

Director of the Research Center

Prof. Dr. Paul-Peter Tak

**Institution**

Division of Clinical Immunology and Rheumatology
Academic Medical Center/University of Amsterdam, F4-218
P.O. Box 22700
1100 DE Amsterdam
The Netherlands
Tel. +31 20 566 2171/ +31 20 566 8998
Fax +31 20 691 9658
E-mail: P.P.Tak@amc.uva.nl

Members of the Center***Rheumatologists***

Dr. Dominique Baeten, MD PhD	d.i.baeten@amc.uva.nl
Dr. Huib Dinant, MD PhD	h.j.dinant@slz.nl
Dr. Danielle Gerlag, MD	d.m.gerlag@amc.uva.nl
Dr. Christina Jonckheere, MD	C.L.Jonckheere@amc.uva.nl
Dr. Arno van Kuijk, MD	a.w.vankuijk@amc.uva.nl
Dr. Philip Remans, MD PhD	p.h.remans@amc.uva.nl
Dr. Koen Vos, MD PhD	k.vos@amc.uva.nl
Dr. Niek de Vries, MD PhD	niek.devries@amc.uva.nl

Basic Scientists

Lisette Bevaart, PhD	bevaart@arthrogen.nl
Nannette Brouwer, PhD	n.brouwer@amc.uva.nl
Marc Lambermon, PhD	lambermon@arthrogen.nl
Scott Loiler, PhD	loiler@arthrogen.nl
Cristina Lebre, PhD	c.lebre@amc.uva.nl
Margriet Vervoordeldonk, PhD	m.j.vervoordeldonk@amc.uva.nl
Kris Reedquist, PhD	k.a.reedquist@amc.uva.nl

Current Fields of Research

The research in AMC's Division of Clinical Immunology and Rheumatology is organized in different teams with very close interactions. The teams focus on: innovative trials with synovial biomarkers; pathogenesis of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis; immunogenetics; signal transduction pathways; dendritic cell biology; and gene therapy.

Clinicians, basic researchers and technicians are working together on clinical research (pathogenetic studies and development of innovative treatment) and more basic research. Contacts between clinicians and basic researchers take place on a daily basis. Research in our group is performed at three different tiers:

Clinical studies: The aim of these studies is to provide more insight into the pathogenesis of various forms of arthritis by analysis of clinical samples of well defined patient groups. Examination of arthroscopic synovial tissue samples plays a key role in the research program. The use of serial synovial biopsies is also used to evaluate the effects of innovative treatment with targeted treatment. These studies give crucial information about the mechanism of action at the site of inflammation. Moreover, the use of biomarkers in the tissue samples is used to predict potential clinical efficacy in small proof of principle studies. This approach is also used to identify possible predictors of efficacy of biological treatment. We have set up a professional unit for arthroscopy, synovial tissue analysis, and digital image analysis for evaluation of stained sections. This unit is also very active in training international fellows.

Animal studies: We regularly perform studies in a variety of animal models of arthritis, including murine collagen-induced arthritis (CIA), rat adjuvant arthritis (AA), streptococcal cell wall induced arthritis (monoarticular and polyarticular), as well as antigen-induced arthritis in rabbits. These animal models are a feasible tool for studying the complex interplay of inflammation and joint destruction during arthritis and the effect of different therapies hereon.

In vitro studies: Fibroblast-like synoviocytes (FLS) isolated from synovial tissue biopsies of rheumatoid arthritis patients are of particular interest as they are highly activated and exhibit certain features of transformed cells. Furthermore, we use synovial fluid and peripheral blood mononuclear cells as well as synovial biopsy culture to perform in vitro/ex vivo experiments.

Combination of these three areas of research provides an excellent environment for the development of translational research.

Selected Publications

1. Saychaudhuri S, Remmers EF, Lee AT, Hackett R, Guiducci C, Burtt NP, Gianniny L, Korman BD, Padyukov L, Kurreeman FAS, Chang M, Catanese JJ, Ding B, Wong S, van der Helm-van Mil AHM, Neale BM, Coblyn J, Cui J, Tak PP, Wolbink GJ, Crusius JBA, van der Horst-Bruinsma IE, Criswell LA, Amos CI, Seldin MF, Kastner DL, Ardlie KG, Alfredsson L, Costenbader KH, Altshuler D, Huizinga TWJ, Shadick NA, Weinblatt ME, de Vries N, Worthington J, Seielstad M, Toes REM, Karlson EW, Begovich AB, Klareskog L, Gregersen PK, Daly MJ, and Plenge RM. Common variants at *CD40* and other loci confer risk of rheumatoid arthritis. *Nature Genetics* (In press)
IF: 25.556
2. Vandooren B, Cantaert T, Noordenbos T, Tak PP, Baeten D. The abundant synovial expression of the RANK/RANKL/Osteoprotegerin system in peripheral spondylarthritis is partially disconnected from inflammation. *Arthritis Rheum* 2008 ;58:718-729
IF: 7.667
3. Lebre MC, Jongbloed SL, Tas SW, Smeets TJ, McInnes IB, Tak PP. Rheumatoid Arthritis Synovium Contains Two Subsets of CD83-DC-LAMP- Dendritic Cells with Distinct Cytokine Profiles. *Am J Pathol.* 2008 172:940-50
IF: 5.487
4. Tas SW, Vervoordeldonk MJ, Hajji N, Schuitemaker JH, van der Sluijs KF, May MJ, Ghosh S, Kapsenberg ML, Tak PP, de Jong EC. Non-canonical NF- κ B signaling in dendritic cells is required for indoleamine 2,3-dioxygenase (IDO) induction and immune regulation. *Blood.* 2007 110:1540-9
IF: 10.896

5. Ludikhuizen J, de Launay D, Groot D, Smeets TJ, Vinkenoog M, Sanders ME, Tas SW, Tak PP, Reedquist KA. Inhibition of forkhead box class O family member transcription factors in rheumatoid synovial tissue. *Arthritis Rheum.* 2007;56:2180-91
IF: 7.667
6. Vos K, Thurlings RM, Wijbrandts CA, van Schaardenburg D, Gerlag DM, Tak PP. Early effects of rituximab on the synovial cell infiltrate in patients with rheumatoid arthritis. *Arthritis Rheum.* 2007;56:772-778
IF: 7.667
7. Adriaansen J, Khoury M, de Cortie CJ, Fallaux FJ, Bigey P, Scherman D, Gould DJ, Chernajovsky Y, Apparailly F, Jorgensen C, Vervoordeldonk MJ, Tak PP. Reduction of arthritis following intra-articular administration of an adeno-associated virus serotype 5 expressing a disease-inducible TNF-blocking agent. *Ann Rheum Dis.* 2007;66:1143-50
IF: 6.411
8. Bonarius HP, Baas F, Remmerswaal EB, van Lier RA, Berge IJ, Tak PP, de Vries N. Monitoring the T-cell receptor repertoire at single-clone resolution. *PLoS ONE.* 2006 Dec 20;1:e55.
IF: N/A
9. Remans PH, Wijbrandts CA, Sanders ME, Toes RE, Breedveld FC, Tak PP, van Laar JM, Reedquist KA. CTLA-4IG suppresses reactive oxygen species by preventing synovial adherent cell-induced inactivation of Rap1, a Ras family GTPase mediator of oxidative stress in rheumatoid arthritis T cells. *Arthritis Rheum.* 2006;54:3135-43
IF: 7.667
10. Gerlag DM, Haringman JJ, Smeets TJ, Zwinderman AH, Kraan MC, Laud PJ, Morgan S, Nash AF, Tak PP. Effects of oral prednisolone on biomarkers in synovial tissue and clinical improvement in rheumatoid arthritis. *Arthritis Rheum.* 2004;50:3783-91
IF: 7.667

Current Funding

American College of Rheumatology
Dana Foundation
Dutch Government, SmartMix
Dutch Arthritis Association
EC Autocure
NWO and ZON-MW Research Foundations
Pharmaceutical industry

Training of Fellows in Research

We have established fellowships dedicated to training in arthroscopy, imaging techniques, immunohistochemistry, digital image analysis, and molecular biology

WebPages

<http://www.amc.nl>
<http://www.amc.nl/index.cfm?pid=2427&contentitemid=447&itemid=166>
<http://www.amc.nl/index.cfm?sid=525>
<http://www.arthrogen.nl>