptors of the innate immune system and liver allograft rejection (€ 18.000)

Current Research Topics

Liver transplantation is on the short-term a successful treatment for end-stage liver diseases, but long-term survival and quality of life are severely impaired by complications caused by continuous immunosuppressive treatment. Our current studies focus on:

1. Defining genetic and immunological parameters that predict the risk of rejection, in order to enable individualization of immunosuppressive therapy. Immune parameters are studied preferentially in the graft itself, using the Fine Needle Aspiration Biopsy technique. We develop an innovative technique to quantify the recipient T-cell response against indirectly presented donor MHC, making use of recipient DC genetically transduced with donor MHC-genes.

2. Promoting immunological conditions that are required for the development of tolerance against liver grafts by modulation of donor- and recipient dendritic cells (DC). We extensively investigate the suitability of Intravenous Immunoglobulins for this purpose.

International Collaboration

Prof I. Lautenschlager, Surgery and Virology, Helsinki, Finland

Prof D.H. Adams, MRC Centre for Immuregulation, Birmingham, UK

Prof. C.P. Day, Centre for Liver Research, Newcastle, UK

Prof. K. Thielemans, Physiology-Immunology, Brussel, Belgium

Name

dr. Luc JW van der Laan

CV

Luc J.W. van der Laan receiving his PhD degree at the Vrije University in Amsterdam (1998) and worked as a post-doc at the Scripps Research Institute (La Jolla, California). Here he worked for three years on the transplantation of human and pig pancreatic islet as a therapy for diabetes, studying the risk of xeno-infection by porcine endogenous retroviruses. In 2001 he received a post-doc fellowship from the Dutch Science Organization (NWO) and in 2002 he became assistant professor at the department of Surgery, Erasmus MC-University Medical Center, Rotterdam, to continue research on transplantation and viral infections. Recently he received several awards including the ESOT "Best abstract in basic science" and the ILTS "Rising star" award.

Selected Publications

- Henry SD, HJ Metselaar, RCB Lonsdale, A Kok, BL Haagmans, HW Tilanus and LJW van der Laan (2006) Mycophenolic acid inhibits hepatitis C virus replication and acts in synergy with cyclosporin A and interferon- α . *Gastroenterology*. 131: no5 (IF 12.4)
- Henry SD, PG van der Wegen, HJ Metselaar, HW Tilanus, BJ Scholte and LJW van der Laan (2006) Simultaneous targeting of HCV replication and viral binding with a single lentiviral vector containing multiple RNA interference expression cassettes. *Mol. Ther.* 14: 485-93 (IF 5.4)
- Demirkiran A., A. Kok, J. Kwekkeboom, J.G. Kusters, H.J. Metselaar, H.W. Tilanus and L.J.W. van der Laan (2006) Low circulating regulatory t cells levels after acute rejection in liver translatation. *Liver Transplant*. 12: 277-84 (IF 4.4)
- Stoop J.N., R.G. van der Molen, C.C. Baan, L.J.W. van der Laan, E.J. Kuipers, J.G. Kusters, and H.L.A. Janssen (2005) Regulatory T cells play a role in the impaired immune response in patients with a chronic Hepatitis B Virus infection. *Hepatology* 41: 771-778 (IF 10.4)
- van der Laan L.J.W., C. Lockey, B.C. Griffeth, F.S. Frasier, C.A. Wilson, D.E. Onions, B.J. Hering, Z. Long, E. Otto, B.E. Torbett and D.R. Salomon (2000) Infection by porcine endogenous retrovirus after islet xenotransplantation in SCID mice. *Nature* 407: 90-94 (IF 32.1)

PhD Students

- Michiel C. Warle (2000-2004)
- Ahmet Demirkiran (Nov 2002-planed defense end 2007)
- Scot Henry (Juli 2004-medio 2008)
- Varsha Segobind, together with dr. C. Baan and prof. W. Weimar (2006-2009)
- Vacancy, together with prof. H. Janssen (start March 2007)

(International) Awards

- 2006 Rising Star award as mentor at the International Liver Transplantation Congres (Milan, 3-6 May) (\$3.000)
- 2005 Biotest award for the best abstract in basic science at the European Society of Organ Transplantation Congres (Geneva, 15-19 Oct) (€2.500)
- 2005 Rising Star award as mentee at the International Liver Transplantation Congres (Los Angeles, 20-23 July) (\$3.000)

- 2005 Best presentation of session: Boot Congres of the Dutch transplantation society (Rolduc, 9-11 march) (€300)
- 2000 Research encouragement award from the Diabetes transplant fund (Washington, USA) (\$500)

Current Research Grant Support

- Erasmus MC Revolving Fund "monitoring donor reactivity in liver transplant patients" (€68.000)
- Gastro Start grant of the Dutch Gastroenterology Society for A. Demirkiran (€7.500)
- Erasmus MC *Translatieoneel Onderzoek* fund "Gene therapy for HCV recurrence" (€125.000)
- Erasmus MC *Translatieoneel Onderzoek* fund together with Dr. Carla Baan, Dept. Internal Medicine for a PhD project entitled "Induction of regulatory T cells for transplantation tolerance" (€150.000)
- Erasmus grants (de Jonge/vanderlaan) entitled "Accelerated liver regeneration in living-donor liver transplantation using cytokine priming and mobilized hepatic progenitor cells" (€50.000)
- Genmab (Utrecht) support for research on therapeutic hepatitis C virus antibodies (€57.000)
- Stichting SLO (Delta study, €40.000) funding research "Gene therapy for HCV recurrence"
- Novartis Pharma, Basel "preclinical research CsA and HCV" (€37.500)
- Annual material budget, depart of Surgery (€25.000).

Current Research Topics

Liver transplantation is the only adequate treatment for end-stage liver diseases. On the short-term it is a successful treatment, but long-term survival and quality of life is severely impaired by complications caused by continuous immunosuppressive treatment and hepatitis virus re-infection. These clinical problems are the bases of my research, which is focused on the role of regulatory T cells (Treg) in transplantation tolerance and the impact of immunosuppressive drugs on these cells and the replication of hepatitis C virus (HCV). The long-term objectives are to defining parameters that predict immune tolerance in order to optimize immunosuppressive therapy and to develop gene therapy and hepatic stem cells mobilization as novel therapies for prevention of HCV-recurrence and the acceleration of liver regeneration.

International Collaboration

- University of Heidelberg, Germany: Prof. Dr. R. Bartenschlager
- Kumamoto University, Japan: Prof. Dr. M. Takeya
- Karolinska Institute, Stockholm, Sweden: Prof. Dr. K. Tryggvason
- Scripps Research Institute, La Jolla, CA: Dr D.R. Salomon

Name

Jon Laman

CV

Doctoraal Medische Biologie, specialisaties immunologie en celbiologie, Vrije Universiteit Amsterdam 1987

Promotie traject afd. Celbiologie Vrije Universiteit

Promotie Erasmus Universiteit Rotterdam "Antibody formation and follicular immune complexes" 1992 (promotor prof.dr. J.J. Haaijman, copromotores dr. E. Claassen, dr. W.J.A. Boersma)

Postdoctoral fellow bij dr. R.J. Noelle, Dartmouth College (Ivy League), Lebanon, New Hampshire, USA 1993-1994

Wetenschappelijk medewerker TNO Preventie en Gezondheid, Leiden, 1995-1997

Universitair docent/hoofddocent afd. Immunologie Erasmus Universiteit/Erasmus MC, vanaf 1997

Bijzonder hoogleraar Immuunregulatie Erasmus Universiteit/Erasmus MC 2005

Selected publications

CD40-CD40 ligand interactions in experimental allergic encephalomyelitis and multiple sclerosis. K. Gerritse, J.D. Laman, R.J. Noelle, A. Aruffo, J.A. Ledbetter, W.J.A. Boersma and E. Claassen. Proceedings National Academy of Sciences USA 93:2499-2504 (1996)

A new primate model for multiple sclerosis in the common marmoset. B.A. 't Hart, M. van Meurs, H.P.M. Brok, L. Massacesi, J. Bauer, L. Boon, R.E. Bontrop and J.D. Laman. Immunology Today 21:290-297 (2000)

Transfer of central nervous system autoantigens and presentation in secondary lymphoid organs. A.F. de Vos, M. van Meurs, H.P. Brok, L.A. Boven, R.Q. Hintzen, P. van der Valk, R. Ravid, S. Rensing, L. Boon, B.A. 't Hart and J.D. Laman. Journal of Immunology 169:5415-5423 (2002)

Myelin-laden macrophages are anti-inflammatory consistent with foam cells in multiple sclerosis. L.A. Boven, M. van Meurs, M. van Zwam, A. Wierenga-Wolf, R.Q. Hintzen, R.G. Boot, J.M. Aerts, S. Amor, E.E. Nieuwenhuis and J.D. Laman. Brain 129:517-526 (2006)

Phagocytes containing a disease-promoting Toll-like receptor/Nod ligand are present in the brain during demyelinating disease in primates. L. Visser, M.J. Melief, D. van Riel, M. van Meurs, E.A. Sick, S. Inamura, J.J. Bajramovic, S. Amor, R.Q. Hintzen, L.A. Boven, B.A. 't Hart and J.D. Laman. The American Journal of Pathology 169:1671-1685 (2006)

PhD studenten

- ir. Marloes van Zwam
- drs. Yolanda Kap
- drs. Eveline de Geus
- vacature nieuw project

Current research support

- Programma subsidie Stichting MS Research (hoofdaanvrager dr. R.Q. Hintzen)
- PhD project Stichting MS Research (start 1 januari 2007)
- Fellowship Stichting MS Research dr. L.A. Boven

Name

Bart N. Lambrecht, professor MD PhD

Department of Respiratory Diseases
University Hospital Ghent
De Pintelaan 185
B9000 Gent Belgium

tel (32)93328784

b.lambrecht@erasmusmc.nl

Born in Ghent, Belgium on 19/04/1968

Qualifications

- Doctor of Medicine, Surgery and Obstetrics (M.D.) from the University of Ghent, summa cum laude (July 1993).
- Doctor in Biomedical Sciences (PhD), from the University of Ghent, summa cum laude (December 1999).
- Registered as Pulmonary Physician by the Dutch Society of Tuberculosis and Pulmonary Medicine (NVALT) and the Medical Specialist Registration Commission (MSRC) from september 2002.
- Registered as Pulmonary Physician in Belgium since october 2007.
- United States Medical Licensing Examination (USMLE) step 1 and step 2
- Educational Commission for Foreign Medical Graduates (ECFMG) certificate in may 1996.

Current employment

- Since july 2005 Professor of Pulmonary Medicine, holding a special chair in 'Immunopathology of the lung' at Erasmus University Medical Center, Rotterdam, The Netherlands (bijzonder hoogleraar)
- Since october 2007 Full Professor of Pulmonary Medicine, Ghent University, Belgium (gewoon hoogleraar)

Prior employment

- October 1993-september 1994 : Residency in Internal Medicine
- October 1994-september 1998 : PhD project on "the contribution of dendritic cells to the induction and maintenance of eosinophilic airway inflammation under the supervision of Prof. Dr. R. Pauwels, University of Ghent, Belgium.
- October 1998-august 2002 : Fellow in training in Pulmonary Medicine at the Department of Pulmonary and Critical Care Medicine, Erasmus University Rotterdam, Dijkzigt and Daniel den Hoed Hospitals, Rotterdam under the supervision of Prof. Dr. H.C. Hoogsteden.
- October 1998-august 2002 : Research Fellow (Postdoc) in charge of animal models of airway inflammation, Pulmonary Medicine Research Lab, Erasmus University Rotterdam.
- September 2002-june 2005 appointment as staff Pulmonary Physician at Erasmus MC, Chief Academic Specialist level.
- March 2002-oct 2007 head of the laboratory of Pulmonary Medicine, leading a group of 20 scientists and technicians.
- May 2005-oct 2007, Adjunct-trainer in Pulmonary Medicine (plaatsvervangend opleider), with a legal status to train specialists in pulmonary medicine.

Academic activities

Royal Academy of Arts and Sciences

- Since 2005 elected as member of the Royal Dutch Academy of arts and Sciences (KNAW) Junior Academy member. Appointed for 5 years. It is the mission of this Academy to promote and analyze science in The Netherlands through a multidisciplinary approach

International Scientific committees

- Founding member of the Junior Member Assembly (JMA) of the European Academy of Allergy and Clinical Immunology (EAACI).
- Member of the Asthma Panel of the EAACI, with a responsibility in generating didactic materials and guidelines, writing and evaluating position papers, collaborating with other international societies (American Thoracic Society/European Respiratory Society), and providing part of the scientific program of the yearly EAACI meeting.
- Member of the planning committee of the European Respiratory Society Allergy and Immunology section
- Member of the Pharmacia Allergy Research Foundation

National Scientific committees

- Former Chairman of the Experimental and Descriptive Research Program working group of the Dutch Asthma Foundation (NAF). 2003-2007.
- Secretary of the Asbestos Cancer Foundation, Rotterdam. It is the mission of this foundation to improve the diagnosis and management of mesothelioma.

Editorial Boards

- Advisory Editor, The Journal of Experimental Medicine
- Associated Editor, Mucosal Immunology (Nature Publishing Group)
- Member of the editorial board of Clinical and Experimental Allergy,
- Member of the editorial board of Allergy

Organizing Meetings

- **Keystone Symposium on Allergy and Allergic Diseases** I will organize this meeting in January 2009 together with Dr Catherine Hawrylowicz and Dr Stephen Galli.
- **Keystone symposium on 'Eicosanoids in Inflammation and Immunity'** January 2008 together with G. Fitzgerald and R. Soberman.
- **Frontiers of Mucosal Immunology.** Organized in 2006 and 2004 together with Dr E. Nieuwenhuis in Rotterdam. This meeting had international speakers and a two day interactive workshop programme.

Awards and scholarships

- The Antoine Faes Award 2008
- The InBev-Baillet Latour award 2008
- The 'Vlaamse Liga tegen Kanker' chair in experimental cancer medicine 2008-2009
- The European Respiratory Society 'Romain Pauwels' Research Award 2005 (50.000 euro)
- The Pharmacia Allergy Research Foundation Award 2004 (Highest international scientific award in the field of allergy worldwide, 50.000 USD)
- The Pharmacia Award (Belgium) for best PhD thesis period 1999-2000, University of Ghent, 2001.

- The 13th Boehringer Ingelheim Award for Respiratory Medicine, Belgian Society of Pulmonary Medicine, Brussels, 2000 (Highest scientific award for pulmonary medicine in Belgium, 15.000 Euro)
- The R. de Beule Prize 2000, The Flemish and Dutch Study Group of Allergologists, Bilzen, 2000.
- Honourable Mention and scholarship award, Pharmacia Allergy Research Foundation, Sydney, 2000.
- Shering Plough Respiratory 2000 International Young Investigator Award, New York, 1998.
- The 1998 European Respiratory Society annual allergy and immunology award, ERS meeting , Geneva, 1998.
- Best Presentation Award, Belgian Immunological Society (BIS) Meeting, 1998
- Respiratory Basic Science Award, Belgian Society of Pulmonary Medicine, 1998
- Horlait-Dapsens Scholarship for Extended Study Abroad, 1996.
- Senior Lecturer award , Belgian Society of Pulmonary Medicine, 1996.

Grants acquired

- Fund for Scientific Research Vlaanderen (FWO Vlaanderen) Aspirant Onderzoeker from 1994-1998. This grant was awarded to pay the applicant's salary and consumables during the PhD period and was awarded based on personal curriculum and scientific merit of the project.
- Dutch Asthma Foundation Grant Nr 99.37. entitled "Contribution of antigen presenting cells to the secondary phase of the allergic immune response in an experimental model of allergic asthma: target for new anti-asthma therapy?" (Applicants Lambrecht BN, Prins JB and Hoogsteden HC). Awarded 272.000 €, for 1 PhD student and 1 technician, end march 2003.
- Dutch Asthma Foundation Grant Nr. 32.00.45 Entitled "Gene-modified dendritic cells as tools for improving immunotherapy of asthma" (Applicants Lambrecht BN, Prins JB and Hoogsteden HC). Awarded 270.000 € for 1 PhD student and 1 technician, end march 2004.
- European Union (Marie Curie Foundation HPMF-CT-2000-01017) Entitled "Co-stimulatory molecules and sensitization to inhaled antigen" (Applicants Lambrecht BN and Hammad H). Awarded 142.000 € for 1 Post-doc, end september 2003.
- Dutch science foundation ZonMW program grant co-applicant (Applicants Yazdanbakhsh M, LUMC; Tielens AGM, UU; Lambrecht BN, EUR) "The expanding world of immunomodulation: molecular mechanisms and manipulation of inflammatory diseases by helminth-derived glycoconjugates and lipids". 1PhD student, 2 post-docs based at LUMC, Start 2003.
- Dutch science foundation ZonMW Replacement of animal experimentation program. "In vitro model for immunomodulation by RSV virus and vaccins" (Applicant Ruwaard D, RIVM). Project leader for part of the project. Start 2003.
- Dutch science foundation **Zon MW VIDI grant** (N W O) 2003 "The hygiene hypothesis of atopy : dendritic cells come clean". This project will run for 4 years, employing a postdoc, PhD student, and technician. (600.000 €)
- Dutch ICES/KIS Viral Genomics (VIRGO) co-applicant and work group leader for work package 2, studying the role of airway DCs in viral pathogenesis. 1 postdoc and technician. 620.000 €, start 1/5/2004.
- Dutch asthma foundation Grant 3.2.03.65. Use of plasmacytoid DCs to induce long lasting tolerance to inhaled allergens. 1 PhD student and technician for 4 years. 217.000 € Start april 2004.

- Mesothelioma Research Foundation of America (MARF) DCs as clinical vaccines in mesothelioma. 1 PhD student for 2 years, 100.000 \$, start 1/1/2004
- Deutsche Forschungsgemeinschaft (DFG) Grant to host a German Scientist for 3 years (Grant awarded to Dr Marco Idzko)
- Schweizerische National Fund (SNF) grant to host a Swiss scientist for 1 year (grant awarded to Dr Peter Gerber)
- European Respiratory Society long term fellowship grant to host Dr Peter Gerber for an additional 1 year.
- Mesothelioma Research Foundation of America (MARF) DCs as clinical vaccines in mesothelioma : initiation of clinical trial. 1 PhD student for 2 years, 100.000 \$, start 1/1/2006
- Several company sponsored grants to perform contract research or educational research grants (Millennium Pharmaceuticals, Procter and Gamble, AstraZeneca, Medimmune, Genfit, Novartis, Actogenix, GSK)
- Grant “Mechanism of Schistosoma mansoni induced suppression of allergic asthma” by Dutch asthma foundation, 1 PhD and technician, 217000 Euro, starts february 2007.
- Grant “**Odysseus I**” Application of dendritic cell biology to design of new immunotherapeutic interventions” This grant was awarded by the Flemish Government to attract scientists to Belgium, 7.5 million Euro, starts at Ghent University october 2007. This is the largest possible grant in Belgium.

PhD Thesis

- **Contribution of dendritic cells to the induction and maintenance of eosinophilic airway inflammation.** Promotor : Prof. Dr. Romain Pauwels, Director Department of Respiratory Diseases, University Hospital Ghent, Belgium, december 1999.
- Since 1998 co-promotor or promotor of 8 PhD students.

Selected Publications 2003-2008

- **The other cells in asthma : dendritic cells and epithelial cell crosstalk.** Lambrecht BN, Hammad H. Curr Opin Pulmon Med. 2003, 9:34-41
- **LPS-induced suppression of airway Th2 responses does not require IL-12 production by dendritic cells.** Kuipers H, Hijdra D, de Vries VC, Hammad H, Prins J.-B., Hoogsteden HC, Lambrecht BN. J. Immunol. 2003, 171:3645-3654
- **Airway eosinophils accumulate in the mediastinal lymph nodes but lack antigen-presenting potential for naive T cells.** Van Rijt LS, Vos N, Hijdra D, de Vries VC, Hoogsteden HC, Lambrecht BN. J. Immunol 2003, 171:3372-3378
- **Prostaglandin D2 inhibits airway dendritic cell migration and function in steady state conditions by selective activation of the D prostanoid receptor 1.** Hammad H, de Heer HJ, Souillie T, Hoogsteden HC, Trottein F, Lambrecht BN. J. Immunol. 2003, 171:3936-3940
- **Taking our breath away : dendritic cells in the pathogenesis of asthma.** Lambrecht BN, Hammad H. Nature Rev Immunol 2003, 3 (12):994-1003
- **Activation of peroxisome proliferators-activated receptor gamma in dendritic cells inhibits the development of eosinophilic airway inflammation in a mouse model of asthma.** Hammad H, de Heer HJ, Souillie T, Angeli V, Hoogsteden HC, Trottein F, Lambrecht BN. Am. J. Pathol. 2004, 164:263-271
- **Proteomic analysis of exosomes isolated from human malignant pleural effusions.** Bard MPL, Hegmans JPJJ, Luider TM, Willemsen R, Burgers SA, Severijnen EA, van Meerbeek JP, Hoogsteden HC, Lambrecht BN. Am J Respir Cell Mol Biol, 2004 31:114-121

- **Proteomic analysis of exosomes secreted by human mesothelioma cells.** Hegmans JP, Bard M, Luider TM, Burgers S, Hoogsteden HC, Lambrecht BN. *Am. J. Pathol.* 2004; 164:1807-1815
- A rapid flow cytometric method for determining the cellular composition of bronchoalveolar lavage fluid cells in mouse models of asthma¹ **van Rijt LS, Kuipers H, Vos N, Hijdra D, Hoogsteden HC, Lambrecht BN, *J. Immunol Meth*, 2004; 288:111-121**
- Essential role of dendritic cell CD80/CD86 costimulation in the induction but not reactivation of Th2 effector responses in a mouse model of asthma **van Rijt LS, Mariëtte Oosterwegel², Monique Willart, Alex KleinJan¹, Nanda Vos¹, Coyle AJ, Hoogsteden HC, Lambrecht BN, *J Allergy Clin Immunol* 2004; 114:166-73**
- **Dendritic cells in the pathogenesis of asthma** Lambrecht BN, Kuipers H, van Rijt L, Hammad H. *Clin Exp Allergy Rev* 2004; 4:1-6
- **Essential role of lung plasmacytoid dendritic cells in preventing asthmatic reactions to harmless inhaled antigen.** De Heer HJ, Hammad H, Souillie T, Hijdra D, Vos N, Willart MAM, Hoogsteden HC, Lambrecht BN. *J. Exp. Med* 2004; 200:89-98
- **Differential capacity of CD8a+ or CD8a- dendritic cell subsets to prime for eosinophilic airway inflammation in the Th2 prone milieu of the lung.** Hammad H, de Vries VC, Maldonado-Lopez R, Moser M, Maliszewski C, Hoogsteden HC, Lambrecht BN. *Clin Exp Allergy* 2004; 34:1834-1840
- **Dendritic cells retrovirally overexpression IL-12 induce strong Th1 responses to inhaled antigen in the lung but fail to revert established Th2 sensitization.** Kuipers H, Hijdra D, Muskens F, Heirman C, de Meirvenne S, Thielemans K, Hoogsteden HC and Lambrecht BN. *J. Leukocyte Biol*, 2004; 76:1028-1038
- **The interplay of dendritic cells, Th2 cells and regulatory T cells in asthma.** Kuipers H, Lambrecht BN. *Curr. Opin Immunology* 2004; 16(6):702-708
- **Dendritic cells and the regulation of the allergic immune response.** Lambrecht BN. *Allergy*, 2005; 60: 271-282
- **In vivo depletion of lung CD11c⁺ dendritic cells during allergen challenge abrogates the characteristic features of asthma**
- van Rijt LS, Jung S, Kleinjan A, Vos N, Willart M, Duez C, Hoogsteden HC, Lambrecht BN, *J. Exp. Med*, 2005, 201:981-991
- **Immunotherapy of murine malignant mesothelioma using tumor lysate pulsed dendritic cells.** Hegmans J, Hemmes A, Hoogsteden HC, Lambrecht BN. *Am. J. Respir. Crit. Care Med.* 2005, 171(10):1168-77.
- **Dendritic cell subsets and immune regulation in the lung.** De Heer HJ, Hammad H, Kool M, Lambrecht BN. *Seminars in Immunol*, 2005, 17(4):295-303.
- **Respiratory viral infections and asthma pathogenesis: a critical role for dendritic cells?** Van Rijt LS, Lambrecht BN. *J. Clin. Virol*, 2005, 34(3):161-9.
- **Modification of dendritic cell function as a tool to prevent or treat allergic asthma.** Kuipers H, Lambrecht BN. *Vaccine*, 2005, 23(37):4577-88.
- **Dendritic cells in asthma: a function beyond sensitization** Van Rijt LS, Lambrecht BN, *Clin Exp Allergy*, 2005. 35:1125-1134
- **An unexpected role for the anaphylatoxin C5a receptor in allergic sensitization.** Lambrecht BN. *J. Clin. Invest.* 2006 116:628-632
- **Alveolar macrophages in the driver's seat.** Lambrecht BN. *Immunity* 2006. 24:366-368

- **Mesothelioma environment comprises cytokines and Treg cells that suppress immune responses.** Hegmans J, Hemmes A, Hammad A, Boon L, Hoogsteden HC, Lambrecht BN. *Eur Respir J.* 2006; 27:1086-1092.
- **Essential role for nasal dendritic cells in human and experimental allergic rhinitis.** Kleinjan A, Willart M, van Rijt LS, Braunstahl G, Hoogsteden HC, Lambrecht BN. 2006. *J Allergy Clin Immunol.*2006, 118:1117-1125.
- **Recent progress in the biology of airway dendritic cells and implications for understanding the regulation of asthmatic inflammation.** Hammad H, Lambrecht BN. *J Allergy Clin Immunol* . 2006, 118:331-336
- **Contribution of the PD-1 ligands/PD-1 signaling pathway to dendritic cell-mediated CD4 + T cell activation.** Kuipers H, Muskens F, Willart M, Hijdra D, Van Assema FB, Coyle AJ, Hoogsteden HC, Lambrecht BN. *Eur J. Immunol.* 2006, 36:2472-2482
- **Local application of FTY720 to the lung abrogates experimental asthma by altering dendritic cell function.** Idzko M, Hammad H, van Nimwegen M, Souillie T, Hoogsteden HC, Lambrecht BN. *J. Clin Invest* 2006, 116:2935-2944
- **Dendritic cells in asthma : a target for novel therapeutics ?.** Leonie S.,Van Rijt. and Lambrecht BN. *Drug Discovery Today: therapeutic strategies*, 2006: 299-307
- **Mouse Models of asthma and rhinitis to study the role of dendritic cells in sensitization and development of inflammation.** Lambrecht BN, Kleinjan A. *Drug Discovery Today : disease models* 2006: 1-7
- **The pressure mounts on lung dendritic cells** Lambrecht BN, van den Toorn L. *Eur Resp J.* 2007 :29:1-3
- **Inhaled iloprost suppresses the cardinal features of asthma via inhibition of airway dendritic cell function** Idzko M, Hammad H, van Nimwegen M, Kool M, Hoogsteden HC, Lambrecht BN. *J. Clin Invest* 2007, 117:464-472.
- **Activation of the D prostanoid receptor suppresses asthma by modulation of lung dendritic cell function and induction of regulatory T cells.** Hammad H, de Heer HJ, Angeli V, Souillie T, Narumiya S, Trottein F, Hoogsteden HC, Lambrecht BN. *J. Exp. Med.*2007, 204:357-367.
- **HIF1a expression in bronchial biopsies correlates with tumor microvascular saturation determined using optical spectroscopy.** Joachim G. Aerts, Arjen Amelink, Joost P Hegmans, Annabrita Hemmes, Bianca Den Hamer, Dick Sterenberg, Henk C Hoogsteden, Bart N Lambrecht *Lung Cancer*, 2007, 57:317-321
- **Lung dendritic cell migration.** Hammad H and Lambrecht BN. *Adv. Immunol.* 2007, 93:265-278
- **Extracellular ATP triggers and maintains asthmatic airway inflammation by activating dendritic cells** Idzko M, Hammad H, van Nimwegen M, de Ferrara F, di Virgilio F, Virchow JC, Hoogsteden HC, Lambrecht BN. *Nature Medicine* 2007, 13:913-919
- **GATA-1 regulates dendritic cell development and survival** Guttierrez L, Nikolic T, van Dijk T, Hammad, H, Vos N, Willart M, Grosveld F, Philippsen S, Lambrecht BN. *Blood*, 2007, 110(6)1933-41
- **Protective effect of Schistosoma mansoni infection on allergic airway inflammation depends on the intensity and chronicity of infection.** Smits HH, Hammad H, van Nimwegen M, Souillie T, Willart M, Lievers E, Kadouch J, Kool M, Oosterhoud JK, Deelder AM, Lambrecht BN, Yazdanbakhsh M. (equal) *J. Allergy Clin Immunol* 2007, 120:932-940
- **Dendritic cells in asthma and COPD: opportunities for drug development.** Kool, M. and Lambrecht BN. *Curr. Opinion Immunol.* 2007, 19:701-710

- **Lung dendritic cells : from basic biology to clinical applications.** Lambrecht BN, *Acta Clin Belg* 2007, 62:330-334.
- **Dendritic cells and epithelial cells : Linking innate and adaptive immunity in Asthma** Lambrecht BN, and Hammad H. *Nature Rev. Immunol.* 2008, 8: 193-2004
- **Alum adjuvant boosts adaptive immunity by inducing uric acid and activating inflammatory dendritic cells** Kool M, Souillie T, Willart M, Jung S, Henk C. Hoogsteden, Hammad H , Lambrecht BN *J. Exp. Med.* 2008, march 27th issue

Name

Erik Lubberts, PhD

CV

Date of birth: 03-30-1967

Master's (MSc)

University: University of Groningen (RuG), The Netherlands

Year: 1994

Discipline: Biology, Medical Biotechnology

Doctorate (PhD)

University: University of Nijmegen (KuN), The Netherlands

Year: 1999

Supervisor ('Promoter'): Prof. Dr. W.B. van den Berg

Title of thesis: Role of interleukin-4 and interleukin-10 in the regulation of experimental arthritis.

March '05 – present

Head of Rheumatology Research Laboratory; Dept. Rheumatology / Immunology at the Erasmus Medical Center (Erasmus MC), Rotterdam, The Netherlands;

Sept '03-March '05

Program leader "cytokines and immunomodulation in inflammatory arthritis". Dept. of Rheumatology, Rheumatology Research and Advanced Therapeutics at the University Medical Center St Radboud, Nijmegen Center for Molecular Life Sciences (NCMLS);

July/Aug. 2003

Visiting scientist at Harvard Institute of Medicine, Boston, USA in the lab of Prof. E. Gravalles.

Keywords research: KRN arthritis model, transgenic mice, RANKL, osteoclasts; bone erosion;

Nov.2002-June 2003

Visiting scientist at LSU Health Sciences Center, New Orleans, USA in the lab of Prof. J.K. Kolls.

2000-2002

Project leader: "Role of IL-17 in joint inflammation and destruction during arthritis: dependence of RANKL/RANK pathway?". Dept. Rheumatology, University of Nijmegen;

1999-2000

Post-doc: "The role of IL-17 in experimental arthritis". Dept. Rheumatology, University of Nijmegen;

1995-1999

PhD student, Dept. of Rheumatology, University of Nijmegen

Selected Publications

- Koenders MI, Kolls JK, Joosten LAB, Oppers-Walgreen B, Schurr JR, Peschon JJ, Schwarzenberger P, Van den Berg WB, Lubberts E. IL-17 receptor deficiency results in impaired synovial expression of IL-1 and MMP-3,-9-13 and prevents cartilage destruction during chronic reactivated streptococcal cell wall-induced arthritis. *Arthritis Rheum.*, 2005, 52:3239-47.
- Lubberts E, Schwarzenberger P, Huang W, Schurr JR, Peschon JJ, Van den Berg WB, Kolls JK. Requirement of local synovial interleukin-17 receptor signaling in the progression of chronic synovitis and bone erosion. *J. Immunol.*, 2005, 175:3360-68.

- Lubberts E, Koenders MI, Van den Berg WB. The role of IL-17 in conducting destructive arthritis. Lessons from animal models. (Review) *Arthritis Res. & Therapy*, 2005, 7:29-37.
- Lubberts E, Oppers-Walgreen B, Coenen-de Roo CCJ, Van den Bersselaar L, Joosten LAB, Van den Berg WB. Anti-IL-17 treatment after onset of collagen-induced arthritis reduces joint inflammation, cartilage destruction and bone erosion. *Arthritis Rheum.* 50, 650-659, 2004.
- Lubberts E. The role of IL-17 in rheumatoid arthritis. (Review) *Current Opinion in Invest. Drugs* 4, 572-577, 2003.
- Lubberts E, Van den Bersselaar L, Oppers-Walgreen B, Schwarzenberger P, Coenen-de Roo CJJ, Kolls JK, Joosten LAB, Van den Berg WB. IL-17 Promotes Bone Erosion in Murine Collagen-Induced Arthritis Through Loss of the Receptor Activator of NF-kappaB Ligand/Osteoprotegerin Balance. *J. Immunol.* 170:2655-62, 2003.
- Lubberts E, Oppers-Walgreen B, Pettit A, Van den Bersselaar L, Joosten LAB, Goldring SR, Gravallesse EM, Van den Berg WB. Increase in expression of receptor activator of nuclear factor kappaB at sites of bone erosion correlates with progression of inflammation in evolving collagen-induced arthritis. *Arthritis Rheum.* 46:3055-64, 2002.
- Lubberts E, Joosten LAB, Oppers B, Van den Bersselaar L, Coenen-de Roo CJJ, Kolls JK, Schwarzenberger P, Van de Loo FAJ, Van den Berg WB. IL-1 independent role of IL-17 in synovial inflammation and joint destruction during collagen induced arthritis. *J. Immunol.* 167:1004-13, 2001.
- Chaubaud M, Lubberts E, Joosten L, Van den Berg W, Miossec P: IL-17 derived from juxta-articular bone and synovium contributes to joint degradation in rheumatoid arthritis. *Arthritis Res.* 3:168-77, 2001.
- Lubberts E, Joosten LAB, Chabaud M, van den Bersselaar L, Coenen-de Roo CJJ, Richards CD, Miossec P, van den Berg WB: IL-4 gene therapy for collagen arthritis suppresses synovium IL-17 and osteoprotegerin ligand and prevents bone erosion. *J. Clin. Invest.*, 105: 1697-1710, 2000.

PhD Students

- S. Tillemans: The role of auto-antibodies (anti-CCP) in the pathogenesis of arthritis
- F. Cornelissen: Is the novel IL-23/T_H-17 immune pathway critical in changing a self-limiting synovitis into a chronic and destructive arthritis?
- M.Koenders: "The interaction between T cell IL-17 and macrophage mediators such as TNF and IL-1 in the pathogenesis of arthritis" (Radboud University Medical Center, Nijmegen)

(International) Awards

- TALENT-Stipend of the Netherlands Organization for Scientific Research (NWO) to do research abroad (November 2002 – September 2003): performed research in the lab's of Prof J.K. Kolls, LSUHSC, New Orleans for 8 months (see ref. 1+2) and Prof. E. Gravalesse, Harvard Medical School, Boston for 2 months.
- VENI-fellowship: "The role of IL-17 in arthritis: dependence of RANKL-RANK pathway?" (Support of NWO for talented Young Investigators), 2002-2005.
- First prize winner, C. Gordon Van Arman Award, for Excellence in Inflammation Research, 10th National Conference Inflammation Research Association. The Homestead, Virginia, USA, September 27, 2000.
- Bertus Kemp-prize 2000 for the best thesis in the field of connective tissue pathology: "The role of interleukin-4 and interleukin-10 in the regulation of experimental arthritis". Papendal, The Netherlands, June 8, 2000.

Current Research Grant Support

- Erasmus MC grant: The role of auto-antibodies (anti-CCP) in the pathogenesis of arthritis
- Erasmus MC grant: Is the novel IL-23/T_H-17 immune pathway critical in changing a self-limiting synovitis into a chronic and destructive arthritis?

Current Research Topics

- The role of B cell / auto-antibodies (anti-CCP) in the pathogenesis of arthritis
- The role of T cell cytokines in arthritis and other autoimmune diseases
- The role of T_H-17 cells / immune pathway in arthritis and other autoimmune diseases
- osteo-immunology

International Collaboration

Prof. J.K. Kolls, Pittsburgh, USA

Prof. P. Miossec, Lyon, France

Prof. E. Gravallese, Boston, USA

Dr. P. Schwarzenberger, Mobile, USA

Dr. J. Tocker, Seattle, USA

Dr. Ling, Indianapolis, USA

Dr. Heegen, Boston, USA

Dr. N. Ghilardi, San Francisco, USA

Name:

Prof. Dr H.A. Martino Neumann

CV

- Born: July 10, 1950 Voorburg, the Netherlands
- 1976-1980 Student Dermatology by Prof. dr R.H. Cormane in Amsterdam
- Dermatologist at the district hospital in Helmond.
- Head of the department of Dermatology, University Maastricht.
- 2002-.... Head of the department of Dermatology, Erasmus MC.

Selected Publications

Atherosclerosis. 2007 Jan; 190(1):1-9.

Unfavorable cardiovasculair risk profiles in untreated and treated psoriasis patients.

Wakkee M, Thio HB, Prens EP, Sijbrands EJ, Neumann HA.

J Vasc Surg. 2006 Nov; 44(5):1051-4.

Residual varocosis veins below the knee after varicose vein surgery are not related to incompetent perforating veins.

Van Neer P, Kessels A, de Haan E, Estourgie R, Veraart J, Lijnen R, Neumann M.

Dermatol Surg. 2006 Feb;32(2):216-23.

Calculating the pressure and the stiffness in three different categories of class II medical elastic compression stockings.

Van der Wegen-Franken K, Roest W, Tank B, Neumann M.

Arch Dermatol. 2006 Feb;142(2):187-94.

Cost-effectiveness of Mohs Micrographic Surgery vs Surgical Excision For Basal Cell Carcinoma of the Face.

Essers BA, Dirksen CD, Nieman FH, Smeets NW, Krekels GA, Prins MH, Neumann HA.

Lancet. 2004 Nov 13-19;364(9447):1766-72.

Surgical excisions vs Mohs' micrographic surgery for basal-cell Carcinoma of the face: randomised controlled trial.

Smeets NW, Krekels GA, Ostertag JU, Essers BA, Dirksen CD, Nieman FH, Neumann HA.

Dermatol Surg. 2004 May;30(5):729-36; discussion 736.

A method for measuring the dynamic behaviour of medical compression Hosiery during walking.

Stolk R, Wegen van der-Franken CP, Neumann HA.

Br J Dermatol. 2003 Jan;148(1):102-9.

Lamin expression in normal human skin, actinic keratosis, squamousCell carcinoma and basal cell carcinoma.

Tilli CM, Ramaekers FC, Broers JL, Hutchison CJ, Neumann HA.

Dermatol Surg. 2003 Mar;29(3):221-6.

Ambulatory phlebectomy versus compression sclerotherapy: results of A randomized controlled trial.

De Roos KP, Niemann FH, Neumann HA.

J Invest Dermatol. 2002 Feb;118(2):239-45.

PpIX fluorescence kinetics and increased skin damage after intracutaneous injection of 5-aminolevulinic acid and repeated illumination.

Thissen MR, de Blois MW, Robinson DJ, de Bruijn HS, Dutrieux RP, Star WM, Neumann HA.

J Invest Dermatol. 2002 Jul;119(1):64-9.

Discriminating basal cell carcinoma from its surrounding tissue by Raman spectroscopy. Nijssen A, Bakker Schut TC, Heule F, Caspers PJ, Hayes DP, Neumann MH, Puppels GJ.

PhD Students

2000 M.R.T.M. Thissen

Treatment of basal cell carcinoma in the light of photodynamic therapy.

2001 A. Sommer

Laser Doppler imaging in dermatology: experimental and clinical application

2003 K-P. de Roos

Ambulatory Phlebectomy

2003 C.M.L.J. Tilli

Apoptosis and proliferation in basal cell carcinoma

2003 D.N. Kolbach

Leg symptoms after deep vein thrombosis; The complexity of a simple syndrome

2004 T. Raveh

Optimization of Incisions in Cutaneous Surgery including Mohs' Micrographic Surgery; The validity of paradigms in skin Surgery

2004 E.M. van der Snoek

STDs and HIV infection in men who have sex with men; Rotterdam cohort study

2004 N.W.J. Smeets

Refining Indications for Mohs Micrographic Surgery in Treatment of Basal Cell Carcinoma

2004 C.A. Schroeter

The Intense Pulse Light Systems: New treatment possibilities for vascular, pigmented lesions and hair removal

2005 R. Laeijendecker

Oral Lichen Planus

2006 J.U. Ostertag

Laser resurfacing in the treatment of potential malignant skin diseases

2006 P.J.F. Quadvlieg

From actinic keratoses to squamous cell carcinoma: a guideline for the children

2007 D.I.M. Kuipers
Shedding new light on the treatment of basal cell carcinoma

2007 P.A.F.A. van Neer
The role of incompetent perforating veins in varicose veins

2007 Mr. E.R.M. de Haas
ALA-PDT; the Treatment of Non-Melanoma Skin Cancer Re-illuminated

Current Research Grant Support

Pharmaceutical Grant Pharmo Database

Current Research Topics

- Evidence Based Phlebology
- Non melanoma skin cancer

International Collaboration

Int. Compression Club

Name

Jan Nouwen, MD MSc PhD

CV

Jan Nouwen was born on July 22nd 1963. After finishing Medical School (Erasmus University Rotterdam) in January 1989, he was trained in Internal Medicine and subsequently Infectious Diseases at the Erasmus MC, Rotterdam. Since 1999 he is staff member of the departments of Medical Microbiology & Infectious Diseases and Internal Medicine – Infectious Diseases section. Since January 2006 he is head of the Infectious Diseases section. He finished his PhD on 'Determinants, Risks and Dynamics of *Staphylococcus aureus* nasal carriage' in December 2004. Subsequent research has focused on MRSA eradication (Center of Expertise 'MRSA-eradication' Erasmus MC; SWAB committee 'Treatment of MRSA carriage') as well as HIV and Tuberculosis in research-poor settings with projects in Zambia: **MEET TB (M**acha - **E**rasmus MC **E**pidemiology and **T**reatment of **T**uberculosis) and **HIT-ICT (H**ealthcare **I**mprovement **T**hrough **I**nformation **C**ommunication **T**echnology) in cooperation with Erasmus MC, Macha Mission Hospital, Zambia, Malaria Institute At Macha MIAM), Zambia, Mukinge Hospital, Zambia, TNO-ICT, CDC-Zambia, FIND initiative WHO, Becton-Dickinson and AIDS Relief. He is coordinating the infectious and immune diseases curricula within the medical curriculum of the Erasmus MC and is the program director of the researchmaster programme 'Infection & Immunity' at Erasmus MC. For his efforts in medical education he received the 'teacher of the year award' in 2004.

Selected publications

- Yurtsever L, van Dijk JH, van der Poel MG, Buijtel PCAM, van Soolingen D, Hamahuwa M, Sikwangala P, Spurrier DJ, **Nouwen JL**, Penno MB. The Feasibility of Implementing a Modern Tuberculosis Laboratory in Rural Zambia (abstract 33). In: Program and Abstracts of the 2nd INTEREST Workshop (Dakar, Senegal) 2008.
- van Dijk JH, Spurrier DJ, van den Berge I, Kraak R, **Nouwen JL**. Determinants of mortality in patients on ART in a rural HIV cohort in Zambia. In Programs and Abstracts of the 2nd INTEREST Workshop (Dakar, Senegal) 2008.
- Emonts M, Uitterlinden AG, **Nouwen JL**, Kardys I, Maat MP, Melles DC, Witteman J, Jong PT, Verbrugh HA, Hofman A, Hermans PW, Belkum A. Host polymorphisms in interleukin 4, complement factor H, and C-reactive protein associated with nasal carriage of *Staphylococcus aureus* and occurrence of boils. *J Infect Dis*. 2008 May 1;197(9):1244-53.
- de Steenwinkel FD, Tak HV, Muller AE, **Nouwen JL**, Oostvogel PM, Mocumbi SM. Low carriage rate of group B streptococcus in pregnant women in Maputo, Mozambique. *Trop Med Int Health*. 2008 Mar;13(3):427-9.
- Melles DC, Pauw E, van den Boogaard L, Boelens HA, Peters J, Peeters JK, Witsenboer H, van Leeuwen WB, Verbrugh HA, van Belkum A, **Nouwen JL**. Host-microbe interplay in persistent *Staphylococcus aureus* nasal carriage in HIV patients. *Microbes Infect*. 2008 Feb;10(2):151-8. Epub 2007 Nov 9.
- Van Dijk J, Spurrier J, van den Berge I, Kraak R, **Nouwen JL**. Stavudine based ART regimens are associated with increased mortality in a HIV cohort in rural Zambia. In: Program and Abstracts of the 44th Annual Meeting of the Infectious Diseases Society of America (San Diego, CA) 2007.
- van Belkum A, Emonts M, Wertheim H, de Jongh C, **Nouwen JL**, Bartels H, Cole A, Cole A, Hermans P, Boelens H, Toom NL, Snijders S, Verbrugh H, van Leeuwen W. The role of

human innate immune factors in nasal colonization by *Staphylococcus aureus*. *Microbes Infect.* 2007 Aug 10

- Bogaert D, **Nouwen JL**, Hermans PW, Belkum A. Lack of Interference between *Streptococcus pneumoniae* and *Staphylococcus aureus* in HIV-infected individuals? *J Infect Dis.* 2006 Dec 1;194(11):1617-8.
- van den Akker EL, **Nouwen JL**, Melles DC, van Rossum EF, Koper JW, Uitterlinden AG, Hofman A, Verbrugh HA, Pols HA, Lamberts SW, van Belkum A. *Staphylococcus aureus* nasal carriage is associated with glucocorticoid receptor gene polymorphisms. *J Infect Dis.* 2006 Sep 15;194(6):814-8.
- **Nouwen JL**, Schouten J, Schneebergen P, Snijders S, Maaskant J, Koolen M, van Belkum A, Verbrugh HA. *Staphylococcus aureus* carriage patterns and the risk of infections associated with continuous peritoneal dialysis. *J Clin Microbiol.* 2006 Jun;44(6):2233-6.
- van Belkum A, Melles DC, Snijders SV, van Leeuwen WB, Wertheim HF, **Nouwen JL**, Verbrugh HA, Etienne J. Clonal distribution and differential occurrence of the enterotoxin gene cluster, egc, in carriage- versus bacteremia-associated isolates of *Staphylococcus aureus*. *J Clin Microbiol.* 2006 Apr;44(4):1555-7.
- **Nouwen JL**. Controlling antibiotic use and resistance. *Clin Infect Dis.* 2006 Mar 15;42(6):776-7.
- Wertheim HF, Melles DC, Vos MC, van Leeuwen W, van Belkum A, Verbrugh HA, **Nouwen JL**. The role of nasal carriage in *Staphylococcus aureus* infections. *Lancet Infect Dis.* 2005 Dec;5(12):751-62.
- **Nouwen JL**, Fieren MW, Snijders S, Verbrugh HA, van Belkum A. Persistent (not intermittent) nasal carriage of *Staphylococcus aureus* is the determinant of CPD-related infections. *Kidney Int.* 2005 Mar;67(3):1084-92.
- Claassen M, **Nouwen JL**, Fang Y, Ott A, Verbrugh H, Hofman A, van Belkum A, Uitterlinden A. *Staphylococcus aureus* nasal carriage is not associated with known polymorphism in the Vitamin D receptor gene. *FEMS Immunol Med Microbiol.* 2005 Feb 1;43(2):173-6.
- **Nouwen JL**. Determinants, risks and dynamics of *Staphylococcus aureus* nasal carriage (thesis). Rotterdam: Erasmus MC, 2004 (ISBN 90-8559-013-2)
- **Nouwen JL**, Boelens H, van Belkum A, Verbrugh H. Human factor in *Staphylococcus aureus* nasal carriage. *Infect Immun.* 2004 Nov;72(11):6685-8.
- **Nouwen JL**, Ott A, Kluytmans-Vandenbergh MF, Boelens HA, Hofman A, van Belkum A, Verbrugh HA. Predicting the *Staphylococcus aureus* nasal carrier state: derivation and validation of a "culture rule". *Clin Infect Dis.* 2004 Sep 15;39(6):806-11.
- Burger DM, Aarnoutse RE, Dieleman JP, Gyssens IC, **Nouwen JL**, de Marie S, Koopmans PP, Stek M Jr, van der Ende ME. A once-daily HAART regimen containing indinavir + ritonavir plus one or two nucleoside reverse transcriptase inhibitors (PIPO study). *Antivir Ther.* 2003 Oct;8(5):455-61.
- van Pelt C, **Nouwen JL**, Lugtenburg E, van der Schee C, de Marie S, Schuijff P, Verbrugh H, Lowenberg B, van Belkum A, Vos M. Strict infection control measures do not prevent clonal spread of coagulase negative staphylococci colonizing central venous catheters in neutropenic hemato-oncologic patients. *FEMS Immunol Med Microbiol.* 2003 Sep 22;38(2):153-8.
- Koning S, van Belkum A, Snijders S, van Leeuwen W, Verbrugh H, **Nouwen JL**, Op 't Veld M, van Suijlekom-Smit LW, van der Wouden JC, Verduin C. Severity of nonbullous *Staphylococcus aureus* impetigo in children is associated with strains harboring genetic markers for exfoliative toxin B, Panton-Valentine leukocidin, and the multidrug resistance plasmid pSK41. *J Clin Microbiol.* 2003 Jul;41(7):3017-21.

- Koning S, van Suijlekom-Smit LW, **Nouwen JL**, Verduin CM, Bernsen RM, Oranje AP, Thomas S, van der Wouden JC. Fusidic acid cream in the treatment of impetigo in general practice: double blind randomised placebo controlled trial. *BMJ*. 2002 Jan 26;324(7331):203-6.
- **Nouwen JL**, van Belkum A, Verbrugh HA. Determinants of *Staphylococcus aureus* nasal carriage. *Neth J Med*. 2001 Sep;59(3):126-33.
- **Nouwen JL**, Wielenga JJ, van Overhagen H, Lameris JS, Kluytmans JA, Behrendt MD, Hop WC, Verbrugh HA, de Marie S. Hickman catheter-related infections in neutropenic patients: insertion in the operating theater versus insertion in the radiology suite. *J Clin Oncol*. 1999 Apr;17(4):1304.
- **Nouwen JL**, van Belkum A, de Marie S, Sluijs J, Wielenga JJ, Kluytmans JA, Verbrugh HA. Clonal expansion of *Staphylococcus epidermidis* strains causing Hickman catheter-related infections in a hemato-oncologic department. *J Clin Microbiol*. 1998 Sep;36(9):2696-702.
- Bakker J, van Overhagen H, Wielenga J, de Marie S, **Nouwen JL**, de Ridder MA, Lameris JS. Infectious complications of radiologically inserted Hickman catheters in patients with hematologic disorders. *Cardiovasc Intervent Radiol*. 1998 Mar-Apr;21(2):116-21.

PhD Students

Janneke van Dijk (2006-current)

Feasibility and consequences of improving diagnostic capacity for HIV and TB rural Zambia

Femke Mollema (2007-current)

Methicillin-resistant Staphylococcus aureus (MRSA) in the community: consequences for the efficiency of the Dutch MRSA prevention policy

Reshmie Ramautarsing (2008-current)

Determinants of mortality in ART programs in Zambia and Thailand

Hannelore Bax (2008-current)

Human host genetic factors in nontuberculous mycobacterial infection

Cox van de Weg (to start in 2009)

Clinical relevance of non-tuberculous mycobacteria

(International) Awards

Juni 2004 Medical Education Council Erasmus MC:
MORE 'Teacher of the Year award' 2003-2004

November 2004 44th Interscience Conference on Antimicrobial Agents and Chemotherapy (Washington, DC):
GSK ICAAC Award 2004

December 2005 45th Interscience Conference on Antimicrobial Agents and Chemotherapy (Washington, DC):
ICAAC Program Committee Award 2005

Oktober 2007 'Futures Hub'

Current Research Topics

Determinants of *Staphylococcus aureus* nasal carriage
Tuberculosis diagnostics and treatment
ART roll-out in resource-poor settings

International Collaboration

Macha Mission Hospital, Zambia
Malaria Institute At Macha, Zambia
AIDSRelief Zambia
CDC-Zambia
Mansa General Hospital, Zambia
University of Zambia / University Teaching Hospital
Queen Elisabeth Teaching Hospital, Blantyre, Malawi
PharmAccess

Name

Edward E. S. Nieuwenhuis, MD, PhD

CV

Research fellowships:

1988 Laboratory of Clinical Immunology, Academic Medical Center, Amsterdam; subject: immune response in cystic fibrosis patients

1992-1993 Laboratory of Immunology, University of Utrecht; subject: cellular-immunological parameters during stress;

1995 Laboratory of Immuno-psychology, University of Newcastle, Australia; subject: immunological parameters during sleep-deprivation.

2000-2002 Research-Fellowship Mucosal Immunology and Gastroenterology at Brigham and Women's Hospital, Harvard Medical School, Boston, USA

Doctorate: September 27th 2002

Thesis: Immunotherapy: Drugs and Bugs

Postdoctoral training:

1986 internship Cardiac Surgery Center "Sant-Jordi", Barcelona, Spain;

1993-1994 Residency Pediatrics, Hospital Infantil Lorencita Villegas de Santos, Bogota, Colombia;

1991-1993 Medical Internships, University of Amsterdam

1994-1999 Residency in Pediatrics at Wilhelmina Children's Hospital, Utrecht and Catharina Ziekenhuis, Eindhoven;

1999-2000 Research-Fellowship Pediatric Immunology at Wilhelmina Children's Hospital, Utrecht Medical Center.

2002-2005 Fellowship Pediatric Gastroenterology.

2005-... Staff pediatric gastroenterologist, Sophia Children's Hospital, Rotterdam

Selectes publications

de Koning BA, van Dieren JM, Lindenberg-Kortleve DJ, van der Sluis M, Matsumoto T, Yamaguchi K, Einerhand AW, Samsom JN, Pieters R, Nieuwenhuis EE. Contributions of mucosal immune cells to methotrexate-induced mucositis. *Int Immunol.* 2006 Jun;18(6):941-9.

Nieuwenhuis EE, Blumberg RS. The role of the epithelial barrier in inflammatory bowel disease. *Adv Exp Med Biol.* 2006;579:108-16.

Damen GM, Hol J, de Ruiter L, Bouquet J, Sinaasappel M, van der Woude J, Laman JD, Hop WC, Buller HA, Escher JC, Nieuwenhuis EE. Chemokine production by buccal epithelium as a distinctive feature of pediatric Crohn disease. *J. Pediatr. Gastroenterol Nutr.* 2006 Feb;42(2):142-9.

Nieuwenhuis EE, Neurath MF, Corazza N, Iijima H, Trgovcich J, Wirtz S, Glickman J, Bailey D, Yoshida M, Galle PR, Kronenberg M, Birkenbach M, Blumberg RS. Disruption of T helper 2-immune responses in Epstein-Barr virus-induced gene 3-deficient mice. *Proc Natl Acad Sci U S A.* 2002 Dec 24;99(26):16951-6.

Heller F, Fuss IJ, Nieuwenhuis EE, Blumberg RS, Strober W. Oxazolone colitis, a Th2 colitis model resembling ulcerative colitis, is mediated by IL-13-producing NK-T cells. *Immunity*. 2002 Nov;17(5):629-38.

Nieuwenhuis EE, Matsumoto T, Exley M, Schleipman RA, Glickman J, Bailey DT, Corazza N, Colgan SP, Onderdonk AB, Blumberg RS. CD1d-dependent macrophage-mediated clearance of *Pseudomonas aeruginosa* from lung. *Nat Med*. 2002 Jun;8(6):588-93.

Name

Professor Dr. A.D.M.E. Osterhaus

CV

Professor Osterhaus started his career in Utrecht (The Netherlands) where he graduated with distinction at the faculty of veterinary sciences. In 1978 he received his PhD degree (with distinction) with Prof. Dr. M.C. Horzinek. He then moved to the RIVM in Bilthoven, where he would stay until 1994. Since then, he has been working at Erasmus MC in Rotterdam. Thirty years of experience in animal and human virology have resulted in a specific interest in viruses that ordinarily affect only animals but that can cross the species barrier. Osterhaus is now a leading authority, able to identify dangerous and elusive new viruses with speed and precision. Osterhaus' team reacted with exceptional speed to the SARS outbreak of 2003 and identified the responsible coronavirus within days. In 1997 Osterhaus and his team silenced sceptics when they proved that Avian Influenza (H5N1) could be transmitted to humans. On the basis of this discovery Osterhaus has enabled health authorities to prepare for potential outbreaks, and, as an individual, has campaigned determinedly for awareness, calling for a global taskforce to prepare for and combat viruses such as H5N1. Throughout his professional career Osterhaus and his team have identified around twenty 'new' viruses (such as the human metapneumovirus, hMPV and a novel human coronavirus, HCoV-NL) as well as countless new possible hosts. His research includes studies on virus reservoirs in wildlife, mechanisms of transmission and pathogenesis of zoonotic viruses. In addition, innovative fundamental research on the natural and vaccine-induced immune response and on antiviral drugs is performed to combat the threat posed by (zoonotic) virus infections. As part of his tireless active interest in public health, Prof. Osterhaus has acted as PhD mentor for ~40 students, written over 650 academic articles, created biotech companies and held several editorial positions. The continuous and groundbreaking work of the so-called 'virus hunter' has helped prevent and control the spread of deadly viruses and will continue to do so, saving countless lives and changing the face of world health today.

Selected Publications

Fouchier R, Kuiken T, Rimmelzwaan G, Osterhaus A.

Global task force for influenza.

Nature May 26;435(7041):419-420 (2005)

Kuiken T, Leighton FA, Fouchier RA, LeDuc JW, Peiris JS, Schudel A, Stohr K, Osterhaus AD.

Public Health. Pathogen surveillance in animals.

Science, Sep. 209(5741):1680-1681 (2005)

Ducatez MF, Olinger CM, Owoade AA, De Landtsheer S, Ammerlaan W, Niesters HG, Osterhaus AD, Fouchier RA, Muller CP.

Avian flu: multiple introductions of H5N1 in Nigeria

Nature Jul 6;442(7098):37-

Olsen B, Munster VJ, Wallensten A, Waldenstrom J, Osterhaus AD, Fouchier RA

Global patterns of influenza a virus in wild birds

Science Apr 21;312(5772):384-388

van Riel D, Munster VJ, de Wit E, Rimmelzwaan GF, Fouchier RA, Osterhaus AD, Kuiken T

H5N1 Virus Attachment to Lower Respiratory Tract

Science Apr 21;312(5772):399- (2006)

Stittelaar KJ, Neyts J, Naesens L, van Amerongen G, van Lavieren RF, Holy A, De Clercq E, Niesters HG, Fries E, Maas C, Mulder PG, van der Zeijst BA, Osterhaus AD
Antiviral treatment is more effective than smallpox vaccination upon lethal monkeypox virus infection
Nature Feb 9;439(7077):745-748 (2006)

Munster VJ, Baas C, Lexmond P, Waldenstrom J, Wallensten A, Fransson T, Rimmelzwaan GF, Beyer WE, Schutten M, Olsen B, Osterhaus AD, Fouchier RA.
Spatial, Temporal, and Species Variation in Prevalence of Influenza A Viruses in Wild Migratory Birds.
PLoS Pathog. 2007 May 11;3(5):e61

Verjans GM, Hintzen RQ, van Dun JM, Poot A, Milikan JC, Laman JD, Langerak AW, Kinchington PR, Osterhaus AD.
Selective retention of herpes simplex virus-specific T cells in latently infected human trigeminal ganglia.
Proc Natl Acad Sci U S A. 2007 Feb 27;104(9):3496-501.

Baras B, Stittelaar KJ, Simon JH, Thoolen RJ, Mossman SP, Pistor FH, van Amerongen G, Wettendorff MA, Hanon E, Osterhaus AD.
Cross-Protection against Lethal H5N1 Challenge in Ferrets with an Adjuvanted Pandemic Influenza Vaccine.
PLoS ONE. 2008 Jan 2;3(1):e1401. PMID: 18167560

de Swart RL, Ludlow M, de Witte L, Yanagi Y, van Amerongen G, McQuaid S, Yüksel S, Geijtenbeek TB, Duprex WP, Osterhaus AD.
Predominant infection of CD150+ lymphocytes and dendritic cells during measles virus infection of macaques.
PLoS Pathog. 2007 Nov;3(11):e178.

PhD students

- 2001 Thesis Dr.K.J.Stittelaar, Erasmus University Rotterdam (“Vaccination against measles. Evaluation of novel approaches”)
- 2001 Thesis Dr.P.P.Heinen, University of Utrecht (“Protective immunity against influenza in pigs”)
- 2002 Thesis Dr.C.A.van Baalen, Erasmus University Rotterdam (“Capacity of cytotoxic T lymphocytes to control the reproduction of human immunodeficiency virus”)
- 2002 Thesis Dr.L.Remeijer, Erasmus University Rotterdam (“Human herpes simplex virus keratitis: The pathogenesis revisited”)
- 2002 Thesis Dr.J.Maertzdorf, Erasmus University Rotterdam (“Pathogenesis of herpes simplex virus infections of the cornea”)
- 2003 Thesis B.Martina, University of Utrecht (“Seal herpesviruses: Characterisation, host susceptibility and vaccine development”)
- 2003 Thesis Dr. A.C.M. Boon, Erasmus MC Rotterdam (“Cytotoxic T Lymphocyte Mediated Immunity to Influenza”)
- 2003 Thesis Dr. L. de Waal, Erasmus MC Rotterdam (“Respiratory Syncytial Virus Anti-viral immunity in humans and macaques”)
- 2004 Thesis Dr. I. Van Benten, Erasmus MC Rotterdam

- 2004 Thesis Dr. M. Barends, Erasmus MC Rotterdam (“Respiratory Syncytial Virus (RSV) and Asthma”)
- 2004 Thesis Dr. B. van den Hoogen, Erasmus MC Rotterdam (“Human Metapneumovirus. Discovery, Characterisation and Associated Disease”)
- 2006 Thesis Dr. A.T.A. Mairuhu, Radboud University Nijmegen (“ Studies on clinical and pathophysiological aspects of dengue virus infection”)
- 2006 Thesis Dr. V. Munster, Erasmus MC Rotterdam (“Ecology, Evolution and Pathogenesis of Avian Influenza Viruses”)
- 2006 Thesis Dr. E. de Wit, Erasmus MC Rotterdam (“Molecular determinants of influenza A virus replication and pathogenesis”)
- 2007 Thesis Dr. E.G.M. Berkhoff, Erasmus MC Rotterdam (“ Evasion from human T cell immunity by influenza A viruses”)
- 2007 Thesis Dr. P. Koraka, Erasmus MC Rotterdam (“Dengue virus specific immune response: implications for laboratory diagnosis and vaccine development”)
- 2007 Thesis Dr. J. Philippa, Erasmus MC Rotterdam (“Vaccination of non-domestic species against emerging infectious diseases”)

(International) Awards

- 1985 Schimmel-Viruly Award: Faculty of Veterinary Medicine, Utrecht
- 1989 Heine-Medin Award: European Society against Virus Diseases
- 1992 Ciba Geigy Prize for Research in Animal Health
- 1993 Laureate Van Loghem lecture, Dutch Society for Immunology
- 1995 Firkin Oration, Australian Society for Medical Research
- 1998 M.W.Beijerinck Virology Award, Royal Dutch Academy of Sciences
- 2000 UK Royal Society invited lecture on Catastrophes after crossing species barriers
- 2000 Mulder-Masurel Award on influenza research
- 2002 The ESCV Gardner Lecture – Viruses emerging from animal reservoirs
- 2003 Commander in the Order of the Dutch Lion - Royal decoration
- 2004 James H. Nakano Citation – CDC prize for exceptional scientific publications.
- 2004 Dr. Saal van Zwanenberg-Oragon prize for exceptional achievement in promoting scientific research
- 2004 Reinier de Graaf medal – for exceptional contribution to medicine
- 2006 Federa prize – for original and exceptional research achievements
- 2006 European Respiratory Society – European Lung Foundation Award – recognition of the contribution to the public lung health in Europe
- 2007 Prix scientifique Louis D – Académie des sciences de l’Institut de France – research done in the field of transmissible diseases from man to animals, anthroozoonoses.

Name

E.P. Prens, MD, PhD

CV

Errol Prens (1956) earned his MD degree in 1981 at the University of Groningen and became a certified Dermatologist in 1985 after receiving his training in the department of Dermatology and Venerology in the Erasmus University Medical Center in Rotterdam. He joined the department of Immunology of the same hospital for research on skin inflammation, resulting in his thesis 'Immunopathophysiology of psoriasis; studies on accessory cells, cytokines and their receptors', Erasmus University Rotterdam (1992). Certification as an Immunologist followed in 1993 (SMWBO). He combined his position as a postdoctoral fellow and leader of the Experimental Immunodermatology group in the department of Immunology of the Erasmus MC, with his work as an all-round dermatologist in Ziekenhuis Walcheren in Vlissingen. In 2005 he was appointed professor of Experimental Dermatology at the Erasmus University and Medical Center Rotterdam. He is an author of over 50 peer reviewed papers and reviewer for several international Dermatological and Immunological journals, co-founder and board member of the Dutch Society for Experimental Dermatology, and member of the scientific committee of the international congress "Psoriasis from Gene to Clinic" in London, which is organized every three years.

Selected Publications

- Companjen AR, Prens E, Mee JB, Groves RW. Expression of IL-18 in human keratinocytes. *J Invest Dermatol.* 2000;114:598-9.
- Companjen AR, van der Wel LI, Wei L, Laman JD, Prens EP. A modified ex vivo skin organ culture system for functional studies. *Arch Dermatol Res.* 2001; 293:184-90.
- Companjen AR, van der Wel LI, Boon L, Prens EP, Laman JD. CD40 ligation-induced cytokine production in human skin explants is partly mediated via IL-1. *Int Immunol.* 2002;14:669-76.
- Van der Fits L, Van der Wel LI, Laman JD, Prens EP, Verschuren MCM. Psoriatic lesional skin exhibits an aberrant pattern of Interferon Regulatory Factor-2 (IRF-2). *J Pathol* 2003,199: 107-114.
- Van der Fits L, van der Wel LI, Laman JD, Prens EP, Verschuren MC. In psoriasis lesional skin the type I interferon signaling pathway is activated, whereas interferon-alpha sensitivity is unaltered. *J Invest Dermatol.* 2004, 122:51-60
- Knijff EM, Kupka RW, Ruwhof C, Breunis N, Prens EP, Nolen WA, Drexhage HA. Evidence that the immunopathogenic mechanism of lithium-induced psoriasis differs from that of regular psoriasis. *Bipolar Disorders* 2005; 7: 388-389.
- Bos WE, Thio HB, Neumann HA, van der Fits L, Prens EP. The pathogenesis of inflammatory dermatoses, especially psoriasis. *Ned Tijdschr Geneesk.* 2006;150:179-83. Review Dutch
- Bos WE, Thio HB, Neumann HA, van der Fits L, Prens EP. New systemic treatments for psoriasis: etanercept, infliximab, adalimumab, efalizumab and alefacept. *Ned Tijdschr Geneesk.*2006; 150:1065-70. Review Dutch.
- Wakkee M, Thio HB, Prens EP, Sijbrands EJ, Neumann HA. Unfavorable cardiovascular risk profiles in untreated and treated psoriasis patients. *Atherosclerosis.* 2007;190:1-9.Review.
- Van der Fits L, Kant M, Van der Wel LI, Prens EP. Polymorphisms in the Interferon Regulatory Factor-1 Promoter are not associated with Psoriasis, and do not influence IFN- α -induced Th1 Polarization. *J Interferon & Cytokine Research,* 2007

PhD Students

- Companjen
- E. Rácz
- E. Baerveldt

Current Research Topics:

Skin inflammation with emphasis on the innate skin immune response and its molecular regulation

International Collaboration:

J.T. Elder, Ann Arbor, USA

M. Girardi, New Haven, USA

R. Edelson, New Haven, USA

L. VandenAbeelee, Leuven, Belgium

M. Parmentier, Brussel, Belgium

G. Girolonimo, Rome, Italy

Name

Guus Rimmelzwaan

CV

Guus Rimmelzwaan MSc PhD, received his MSc degree in Biology (Cum Laude) from the Free University of Amsterdam (1985) and he defended his PhD thesis (on Canine parvovirus infections) successfully at the University of Utrecht (1990). From 1990-1992 he was a postdoctoral fellow at the National Institute of Public Health and Environmental Protection in Bilthoven and from 1992-1994 at the Faculty of Medicine, University of Amsterdam, working on lentivirus vaccine development. During this period he worked at the National Cancer Institute in Frederick, MD, USA for 1½ year. Since 1994 he works as project leader in the department of virology at the Erasmus Medical Center, which also harbors the WHO-National influenza center (NIC). He is responsible for the workgroup influenza immunology and the NIC activities and co-authored > 130 international peer-reviewed papers. Since 2002 he is head of the research unit of the department of virology

Selected Publications

- Rimmelzwaan GF, Kuiken T, van Amerongen G, Bestebroer TM, Fouchier RAM and Osterhaus ADME. The pathogenesis of influenza A (H5N1) virus infection in a primate model. *J. Virol.* 75(14):6687-6691 (2001)
- Boon ACM, de Mutsert G, Grauss YMF, Fouchier RAM, Sintnicolaas K, Osterhaus ADME and Rimmelzwaan GF. The magnitude and specificity of influenza A virus-specific cytotoxic T-lymphocyte response in humans is related to HLA-A and B phenotype. *J. Virol.* 76(2):582-590 (2002)
- Gog J, Rimmelzwaan GF, Osterhaus ADME and Grenfell B
- Population dynamics of rapid fixation in CTL escape mutants in influenza A
- *Proc. Natl. Acad. Sci. USA*, 100 (19):11143-11147 (2003)
- 4.. Boon ACM, de Mutsert G, van Baarle D, Sintnicolaas K, Smith D, Lapedes A, Fouchier RAM, Osterhaus ADME, and Rimmelzwaan GF. Recognition of homo and heterosubtypic variants of influenza A viruses by human CD8+ T cells. *J. Immunol.* 172:2453-2460 (2004)
- Boon ACM, de Mutsert G, Fouchier RAM, Sintnicolaas K, Osterhaus ADME and Rimmelzwaan GF. Preferential HLA usage in the influenza virus specific cytotoxic T lymphocyte response. *J. Immunol.* 172(7):4435-4443 (2004)
- Berkhoff EGM, Boon ACM, Nieuwkoop NJ, Fouchier RAM, Sintnicolaas K, Osterhaus ADME and Rimmelzwaan GF. A mutation in the HLA-B*2705 restricted NP₃₈₃₋₃₉₁ epitope affects the human influenza A virus specific CTL response in vitro. *J. Virol.* 78(10):5216-5222 (2004)
- Rimmelzwaan GF, Berkhoff EGM, Nieuwkoop NJ, Fouchier RAM and Osterhaus ADME. Functional compensation of a detrimental amino acid substitution in a CTL epitope of influenza A viruses by co-mutations. *J. Virol.* 78(16):8946-8949 (2004)
- Berkhoff EGM, de Wit E, Geelhoed-Mieras MM, Boon ACM, Fouchier RAM, Osterhaus ADME and Rimmelzwaan GF. Functional constraints of influenza A virus CTL epitopes limit escape from Cytotoxic T Lymphocytes. *J. Virol.* 79(17):11239-46 (2005)
- Rimmelzwaan GF, van Riel D, van Amerongen G, Baars M, Fouchier R and Osterhaus A, Kuiken T. Influenza A virus (H5N1) infection in domestic cats causes systemic disease with possible novel routes of virus spread within and between hosts. *Am. J. Pathol.* 168:176-183 (2006)

- Boon ACM, de Mutsert G, Fouchier RAM, Osterhaus ADME and Rimmelzwaan GF. The hyper variable NP₄₁₈₋₄₂₆ epitope from the influenza A virus nucleoprotein is recognized by cytotoxic T lymphocytes with high functional avidity J. Virol. 80(12):6024-6032 (2006)

PhD Students

- J.T.M. Voeten. Influenza, New vaccines and antiviral Immunity (2000)
- A.C.M. Boon. Cytotoxic T lymphocyte-mediated immunity to influenza (2003)
- E.G.M. Berkhoff. Evasion of influenza A viruses from human T-cell immunity (2007)
- J.H.C.M. Kreijtz. Immunity to influenza virus infections (2005-present)

Current Research Grant Support

- Nivarec ZonMW grant
- AIDS-fonds
- EU grant FLUVAC
- TI PHARMA

Current Research Topics

- Influenzavirus vaccine development,
- Development of animal models for influenza and pathogenesis
- immunity to influenza viruses, cell-mediated immunity in particular
- influenza virus epidemiology,
- virus host interactions.

International Collaboration

- Paul Ehrlich Institute, Dr. G. Sutter
- Institute Nationale de recherche Agronomique (INRA), Dr. B. Riteau
- University of Cambridge, Dr. D. Smith, Dr. J. Gog
- Pennstate University, Dr. B. Grenfell
- Karolinska Institute, Dr. K. Ljungberg
- University of Perugia, Dr. AM. Iorio
- WHO collaborating reference Center London, Dr. A.Hay

Name

Janneke N. Samsom

CV

Jan. 2005 until now: Assistant professor (1fte, tenured) at the dept. of Pediatric Gastroenterology and Nutrition ErasmusMC Rotterdam.

2003 – Dec. 2004: Assistant professor (1fte, tenured) at the department of Molecular Cell Biology and Immunology (MCBI), VUMC, Amsterdam.

Primary interest: investigating differentiation, fate and plasticity of regulatory T cells during mucosal tolerance. Research performed in a group with supervision (co-promotor) of 2 PhD students (both have defended their thesis in 2004); 2 technicians; several under-graduate students.

2002 – 2003: Senior Researcher (1fte, fixed-term) at the department of MCBI VUMC

1998 – 2002: Post-doctoral research position (1 fte, fixed-term) at the department of MCBI under supervision of Prof. Dr. G. Kraal.

1997 -1998: Post-doctoral research position (1 fte, fixed-term) at the department of mammalian Virology at the institute for animal science and health.

Dec. 4th 1996: Doctorate date: Leiden University, Dept of infectious diseases

Supervisor Prof Dr R. van Furth.

Selected Publications

- van Dieren JM, van der Woude CJ, Kuipers EJ, Escher JC, Samsom JN, Blumberg RS, Nieuwenhuis EE. Roles of CD1d-restricted NKT cells in the intestine. *Inflamm Bowel Dis*. 2007 May 2
- Kraal G, Samsom JN, Mebius RE. The importance of regional lymph nodes for mucosal tolerance. *Immunol Rev*. 2006 Oct;213:119-30. Review.
- van Dieren JM, Kuipers EJ, Samsom JN, Nieuwenhuis EE, van der Woude CJ. Revisiting the immunomodulators tacrolimus, methotrexate, and mycophenolate mofetil: their mechanisms of action and role in the treatment of IBD. *Inflamm Bowel Dis*. 2006 Apr;12(4):311-27.
- Hauet-Broere F, Unger WW, van Berkel LA, Garssen J, Hoijer MA, Kraal G, Samsom JN. New cohorts of naive T cells exacerbate ongoing allergy but can be suppressed by regulatory T cells. *Allergy*. 2005 Dec;60(12):1530-6.
- Samsom JN, van Berkel LA, van Helvoort JM, Unger WW, Jansen W, Thepen T, Mebius RE, Verbeek SS, Kraal G. Fc gamma RIIB regulates nasal and oral tolerance: a role for dendritic cells. *J Immunol*. 2005 May 1;174(9):5279-87.
- Samsom JN. Regulation of antigen-specific regulatory T-cell induction via nasal and oral mucosa. *Crit Rev Immunol*. 2004;24(3):157-77. Invited review.
- van Helvoort JM, Samsom JN, Chantry D, Jansen W, Schadee-Eestermans I, Thepen T, Mebius RE, Kraal G. Preferential expression of IgG2b in nose draining cervical lymph nodes and its putative role in mucosal tolerance induction. *Allergy*. 2004 Nov;59(11):1211-8.
- Unger WW, Hauet-Broere F, Jansen W, van Berkel LA, Kraal G, Samsom JN. Early events in peripheral regulatory T cell induction via the nasal mucosa. *J Immunol*. 2003 Nov 1;171(9):4592-603.
- Hauet-Broere F, Unger WW, Garssen J, Hoijer MA, Kraal G, Samsom JN. Functional CD25- and CD25+ mucosal regulatory T cells are induced in gut-draining lymphoid tissue within 48 h after oral antigen application. *Eur J Immunol*. 2003 Oct;33(10):2801-10.

- Unger WW, Jansen W, Wolvers DA, van Halteren AG, Kraal G, Samsom JN. Nasal tolerance induces antigen-specific CD4+CD25- regulatory T cells that can transfer their regulatory capacity to naive CD4+ T cells. *Int Immunol.* 2003 Jun;15(6):731-9.

PhD Students

- J. van Dieren: Immunoregulation in IBD (collaboration with Prof. dr. E. Kuipers)
- J. Hol: Commensal-Host Interactions in Pediatric Allergy Patients (collaboration with Prof. dr. J.C. de Jongste, Senter)
- G. Damen: The role of the Epithelial Barrier in Pediatric IBD
- R. Louwen: Pathogen Host Interactions in the Guillain-Barré Syndrome (coll. with Prof. dr. A. van Belkum)
- P. van Lierop: Mucosal Antigen Presentation in IBD (collaboration with Prof. dr. B.N.M. Lambrecht; MRACE)
- M. Kuif: Dendritic Cell Function in the Guillain-Barré Syndrome (collaboration with Dr. B.C. Jacobs, MRACE)
- F. du Pré: Identification of human mucosal regulatory T-cells (SSWO 470)
- F. Hauet-Broere, (defense May 7th 2004) Thesis entitled: Regulatory T cells in oral tolerance
- W. Unger, (defense November 5th 2004) Thesis entitled: Induction, fate and function of TR cells induced via the nasal mucosa.

Current Research Grant Support

- December 2006: Stichting Sophia Kinderziekenhuis Fonds (technician) *"Inflammatory Bowel Disease: Gain of function or loss of function? A study in a novel Zebrafish Colitis model"* (euro 111.000)
- December 2006: Stichting Sophia Kinderziekenhuis Fonds (technician) *"Regulation of the T-cell response to gluten."* (euro 111.000)
- July 2006: Erasmus MC Grants 2006: *"Regulation of the T-cell response to gluten."* (euro 50.000)
- July 2006: Erasmus MC Grants 2006: *"Cellular mechanism driving the antibody response to Campylobacter jejuni causing the Guillain-Barré syndrome"*. (euro 213.256) (project leader: dr. B. Jacobs Neurology)
- December 2005: Maag Lever Darm Stichting MWO 05-29 *"immune regulation of remission during IBD"* (euro 119. 461)
- January 2004: Sophia BV *"Immunosuppressive activity of Phosphatidyl-inositol"* (euro 898.000)
- November 2004: Stichting Sophia Kinderziekenhuis Fonds (pHD student): *Identification of human mucosal regulatory T-cells* (euro 250.000)

Current Research Topics

Major research interest

The laboratory of Pediatric Gastroenterology has chosen to fully direct its research to mucosal immunology. The lab. has established an ideal setting to investigate the intricate networks of mucosal immune regulation from the patient to fundamental mouse model and from a cellular to a molecular level. The two main lines of research are aimed at identifying innate immune regulatory factors on one hand and adaptive regulatory processes on the other hand. Our research will lead to identification of innate and adaptive processes that are pivotal in gastro-intestinal homeostasis and provide novel opportunities to enhance immune regulation in several phases of disease.

The translation to the clinic

Of great value is the solid, very direct link of research with the clinic. Our department of Pediatric Gastroenterology, ErasmusMC serves as coordinating center for the European Registry of *Pediatric IBD* patients. This initiative aims at establishing a forum facilitating collaborative European studies in Pediatric IBD. Together with Dr. J.C. Escher we aim at developing a bidirectional approach: key questions from the clinic concerning pathology, diagnosis and treatment of IBD are translated to an experimental setting. In parallel, similar initiatives are developed in the field of *Celiac disease* by taking advantage of the recently acquired knowledge and expertise in translational IBD research.

International Collaboration

We have a close collaboration with Prof. Dr. RS Blumberg, Harvard Medical School, Boston USA (mucosal immunology) ; Prof. Dr. CE Elson, University of Alabama at Birmingham, USA expert in Mucosal Immunology (IBD and intestinal Microbiota); Dr. F. Lund Trudeau Institute, Saranac Lake, NY, USA (molecular immunology). Prof. dr. Lars Fugger MRC Human Immunology Unit and Department of Clinical Neurology, Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, University of Oxford, United Kingdom. (humanized mouse models)

Name

Prof.dr. Peter Sillevius Smitt

CV

Peter Sillevius Smitt, MD PhD, is a full professor in Neurology and head of the Department of Neurology since 2002. He received his clinical Neurology and PhD training (1987 – 1992) at the University of Amsterdam and subsequently trained in Neuro-oncology at the Memorial Sloan-Kettering Cancer Center in New York (1992 – 1995). His major scientific interest are in molecular pathways involved in carcinogenesis and anti-tumor immunity. He is currently member of the Board of the Molecular Medicine research school.

Selected peer-reviewed publications

1. de Graaf M, de Beukelaar J, Bergsma J, Kraan J, van den Bent M, Klimek M, van Norden Y, Kusuma A, Smitt PS, Gratama JW. B and T cell imbalances in CSF of patients with Hu-antibody associated PNS. *J Neuroimmunol* 2008; 195:164-70.
2. French PJ, Peeters J, Horsman S, Duijm E, Siccama I, van den Bent MJ, Luider TM, Kros JM, van der Spek P, Sillevius Smitt PA. Identification of differentially regulated splice variants and novel exons in glial brain tumors using exon expression arrays. *Cancer Res* 2007; 67:5635-42.
3. ter Horst M, Verwijnen SM, Brouwer E, Hoeben RC, de Jong M, de Leeuw BH, Sillevius Smitt PA. Locoregional delivery of adenoviral vectors. *J Nucl Med* 2006; 47:1483-9.
4. French PJ, Swagemakers SM, Nagel JH, Kouwenhoven MC, Brouwer E, van der Spek P, Luider TM, Kros JM, van den Bent MJ, Sillevius Smitt PA. Gene expression profiles associated with treatment response in oligodendrogliomas. *Cancer Res* 2005; 65:11335-44.
5. Dekker LJ, Boogerd W, Stockhammer G, Dalebout JC, Siccama I, Zheng P, Bonfrer JM, Verschuuren JJ, Jenster G, Verbeek MM, Luider TM, Smitt PA. MALDI-TOF mass spectrometry analysis of cerebrospinal fluid tryptic peptide profiles to diagnose leptomeningeal metastases in patients with breast cancer. *Mol Cell Proteomics* 2005; 4:1341-9.
6. de Beukelaar JW, van Arkel C, van den Bent MJ, van't Veer MB, van Doornum GJ, Cornelissen JJ, Sillevius Smitt PA, Gratama JW. Resolution of EBV(+) CNS lymphoma with appearance of CSF EBV-specific T cells. *Ann Neurol* 2005; 58:788-92.
7. Smitt PS, Driessse M, Wolbers J, Kros M, Avezaat C. Treatment of relapsed malignant glioma with an adenoviral vector containing the herpes simplex thymidine kinase gene followed by ganciclovir. *Mol Ther* 2003; 7:851-8.
8. Nanda D, Vogels R, Havenga M, Avezaat CJ, Bout A, Smitt PS. Treatment of malignant gliomas with a replicating adenoviral vector expressing herpes simplex virus-thymidine kinase. *Cancer Res* 2001; 61:8743-50.
9. Sillevius Smitt P, Kinoshita A, De Leeuw B, Moll W, Coesmans M, Jaarsma D, Henzen-Logmans S, Vecht C, De Zeeuw C, Sekiyama N, Nakanishi S, Shigemoto R. Paraneoplastic cerebellar ataxia due to autoantibodies against a glutamate receptor. *N Engl J Med* 2000; 342:21-7.

PhD Students

Rosso SM.

Frontotemporal dementia in the Netherlands

Thesis, Erasmus University Rotterdam, the Netherlands (2003, March 26th)

Supervisors: Niermeijer MF, Sillevius Smitt PAE, van Swieten JC, Heutink P.

ISBN 90-6734-187-8.

Dekker LJM.

Proteomics of body fluids.

Thesis, Erasmus University Rotterdam, the Netherlands (2007, October 10th)

Supervisors: Sillevs Smitt PAE, Bangma C, Luider TM, Jenster G.

ISBN-978-90-9022111-3.

Beukelaar JWK de.

The role of T Lymphocytes in the pathogenesis of Hu antibody associated Paraneoplastic Neurological Syndromes.

Thesis, Erasmus University Rotterdam, the Netherlands (2007, June 13th)

Supervisors: Sillevs Smitt PAE, Gratama JW.

ISBN-978-90-8559-290-7.

Verwijnen SM.

Improvement of malignant glioma treatment: preclinical evaluation of adenoviral gene therapy and PRRT.

Thesis, Erasmus University Rotterdam, the Netherlands (2007, December 12th)

Supervisors: de Jong M, Sillevs Smitt PAE.

ISBN-978-90-8559-327-0

Horst M ter.

Gene therapy of malignant gliomas.

Thesis, Erasmus University Rotterdam, the Netherlands (2008, January 9th)

Supervisors: Sillevs Smitt PAE, de Jong M, de Leeuw B.

ISBN-978-90-8559-337-9

Nanda D.

Gene therapy for gliomas.

Thesis, Erasmus University Rotterdam, the Netherlands (2008, June 25th)

Supervisor: Sillevs Smitt PAE.

Current grant support includes

- Gratama Stichting: "Analyse van specifieke T-lymfocyten respons bij Paraneoplastische Neurologische Syndromen geassocieerd met anti-Hu antistoffen" (200 k€)
- Internationale Samenwerking: "Development of a Novel Diagnostic Platform Technology Through Mass Spectrometry Interrogation of Combinatorial Constrained Peptide Arrays"(850 k€)
- Internationale Samenwerking: "EURECAL" (875 k€)

Current research topics

Current research focuses on primary brain tumors and neurological complications of cancer, including cancer and neuropathic pain. Current topics are:

- Molecular mechanisms driving gliomagenesis
- Molecular characterization of gliomas for prognosis and prediction of treatment response
- Gene therapy for malignant gliomas
- Role of cellular immunity in the pathogenesis of central nervous system inflammation associated with cancer

- Role of the fine specificity of paraneoplastic antineuronal antibodies
- The role of gene polymorphisms in cancer and neuropathic pain

International collaborations

Prof. Cesc Graus, Dpt. Neurology, Hopital i Clinic, Barcelona, Spain

Prof. Joseph Dalmau, Dpt. Neurology, U. Pennsylvania, USA

Prof. Jean-Yves Delattre, Dpt. Neurology, Hospital Salpetriere, Paris, France

Prof. Geof Manley, Dpt. Neurosurgery, UCSF, USA

Name

Prof. dr. André Uitterlinden,
Professor of Complex Genetics
Genetic Laboratory, Department of Internal Medicine

CV

André Uitterlinden is a Professor of Complex Genetics at Erasmus Medical Centre, Rotterdam. He graduated from Leiden University in 1985 where he also obtained his PhD in 1993 after working at TNO, a Dutch Research Organisation, as well as both US and Dutch Biotech firms. In 1994 he joined Erasmus MC at the Department of Internal Medicine, where he now also holds positions in the Department of Epidemiology & Biostatistics and the Department of Clinical Chemistry.

His research is focussing on identification and characterization of genetic factors for common traits and diseases, including anthropometry, endocrine disorders and locomotor disease such as osteoporosis and osteoarthritis. He is also in charge of a high-throughput human genotyping facility at Erasmus MC (DNA isolation, formatting, and genotyping with Illumina, Sequenom, Taqman), and is coordinating all molecular genetic analyses in the Rotterdam Study. Within this framework he is collaborating with many (large) epidemiological study populations at Erasmus MC, and abroad involved in several consortia on complex traits and diseases including GEFOS, TREAT OA, ENGAGE, CHARGE, GIANT. Prof. Uitterlinden is coordinator of the EU-sponsored GENOMOS/GEFOS consortium, involving >150.000 subjects to identify genetic risk factors for osteoporosis by prospective meta-analyses. Prof. Uitterlinden has published 180 papers in refereed journals and is a member of the editorial board of Calcified Tissues International (CTI), Human Genomics and Proteomics (HGP), and chief co-editor of the Dutch Journal for Calcium and Bone metabolism (NTCB). He is also organising an annual international SNP-course at Erasmus MC (with >70 international participants) and organiser of a bi-annual symposium on genetic variation and complex disease.

Academic Record

1981	B.Sc. Biology, State University Leiden, Leiden, The Netherlands
1984	M.Sc. Molecular Biology, State University Leiden Leiden, The Netherlands
1993	Ph.D. Medicine, State University Leiden, Leiden, The Netherlands "Genome analysis by Two-dimensional DNA typing", Promotor: Prof.Dr.Ir. P.H.M.Lohman (Department of Radiation Genetics, State University Leiden)
2004	Appointment as Associate Professor, Erasmus MC, Rotterdam, The Netherlands
2007	Appointment as Full Professor (Complex Genetics of common diseases), Erasmus MC, Rotterdam, The Netherlands

Professional positions

1. TNO Institute for Experimental Gerontology (TNO-IvEG; Rijswijk, The Netherlands)
1984-1985: Research Associate working at Lifecodes, Corp. (Valhalla, New York, USA).
1985-1988: Research Associate at TNO IvEG
1988-1990: Head of the section Genome Analysis at TNO-IvEG

2. INGENY B.V. (Leiden, The Netherlands)

1990-1994: Head of the Department of Genetic Diagnostics

3. Erasmus Medical Centre Rotterdam, Academic Hospital Dijkzigt Rotterdam

1994 - 2000: Senior Research Fellow, Department of Internal Medicine,
Calcium and Bone Metabolism Group

1998 - Honorary position at Department of Epidemiology & Biostatistics as
Senior Research Fellow

2000 - Staff member Department of Internal Medicine (0.7 fte)

2000 - Staff member Department of Clinical Chemistry (0.3 fte)

2001 - Head of the Genetic Laboratory Internal Medicine

2004 -2007 Associate Professor

2007 - Full Professor Complex Genetics

PhD students

Past:

Edgar Collin (1999-thesis 2002),

Angelique Weel (1999-thesis 2002)

Stephanie Schuit (2000-thesis June 2004)

Fernando Rivadeneira (2000-thesis november 2004)

Yue Fang (1997-thesis december 2005)

Nahid Yazdanpanah (2005-thesis 2007)

Present:

Arjan Bergink (1999-thesis planned spring 2009)

Wietske Ester (2003-thesis planned 2008)

Lisette Stolk (2004-thesis planned 2009)

Carola Zillikens (thesis planned 2009)

Jesus Karol Estrada Gil (2008-)

Marjolein Peters (2008-)

Research Grants

1. "Two-dimensional DNA typing of human individuals for mapping genetic traits"

Principal investigator and coordinator, (authors: Uitterlinden, Kruse, Bolund, Lehrach)

EU Hum Genome Analysis Program, GENO-CT91-0021, 1992-'94 € 250,000.=

2. "Further development of 2-D DNA typing: application in the analysis of genetic linkage
and somatic mutation"

Principal investigator and coordinator, (authors: Uitterlinden, Kruse, Bolund, Lehrach)

EU Hum Genome Analysis Program, PL 93-0041, 1994-97 € 450,000.=

3. "Improvements in single-stranded DNA sequencing by pulsed-field gel electrophoresis:

Comprehension of the implied molecular mechanisms and investigation of new adapted
types of gels"

Investigator, (authors: Sturm, Chiari, Uitterlinden, Brogren)

EU Human Genome Analysis Program, PL 93-0024, 1994-1997 € 80,000.=

4. "Vitamin D receptor gene polymorphisms: prognostic value and functional significance"

- Advisor (authors: Pols, Birkenhäger, van Leeuwen)
NWO 950-10-618,1996-1999, € 127.058,=
5. "Vitamin D and Estrogen receptor gene polymorphisms: significance for screening on and treatment of osteoporosis"
Investigator, (authors: Pols, van Leeuwen, Uitterlinden)
Praeventiefonds/ZON, 28.24.890, 1997-1998, € 88.941,=
6. "Genetic marker analysis of osteoporosis: COLIA1 polymorphisms in relation to bone mass"
Principal investigator, (authors: Uitterlinden, Pols)
JANIVO Stichting,1996.069, 1998-2000, € 108.453,=
7. "Characterization of Vitamin D receptor gene variants"
Principal investigator (author: Uitterlinden)
NWO, 903-46-178,1998-2002, € 103.462,=
8. "Osteoarthritis: gene-environment interaction of the Vitamin D ligand-receptor complex and collagen type II α 1 gene locus polymorphisms"
Principal investigator (authors: Pols, Uitterlinden)
NWO, 925-01-010,1998-2002, € 245.041,=
9. "Research Institute Diseases in the Elderly: The role of endocrine factors in the pathogenesis of diseases of the elderly"
Investigator (authors: Pols, Lamberts)
NWO, 014-90-001, 2000-2004, € 453.781,=
10. "Genetic association analysis of polymorphisms at the SCL/SOST/BEER locus"
Principal Investigator
Celltech-Chiroscience, USA (2000-2003) € 181.512,=
11. "Strategic Collaboration Agreement"
Programme Manager
Oxagen Ltd., UK € 910.000,=
12. "Network in Europe on Male Osteoporosis NEMO" (QLK6-CT-2002-00491)
Participant
European Union FP5, 2002-2004 € 50.000,=
13. "IMPACT genotyping"
Principle Investigator
Aventis Pharmaceuticals € 270.000,=
14. Sponsored Celera subscription
NWO, 050-20-113, 2003 € 20.000,=
15. "Genetic Markers for Osteoporosis GENOMOS" (QLK6-CT-2002-02629)
Coordinator, participant
European Union FP5, 2003-2007 € 3.000.000,=
16. "Investmentsupport Equipment for SNP platform"
coordinator, participant
NWO 911-03-012, 2003 € 800.000,=
17. "Research Institute Diseases in the Elderly: The role of genetic variation in the estrogen pathway in the pathogenesis of diseases of the elderly"
Principal Investigator
ZonMW/NWO, 014-93-015, 2004-2008, € 250.000,=
18. "Assembly of a genetic risk profile for the prediction of multifactorial diseases: osteoporosis as a model"
Principal Investigator
ErasmusMC , 2005, (internal funding competition; Mrace) € 50.000,=
19. "Genetic association analysis of two GPCR genes"

Principal Investigator		
Organon BV , 2005-2006	€	175.000,=
20. "Pharmacogenetic aspects of ACE inhibition in stable coronary artery disease"		
Co-principal investigator, with prof. Maarten Simoons		
Nederlandse Hartstichting (NHS) , 2006-2010	€	221.210,=
21. "Affymetrix 500K pilot project GWA in ERGO"		
Principal investigator		
Erasmus MC , 2006 (co-funded by several departments)	€	300.000,=
22. Patents sold to Sciona (2006)	€	85.000,=
23. "Pharmacogenetics of cytochrome P450 polymorphisms"		
Co-principal investigator with prof Bruno Stricker		
Ministerie van VWS , 2006-2007	€	200.000,=
24. "A Genome-Wide database of the Rotterdam Study"		
Principal investigator		
NWO , 175.010.2005.011, 2007-2010	€	6.000.000,=
25. "GEFOS" (Health-F2—2008-201865)		
Coordinator		
EU-FP7 , 2007-20011	€	3.000.000,=
26. "TREAT-OA" (Health-F2-2008-22478)		
Participant		
EU-FP7 , 2007-20012	€	500.000,=
27. "Generation R GWA"		
Principal investigator		
Erasmus MC , 2007 (dean; co-funded by several departments)	€	2.500.000,=

Recent key publications

- 1) Richards JB*, Rivadeneira F*, Inouye M*, Pastinen TM, Soranzo N, Wilson SG, Andrew T, Falchi M, Gwilliam R, Ahmadi KR, Valdes AM, Arp P, Whittaker P, Verlaan DJ, Jhamai M, Kumanduri V, Moorhouse M, van Meurs JB, Hofman A, Pols HA, Hart D, Zhai G, Kato BS, Mullin BH, Zhang F, Deloukas P*, Uitterlinden AG*, Spector TD*. Bone mineral density, osteoporosis, and osteoporotic fractures: a genome-wide association study. **Lancet**. 2008;371(9623):1505-12.
- 2) van Meurs JB, Trikalinos TA, Ralston SH, Balcells S, Brandi ML, Brixen K, Kiel DP, Langdahl BL, Lips P, Ljunggren O, Lorenc R, Obermayer-Pietsch B, Ohlsson C, Pettersson U, Reid DM, Rousseau F, Scollen S, Van Hul W, Agueda L, Akesson K, Benevolenskaya LI, Ferrari SL, Hallmans G, Hofman A, Husted LB, Kruk M, Kaptoge S, Karasik D, Karlsson MK, Lorentzon M, Masi L, McGuigan FE, Mellström D, Mosekilde L, Nogue X, Pols HA, Reeve J, Renner W, Rivadeneira F, van Schoor NM, Weber K, Ioannidis JP, Uitterlinden AG; GENOMOS Study. Large-scale analysis of association between LRP5 and LRP6 variants and osteoporosis. **JAMA**. 2008;299(11):1277-90.
- 3) Rivadeneira F, van Meurs JB, Kant J, Zillikens MC, Stolk L, Beck TJ, Arp P, Schuit SC, Hofman A, Houwing-Duistermaat JJ, van Duijn CM, van Leeuwen JP, Pols HA, Uitterlinden AG. Estrogen receptor beta (ESR2) polymorphisms in interaction with estrogen receptor alpha (ESR1) and insulin-like growth factor I (IGF1) variants influence the risk of fracture in postmenopausal women. **J Bone Miner Res**. 2006;21(9):1443-56.
- 4) Ioannidis JP, Gwinn M, Little J, Higgins JP, Bernstein JL, Boffetta P, Bondy M, Bray MS, Brenchly PE, Buffler PA, Casa JP, Chokkalingam A, Danesh J, Smith GD, Dolan S, Duncan R, Gruis NA, Hartge P, Hashibe M, Hunter DJ, Jarvelin MR, Malmer B,

- Maraganore DM, Newton-Bishop JA, O'Brien TR, Petersen G, Riboli E, Salanti G, Seminara D, Smeeth L, Taioli E, Timpson N, Uitterlinden AG, Vineis P, Wareham N, Winn DM, Zimmern R, Khoury MJ. Human Genome Epidemiology Network and the Network of Investigator Networks. A roadmap for efficient and reliable human genome epidemiology. *Nat Genet* 2006;38(1):3-5.
- 5) Fang Y, van Meurs JB, d'Alesio A, Jhamai M, Zhao H, Rivadeneira F, Hofman A, van Leeuwen JP, Jehan F, Pols HA, Uitterlinden AG. Promoter and 3'UTR haplotypes in the vitamin D receptor gene predispose to osteoporotic fracture: the Rotterdam Study *Am J Hum Genet.* **2005;77(5): 807-23.**
- 6) van Meurs JBJ, Dhonukshe-Rutten RAM, Pluijm SMF, van der Klift M, de Jonge R, Lindemans J, de Groot LCPGM, Hofman A, Witteman JCM, van Leeuwen JPTM, Breteler MMB, Lips P, Pols HAP, Uitterlinden AG. Homocysteine levels and the risk of osteoporotic fracture. *New Engl J Med* 2004;350(20):2033-41.

Name

Henri Alexander Verbrugh MD PhD

CV

Born 25 November 1949 in Tj. Pandan, Indonesia, Gymnasium-beta diploma June 1968 St Fransiscus College, Rotterdam; studied Medicine 1968-1975 Erasmus MC Rotterdam, Fellowship in Medical Microbiology 1975-1978 University of Utrecht (supervisor: Prof dr KC Winkler), PhD degree 1979 University of Utrecht (promoter: prof dr J Verhoef); recipient of NIH International Fogarty Fellowship 1980-1982 at University of Minnesota Medical School, Minneapolis, USA (preceptor: prof dr Paul Quie); associate professor University of Utrecht Medical School 1978-1993 and head department of Medical Microbiology, Diaconessen Hospital, Utrecht. Professor of Clinical Microbiology and Head department of Medical Microbiology and Infectious Diseases of Erasmus MC, Rotterdam 1993-present.

Selected Publications

- Man P de, Verhoeven BAN, Verbrugh HA, Vos MC, Anker JN van der. An antibiotic policy to prevent emergence of resistant bacilli. *Lancet* **355**: 973-978, 2000.
- Belkum A van, Braak N van den, Godschalk P, Ang W, Jacobs B, Gilbert M, Wakarchuk W, Verbrugh H, Endtz H. A *campylobacter jejuni* gene associated with immune-mediated neuropathy. *Nature Medicine* **7**: 752-753, 2001.
- Ahmed AO, van Leeuwen W, Fahal A, van de Sande W, Verbrugh H, van Belkum A. Mycetoma caused by *Madurella mycetomatis*: a neglected infectious burden. *Lancet Infect Dis.* 2004 Sep;4(9):566-74. Review.
- Leeuwen WB van, Snoeijers S, Werken-Libregts C van der, Tuij A, Zee A van der, Egberink D, Proost M de, Bik E, Lunter B, Kluytmans J, Gits E, Duyn I van, Heck M, Zwaluw K van der, Wannet W, Noordhoek GT, Mulder S, Renders N, Boers M, Zaat S, Riet D van der, Kooistra M, Talens A, Dijkshoorn L, Reyden T van der, Veenendaal D, Bakker N, Cookson B, Lynch A, Witte W, Cuny C, Blanc D, Vernez I, Hryniewicz W, Fielt J, Struelens M, Deplano A, Landegent J, Verbrugh HA, Belkum A van. Intercenter reproducibility of binary typing for *Staphylococcus aureus*. *J Microbiol Methods* **51**: 19-28, 2002.
- Wertheim HF, Vos MC, Ott A, van Belkum A, Voss A, Kluytmans JA, van Keulen PH, Vandenbroucke-Grauls CM, Meester MH, Verbrugh HA. Risk and outcome of nosocomial *Staphylococcus aureus* bacteraemia in nasal carriers versus non-carriers. *Lancet.* 2004 Aug 21;364(9435):703-5.
- Verbrugh HA. Selective decontamination of digestive tract in intensive care. *Lancet.* 2003 Dec 20;362(9401):2117-8.
- Nouwen J, Boelens H, van Belkum A, Verbrugh H. Human factor in *Staphylococcus aureus* nasal carriage. *Infect Immun.* 2004 Nov;72(11):6685-8.
- Melles DC, Gorkink RF, Boelens HA, Snijders SV, Peeters JK, Moorhouse MJ, van der Spek PJ, van Leeuwen WB, Simons G, Verbrugh HA, van Belkum A. Natural population dynamics and expansion of pathogenic clones of *Staphylococcus aureus*. *J Clin Invest.* 2004 Dec;114(12):1732-40.
- Claassen M, Nouwen J, Fang Y, Ott A, Verbrugh H, Hofman A, van Belkum A, Uitterlinden A. *Staphylococcus aureus* nasal carriage is not associated with known polymorphism in the Vitamin D receptor gene. *FEMS Immunol Med Microbiol.* 2005 Feb 1;43(2):173-176.

- Nouwen JL, Fieren MW, Snijders S, Verbrugh HA, van Belkum A. Persistent (not intermittent) nasal carriage of *Staphylococcus aureus* is the determinant of CPD-related infections. *Kidney Int.* 2005 Mar;67(3):1084-92.
- Van den Akker EL, Nouwen JI, Melles DC, van Rossum EF, Koper JW, Uiterlinden AG, Hofman A, Verbrugh HA, Pols HAP, Lamberts SW, van Belkum A. *Staphylococcus aureus* nasal carriage is associated with glucocorticoid receptor gene polymorphisms. *J Infect Dis.* 2006 Sep 15;194(6):814-8. Epub 2006 Aug 8.
- Ahmed AA, van de Sande WW, Fahal A, Bakker-Woudenberg I, Verbrugh H, van Belkum A. Management of mycetoma: major challenge in tropical mycoses with limited international recognition. *Curr Opin Infect Dis.* 2007 Apr;20(2):146-51.

PhD Students

- N. Posthuma. Biocompatibility of a glucose polymer solution (icodextrin) in continuous cyclic peritoneal dialysis. Free University of Amsterdam, Amsterdam 2000
- N. van den Braak. Glycopeptide resistant enterococci in the Netherlands. Erasmus University Rotterdam, Rotterdam 2001
- R. Schiffelers. Liposomal targeting of antimicrobial agents to bacterial infections. Erasmus University Rotterdam, Rotterdam 2001
- W.B. van Leeuwen. Binary Typing of *Staphylococcus aureus*. Erasmus University Rotterdam, Rotterdam 2002
- E.J. Ruijgrok. Inhalation of amphotericin B for prevention and treatment of invasive pulmonary aspergillosis. Erasmus University Rotterdam, Rotterdam 2002
- R. Mathoera. Stone formation in the infected enterocytosplasty in children. Erasmus University Rotterdam, Rotterdam 2003
- A.O.A. Ahmed. Molecular and biological studies on *Madurella mycetomatis* infection in man and mice, Erasmus University Rotterdam, Rotterdam 2003
- M.J. Becker. Experimental and clinical studies on invasive pulmonary aspergillosis. Pathophysiology, diagnosis and management, Erasmus University Rotterdam, Rotterdam 2004
- J.L. Nouwen. Determinans, risks and dynamics of *Staphylococcus aureus* nasal carriage, Erasmus University Rotterdam, Rotterdam 2004.
- H. Wertheim. *Staphylococcus aureus* infections, lead by the nose, Rotterdam 2005
- MF Filius. Antimicrobial use and resistance patterns in hospitalized patients, Rotterdam 2005

(International) Awards

- Penning Fonds voor Wetenschappelijk Onderzoek Vlaanderen, Juni 2006
- Honorary member of PAMKI (Indonesian Society of Clinical Microbiology), November 2006

Current Research Grant Support

KNAW, ZonMW, Becton Dickinson, Ministry of Agriculture, Nature and Food safety.

Current Research Topics

Staphylococcus aureus carriage, infections and antimicrobial resistance

International Collaboration

- Network on antimicrobial resistance in *Staphylococcus aureus* (NARSA, USA)
- Antimicrobial resistance in Indonesia (AMRIN consortium including University medical centers of Semarang, Surabaya, Malang and Denpasar))

- International Symposium on Staphylococci and Staphylococcal Infections 2008
- European Center for Disease Prevention and Control (ECDC, Stockholm)

Name

C. Vink, PhD

Associate Professor,

Head Laboratory of Pediatrics/Pediatric infectious diseases, Erasmus MC

CV

Dr. Vink graduated (*cum laude*) in Biology at the University of Leiden in 1989. In the same year, he received the Unilever Research Prize. He then worked in the group of Prof. Dr. R.H.A. Plasterk at the Department of Molecular Biology of the Netherlands Cancer Institute (NKI) in Amsterdam. In 1993, he received his PhD for a study on the mechanism by which the AIDS virus, HIV, integrates into the human genome. After working as a postdoc at the NKI, he joined the Department of Medical Microbiology, headed by Prof. Dr. C.A. Bruggeman, at the Maastricht University in 1995. In 2000, he was awarded with a 5-year fellowship from the Royal Netherlands Academy of Arts and Sciences (KNAW). In Maastricht, his major research interests were characterization of the molecular genetics of herpesviruses and, in particular, elucidation of the function of herpesvirus-encoded homologs of G protein-coupled receptors and chemokines. Additionally, Dr. Vink was responsible for both maintenance and development of the molecular diagnostics of infectious diseases within the department of Medical Microbiology. Since August 2006, Dr. Vink was appointed Head of the Laboratory of Pediatrics at the Erasmus MC, leading a research group working on pediatric infectious diseases.

Selected Publications

- Deurenberg, R. H., C. Vink, S. Kalenic, A. W. Friedrich, C. A. Bruggeman, and E. E. Stobberingh. The molecular evolution of methicillin-resistant *Staphylococcus aureus*. *Clin. Microbiol. Infect.* (2006), in press.
- Linssen, C.F., J.A. Jacobs, P. Beckers, K.E. Templeton, J. Bakkers, E.J. Kuijper, W.J. Melchers, M. Drent, and C. Vink. Inter-laboratory comparison of three different real-time PCR assays for the detection of *Pneumocystis jiroveci* in bronchoalveolar lavage fluid samples. *J. Med. Microbiol.* 55 (2006), 1229-1235.
- van Cleef, K.W.R., C. A. Bruggeman, and C. Vink. Chemokines and chemokine receptors encoded by cytomegalovirus. *J. Clin. Virol.* 35 (2006), 343-348.
- Vliegen, I., J.A. Jacobs, E. Beuken, C.A. Bruggeman, and C. Vink. Rapid identification of bacteria by real-time amplification and sequencing of the 16S rRNA gene. *J. Microbiol. Methods* 66 (2006), 156-164.
- Deurenberg R.H., R.F. Nieuwenhuis, C. Driessen, N. London N, F.R. Stassen, F.H. van Tiel, E.E. Stobberingh, and C. Vink. The prevalence of the *Staphylococcus aureus* *tst* gene among community- and hospital-acquired strains and isolates from Wegener's Granulomatosis patients. *FEMS Microbiol Lett.* 245 (2005), 185-189.
- Beisser, P.S., D. Verzijl, Y.K. Gruijthuijsen, E. Beuken, M.J. Smit, R. Leurs, C.A. Bruggeman, and C. Vink. The Epstein-Barr virus BILF1 gene encodes a G protein-coupled receptor that inhibits phosphorylation of PKR. *J. Virol.* 79 (2005), 441-449.
- Penders, J., C. Vink, C. Driessen, N. London, C.Thijs, E. Stobberingh. Quantification of *Bifidobacterium spp.*, *E. coli* and *C. difficile* in faecal samples of breast-fed and formula-fed infants by real-time PCR. *FEMS Microbiology Lett.* 243 (2005), 141-147
- van Cleef, K.W.R., W.M.A. Scaf, K. Maes, S.J.F. Kaptein, E. Beuken, P.S. Beisser, F.R.M. Stassen, G.E.L.M. Grauls, C.A. Bruggeman, and C. Vink. The rat cytomegalovirus homologue of parvoviral rep genes, r127, encodes a nuclear protein with single- and double-

stranded DNA-binding activity that is dispensable for virus replication. *J. Gen. Virol.* 85 (2004), 2001-2013.

- Gruijthuisen, Y.K., E.V.H. Beuken, M.J. Smit, R. Leurs, C.A. Bruggeman, and C. Vink. Mutational analysis of the rat cytomegalovirus R33-encoded G protein-coupled receptor: Identification of amino acid residues critical for cellular localization and ligand-independent signaling. *J. Gen. Virol.* 85 (2004), 897-909.
- Gruijthuisen, Y.K., Casarosa P., D. Michel, P. Beisser, J. Holl, C.P. Fitzsimons, D. Verzijl, C.A. Bruggeman, T. Mertens, R. Leurs, C. Vink, and M.J. Smit. Constitutive signaling of the human cytomegalovirus-encoded receptor UL33 differs from that of its rat cytomegalovirus homolog R33 by promiscuous activation of G proteins of the Gq, Gi as well as Gs class. *J. Biol. Chem.* 278 (2003), 50010-50023.

PhD Students

Currently, the pediatric infectious diseases group harbours the following graduate students:

- V. Hira
- J. Labout
- W. Hendriksen

(International) Awards

Unilever Research Prize (1989)

Current Research Grant Support

Currently, Dr. Vink holds a single NWO-ALW postdoc grant, entitled 'Characterization and manipulation of the function of the G protein-coupled receptor homologs encoded by cytomegalovirus', 2003-2007).

Current Research Topics

As of August 2006, a new line of research has been initiated which focuses on the cell wall-less bacterium *Mycoplasma pneumoniae*. *M. pneumoniae* is a human pathogen that causes a range of respiratory infections, such as tracheobronchitis, pharyngitis, and atypical pneumonia. This bacterium causes up to 40% of community-acquired pneumonias and as many as 18% of cases requiring hospitalization in children.

A crucial step in the initiation of infection by *M. pneumoniae* is the intimate attachment of the bacteria to the respiratory epithelium (cytadherence) of its human host. This process is essential to pathogenesis since cytadherence mutants are avirulent. The most prominent protein (cytadhesin) that is involved in attachment is the P1 protein, which is highly expressed on the surface of a so-called 'tip structure' of *M. pneumoniae*. Interestingly, the gene encoding P1, termed MPN141, contains sequence regions of which multiple sequence variants exist in the bacterial genome. It has been suggested that these variants may recombine with the MPN141 gene, thereby representing a source of sequence variation of this gene. This may ultimately result in differences in the amino acid sequence of P1 at the bacterial surface, which may provide a means for the bacterium to evade the immune system.

The aim of this research line is to understand the underlying mechanism of DNA rearrangements leading to variation in the P1 cytadhesin sequence.

International Collaboration

Collaborations on the novel research line have not yet been initiated.

Name

Margreet Cornelia Vos

CV

Birthdate: 17 februari 1961

1995: Medical microbiologist

1995: staff member department of Medical Microbiology & Infectious Diseases, Erasmus MC

Selected publications

Vos MC, de Haas P.EW, Verbrugh HA, Renders NHM, Hartwig NG, de Man P, Kolk AHJ, van Deutekom H, Yntema JL, Vulto AG, Messemaker M, van Soolingen D.

Nosocomial *Mycobacterium bovis*-Bacille Calmette-Guérin Infections due to contamination of chemotherapeutics: Case finding and route of transmission.

J.Inf Dis 2003;188:1332-1335.

Wertheim HFL, Vos MC, Ott A, van Belkum A, Voss A, Kluytmans JAJW, van Keulen PHJ, Vandembroucke-Grauls CMJE, Meester MHM, Verburg HA.

Risk and outcome of nosocomial *Staphylococcus aureus* bacteraemia in nasal carriers versus non-carriers.

The Lancet 2004;364:703-705.

Wertheim HFL, Vos MC, Ott A, Voss A, Kluytmans JAJW, van Keulen PHJ, Vandembroucke-Grauls CMJE, Meester MHM, van Keulen PHJ, Verburg HA.

Mupirocin prophylaxis against nosocomial *Staphylococcus aureus* infections in nonsurgical patients. Ann Intern Med 2004;140:419-425.

Vos MC, Verbrugh HA.

MRSA : we can overcome, but who will lead the battle ?

Infect Control Hosp Epid 2005;26:117-120.

Vos MC, Endtz HP, Horst-Kreft D, Doorduyn J, Lugtenburg E, Verbrugh HA, Lowenberg B, de Marie S, van Pelt C, van Belkum A.

Candida krusei transmission among hematology patients resolved by adapted antifungal prophylaxis and infection control measures.

J Clin Microbiol 2006;44 (3): 1111-4.

PhD Students

- Heiman Wertheim (2001-2005)
Preventionfund: Prevention of nosocomial bacteraemias and sepsis through elimination of *Staphylococcus aureus* nasal carriage
- Jos Kerremans (2003-2008)
Comparative study into the costeffectiveness and clinical impact of rapid identification and antibiotic resistance testing of pathogenic bacteria.
- Lonneke Bode (2004 - current)

Prevention of nosocomial *Staphylococcus aureus* infections after rapid detection and eradication of *S. aureus* carriage in patients at risk; a randomized placebo controlled multi-centre trial.

- V. Valk (2006 - current)
Determinants of (non-)compliance to standard hospital infections preventive measures in Dutch hospitals. Multicenter trial.
- Femke Mollema (2007-current)
Methicillin-resistant *Staphylococcus aureus* (MRSA) in the community: consequences for the efficiency of the Dutch MRSA prevention policy.

Current Research Grant Support

- ZonMW: Prevention of nosocomial *Staphylococcus aureus* infections after rapid detection and eradication of *S. aureus* carriage in patients at risk; a randomized placebo controlled multi-centre trial; € 465.788
- ZonMw : Comparative study into the costeffectiveness and clinical impact of rapid identification and antibiotic resistance testing of pathogenic bacteria; € 229.074,-
- Prevention fund: Determinants of (non-)compliance to standard hospital infections preventive measures in Dutch hospitals. Multicenter trial; € 290.862
- ZonMW: Early recognition and prevention of CDAD in University and General hospitals in The Netherlands" (LUMC en Cib, RIVM). Multicenter trial; € 541.687
- Developmental medicine (Ontwikkelingsgeneeskunde) € 100,000
- Revolving Fund € 51.800
- 3M €200.000
- Biomerieux € 150,000

Current Research Topics

MRSA

Prevention of nosocomial infections

International Collaboration

See list of publications

Name

Dr. Andrea M. Woltman; Department Gastroenterology and Hepatology (MDL)

CV

Andrea Woltman received her PhD degree at the University of Leiden (2002) on functional modulation of human dendritic cells in renal allograft transplantation and rejection. She continued her research as a post-doc at the Department of Nephrology of the Leiden University Medical Center and focused on dendritic cells as potential tools and targets to prevent renal allograft rejection. In 2005 she received a Veni (ZonMW) to work on the molecular mechanisms regulating human dendritic cell development and survival. In May 2006, she became staff member at the Department of Gastroenterology and Hepatology of the Erasmus MC in Rotterdam working on the immunology and immunopathogenesis of viral hepatitis, especially chronic hepatitis B.

Selected Publications

Woltman AM, Van der Kooij SW, De Fijter JW, Van Kooten C. Maturation-resistant dendritic cells induce hyporesponsiveness in alloreactive CD45RA⁺ and CD45RO⁺ T-cell populations. *Am. J. Transplant.* 6:2580-2591, 2006

Woltman AM, De Fijter JW, Van der Kooij SW, Jie KE, Massacrier C, Caux C, Daha MR, Van Kooten C. MIP-3 α /CCL20 in renal transplantation and its involvement as dendritic cell chemo-attractant in renal allograft rejection. *Am. J. Transplant.* 5:2114-2125, 2005.

Van Kooten C and Woltman AM. Dendritic cells as a target of immunosuppressive drugs. *Transplant. Rev.* 18:70-79, 2004. Review.

Woltman AM, Schlagwein N, van der Kooij SW, van Kooten C. The novel cyclophilin-binding drug sanglifehrin A specifically affects antigen uptake receptor expression and endocytic capacity of human dendritic cells. *J. Immunol.* 172:6482-6489, 2004.

Castellano G, Woltman AM, Nauta AJ, Roos A, Trouw LA, Seelen MA, Schena FP, Daha MR, van Kooten C. Maturation of dendritic cells abrogates C1q production in vivo and in vitro. *Blood* 103:3813-3820, 2004.

Woltman AM, van Kooten C. Functional modulation of dendritic cells to suppress adaptive immune responses. *J. Leukoc. Biol.* 73:428-441, 2003. Review.

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PhD Students

- Jeroen Stoop (May 2003 - 2007)
- Marjolein Op den Brouw (June 2004 - 2008)
- Eric Tjwa (September 2006 – 2009)
- Lianne van de Laar, together with Prof. P.J. Coffe (UMC, Utrecht)(2007-2011)

(International) Awards

- 2002 Proefschriftprijs: Best thesis presented by the Dutch Federation for Nephrology & Dutch Kidney Foundation
- 2002 Novartis Transplantation Grant: Best publication in transplantation research
- 2001 Poster Presentation Award: Basic Science Symposium of the Transplantation Society, 2001 (Switzerland)
- 2001 Best oral presentation Bootcongres; Annual congress Dutch Transplantation Society

Current Research Grant Support

2005 Veni (ZonMW) 'Molecular mechanisms regulating human dendritic cell development' (€200.000,-)

Current Research Topics

Current research is mainly devoted to understanding the apparently inadequate immune response to the hepatitis B virus (HBV). Gaining better understanding of these mechanisms will eventually contribute to innovations in treatment regimens. Research is focused on the role of dendritic cells (DC), (regulatory) T cells and NK cells. Patients with chronic viral hepatitis exhibit an impaired DC function and increased percentages of regulatory T cells as compared to healthy volunteers. This may contribute to the insufficient T cell response in these chronic infections. NK cells also play a pivotal role in anti-viral responses, but their role in anti-HBV responses is as yet largely unknown.

International Collaboration

University of Heidelberg, Germany: Dr. S. Urban
Centre Léon Bérard, Lyon, France: Dr. C. Caux