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Current Fields of Research

Research activities in the Dept. of Rheumatology of the VU Medical Center and Jan van Breemen Research Institute / Reade in Amsterdam cover clinical research, translational research and basic science-directed research, with a special focus on disease targets: rheumatoid arthritis, ankylosing spondylitis, systemic lupus erythematosus, and systemic sclerosis:

- Preclinical state of rheumatoid arthritis
- Early Arthritis (RA, SpA)
- Clinical trials (BeST, COBRA, PREVAS studies)
- Antibodies to biologicals and the clinical consequences
- (Immuno)genetics
- Comorbidity (cardiovascular, osteoporosis)
- Imaging (PET, MRI)
- Clinical epidemiology
- Response-prediction biomarkers
- Disease profiling
- Experimental therapeutics
- Drug resistance

Selected publications

1. Felson DT, Smolen JS, Wells G, Zhang B, van Tuyl LH, Funovits J, Aletaha D, Allaart CF, Bathon J, Bombardieri S, Brooks P, Brown A, Matucci-Cerinic M, Choi H, Combe B, de Wit M, Dougados M, Emery P, Furst D, Gomez-Reino J, Hawker G, Keystone E, Khanna D, Kirwan J, Kvien TK, Landewé R, Listing J, Michaud K, Martin-Mola E, Montie P, Pincus T, Richards P, Siegel JN, Simon LS, Sokka T, Strand V, Tugwell P, Tyndall A, van der Heijde D, Verstappen S, White B, Wolfe F, Zink A, Boers M. American College of Rheumatology / European League Against Rheumatism provisional definition of remission in rheumatoid arthritis for clinical trials. *Ann Rheum Dis* (2011) 70: 404-413.
2. van de Stadt LA, van der Horst AR, de Koning MH, Bos WH, Wolbink GJ, van de Stadt RJ, Pruijn GJ, Dijkmans BA, van Schaardenburg D, Hamann D. The extent of the anti-citrullinated protein antibody repertoire is associated with arthritis development in patients with seropositive arthralgia. *Ann Rheum Dis* (2011) 70:128-133
3. Jamnitski A, Bartelds GM, Nurmohamed MT, van Schouwenburg PA, van Schaardenburg D, Stapel SO, Dijkmans BA, Aarden L, Wolbink GJ. The presence or absence of antibodies to infliximab or adalimumab determines the outcome of switching to etanercept. *Ann Rheum Dis* (2011) 70:284-288
4. Elzinga EH, van der Laken CJ, Comans EF, Boellaard R, Hoekstra OS, Dijkmans BA, Lammertsma AA, Voskuyl AE. 18F-FDG PET as a tool to predict the clinical outcome of infliximab treatment of rheumatoid arthritis: an explorative study. *J Nucl Med* (2011) 52:77-80
5. van Tuyl LH, Voskuyl AE, Boers M, Geusens P, Landewé RB, Dijkmans BA, Lems WF. Baseline RANKL:OPG ratio and markers of bone and cartilage degradation predict annual radiological progression over 11 years in rheumatoid arthritis. *Ann Rheum Dis* (2010) 69:1623-1628
6. Van Baarsen LG, Bos WH, Rustenburg F, van der Pouw Kraan TC, Wolbink GJ, Dijkmans BA, van Schaardenburg D, Verweij CL. Gene expression profiling in autoantibody-positive patients with arthralgia predicts development of arthritis. *Arthritis Rheum* (2010) 62: 694-704
7. Bos WH, Wolbink GJ, Boers M, Tjhuis GJ, de Vries N, van der Horst-Bruinsma IE, Tak PP, van de Stadt RJ, van der Laken CJ, Dijkmans BA, van Schaardenburg D. Arthritis development in patients with arthralgia is strongly associated with anti-citrullinated protein antibody status: a prospective cohort study. *Ann Rheum Dis* (2010) 69: 490-494
8. Peters MJ, Symmons DP, McCarey D, Dijkmans BA, Nicola P, Kvien TK, McInnes IB, Haentzschel H, Gonzalez-Gay MA, Provan S, Semb A, Sidiropoulos P, Kitis G, Smulders YM, Soubrier M, Szekanecz Z, Sattar N, Nurmohamed MT. EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. *Ann Rheum Dis* (2010) 69: 325-331

9. Güler-Yüksel M, Allaart CF, Goekoop-Ruiterman YP, de Vries-Bouwstra JK, van Groenendael JH, Mallée C, de Bois MH, Breedveld FC, Dijkmans BA, Lems WF. Changes in hand and generalised bone mineral density in patients with recent-onset rheumatoid arthritis. *Ann Rheum Dis* (2009) 68:330-336
10. Van der Heijden JW, Oerlemans R, Dijkmans BAC, Van der Laken CJ, Lems WF, Jackman AL, Kraan MC, Tak PP, Ratnam M, Jansen G. Folate receptor- β as potential delivery route for novel folate antagonists to macrophages in synovial tissue of rheumatoid arthritis patients. *Arthritis Rheum* (2009) 60:12-21
11. Van der Heijden JW, Oerlemans R, Tak PP, Assaraf YG, Kraan MC, Scheffer GL, Van der Laken CJ, Lems WF, Scheper RJ, Dijkmans BAC, Jansen G. Involvement of breast cancer resistance protein expression on RA synovial tissue macrophages in resistance to methotrexate and leflunomide. *Arthritis Rheum* (2009) 60:669-677
12. Peters, M.J., van Halm, V.P., Voskuyl, A.E., Smulders, Y.M., Boers, M., Lems, W.F., Visser, M., Stehouwer, C.D., Dekker, J.M., Nijpels, G., Heine, R., Dijkmans, B.A., Nurmohamed, M.T. Does rheumatoid arthritis equal diabetes mellitus as an independent risk factor for cardiovascular disease? A prospective study. *Arthritis Rheumatism* (2009) 61:1571-1579
13. van Eijk, I.C., de Vries, M.K., Levels, J.H., Peters, M.J., Huizerm E.E., Dijkmans, B.A., van der Horst-Bruinsma, I.E., Hazenberg, B.P., van de Stadt, R.J., Wolbink, G.J., Nurmohamed, M.T. Improvement of lipid profile is accompanied by atheroprotective alterations in high-density lipoprotein composition upon tumor necrosis factor blockade: a prospective cohort study in ankylosing spondylitis. *Arthritis Rheumatism* (2009) 60: 1324-1330
14. De Vries, M.K., van Eijk, I.C., van der Horst-Bruinsma, I.E., Peters, M.J., Nurmohamed, M.T., Dijkmans, B.A., Hazenberg, B.P., Wolbink, G.J. Erythrocyte sedimentation rate, C-reactive protein level, and serum amyloid a protein for patient selection and monitoring of anti-tumor necrosis factor treatment in ankylosing spondylitis. *Arthritis Rheumatism* (2009) 61:1484-1490
15. Van Tuyl LH, Lems WF, Voskuyl AE, Kerstens PJ, Garnero P, Dijkmans BA, Boers M. Tight control and intensified COBRA combination therapy in early rheumatoid arthritis: 90% remission in a pilot trial. *Ann Rheum Dis* (2008) 67:1574-1577
16. Van der Laken CJ, Elzinga EH, Kropholler MA, Molthoff CF, van der Heijden JW, Maruyama K, Boellaard R, Dijkmans BA, Lammertsma AA, Voskuyl AE. Noninvasive imaging of macrophages in rheumatoid synovitis using ^{11}C -(R)-PK11195 and positron emission tomography. *Arthritis Rheum* (2008) 58:3350-3355
17. Bos WH, Wolbink GJ, Boers M, Tjhuis GJ, de Vries N, van der Horst-Bruinsma IE, Tak PP, van de Stadt RJ, van der Laken CJ, Dijkmans BA, van Schaardenburg D. Arthritis development in patients with arthralgia is strongly

- associated with anti-citrullinated protein antibody status: a prospective cohort study. *Ann Rheum Dis* (2010) 69: 490-494
18. Güler-Yüksel M, Bijsterbosch J, Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Hulsmans HM, de Beus WM, Han KH, Breedveld FC, Dijkmans BA, Allaart CF, Lems WF. Changes in bone mineral density in patients with recent onset, active rheumatoid arthritis. *Ann Rheum Dis* (2008) 67:823-828
 19. Van der Pouw Kraan TC, Wijbrandts CA, van Baarsen LG, Voskuyl AE, Rustenburg F, Baggen JM, Ibrahim SM, Fero M, Dijkmans BA, Tak PP, Verweij CL. Rheumatoid arthritis subtypes identified by genomic profiling of peripheral blood cells: assignment of a type I interferon signature in a subpopulation of patients. *Ann Rheum Dis*. (2007) 66:1008-1014
 20. Güler-Yüksel M, Bijsterbosch J, Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Roday HK, Peeters AJ, de Jonge-Bok JM, Breedveld FC, Dijkmans BA, Allaart CF, Lems WF. Bone mineral density in patients with recently diagnosed, active rheumatoid arthritis. *Ann Rheum Dis*. (2007) 66:1508-1512
 21. Van Rossum MA, van Soesbergen RM, Boers M, Zwinderman AH, Fiselier TJ, Franssen MJ, ten Cate R, van Suijlekom-Smit LW, Wulffraat NM, van Luijk WH, Oostveen JC, Kuis W, Dijkmans BA: Dutch Juvenile Idiopathic Arthritis Study group. Long-term outcome of juvenile idiopathic arthritis following a placebo-controlled trial: sustained benefits of early sulfasalazine treatment. *Ann Rheum Dis* (2007) 66:1518-1524
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 23. Van Halm VP, Nielen MM, Nurmohamed MT, van Schaardenburg D, Reesink HW, Voskuyl AE, Twisk JW, van de Stadt RJ, de Koning MH, Habibuw MR, van der Horst-Bruinsma IE, Dijkmans BA. Lipids and inflammation: serial measurements of the lipid profile of blood donors who later developed rheumatoid arthritis. *Ann Rheum Dis* (2007) 66:184-188
 24. Vis M, Havaardsholm EA, Haugeberg G, Uhlig T, Voskuyl AE, van de Stadt RJ, Dijkmans BA, Woolf AD, Kvien TK, Lems WF. Evaluation of bone mineral density, bone metabolism, osteoprotegerin and receptor activator of the NFkappaB ligand serum levels during treatment with infliximab in patients with rheumatoid arthritis. *Ann Rheum Dis* (2006) 65:1495-1499
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28. Van Rossum MA, Boers M, Zwinderman AH, van Soesbergen RM, Wieringa H, Fiselier TJ, Franssen MJ, ten Cate R, van Suijlekom-Smit LW, Wulffraat NM, van Luijk WH, Oostveen JC, Kuis W, Dijkmans BA; Dutch Juvenile Idiopathic Arthritis Study Group. Development of a standardized method of assessment of radiographs and radiographic change in juvenile idiopathic arthritis: introduction of the Dijkstra composite score. *Arthritis Rheum* (2005) 52: 2865-2872
29. 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* (2005) 52: 3381-3390

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- Dutch Arthritis Foundation
- Dutch government
- EC Autocure
- Dutch National Science Foundation (NWO)
- ZonMW Research Foundation
- Center for Translational and Molecular Medicine
- Pharmaceutical industry
- EULAR

Training of Fellows in Research

- Clinical fellows participate in courses and receive training in clinical epidemiology, joint examination and laboratory assessments.

WebPages:

www.vumc.nl/afdelingen/reumatologie

www.vumc.nl/afdelingen/CCA-V-ICI

www.move.vu.nl

www.reade.nl