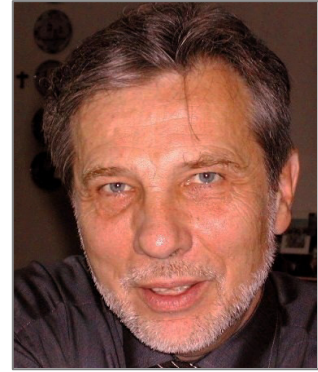


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Current Fields of Research**Connective tissues of synovial joints – regenerative medicine – OA**

The department contributes to research on genetics, cell biology, the biochemistry and the physiology of the connective tissues of bones and joints. Substantial expertise has been obtained on the development and the use of alleged chondroprotective drugs. An alkylated cyclodextrin polysulphate, for which Ghent University obtained the patent, is currently developed for the use in the human clinics of OA and will now enter phase II of the development plan. Therefore, studies on the DMOAD effects of these drugs are conducted on the 'erosive' type of hand OA and "in house" methods have been developed to evaluate the anatomical progression of this disease.

The department is engaged in the development of biodegradable and biocompatible scaffolds for the culture and implantation of different connective tissue cells in an articular environment, e.g. articular cartilage, menisci and tendon-like structures. With the department of orthopedic surgery, the department shares 15 years of experience with regard to heterologous cartilage cell transplantation and the transplantation of meniscal bodies.

We contributed significantly to the development of recommendations for the diagnosis and the management of knee, hip and hand OA and is currently involved in the first therapeutic trials with TNF blockers in erosive OA of the interphalangeal finger joints.

Immunology in animal models of arthritis

The laboratory for molecular immunology and inflammation is focused on studying cellular and molecular mechanisms of joint inflammation and has a genuine interest in the role of natural killer T (NKT) cells, a unique regulatory lymphocyte subset, in health and disease. We have unmasked a pivotal role of the TNF cytokine, lymphotoxin alpha, in NK and NKT cell biology. Our studies highlight the potential of NKT cells to modulate a variety of immune responses, both in a preventive and therapeutic manner.

We currently study cellular and molecular mechanisms of joint inflammation with the specific goal to translate this into therapeutic interventions. As such, we have evaluated a plant derived ligand that binds to glucocorticoid receptor, but unlike classical glucocorticoids does not impose transactivation. As a result, this compound has marked differences in modulating glucocorticoid receptor and serves as a classical selective glucocorticoid agonist, which could therefore have a better efficacy/toxicity ratio compared to classical glucocorticoids. The second approach involves a camelid derived anti-TNF antibody that was able to strongly modulate collagen induced arthritis. Finally, we recently highlighted the role of TNF receptor 1 on mesenchymal cells as a common denominator in regulating combined gut and joint disease in spondyloarthritis. Several new leads unmasked by genome/proteome discovery projects are currently being validated.

Spondylarthropathy - SpA

One of the major objectives in clinical and fundamental research in our department was unravelling the relationship between gut and joint in the spondyloarthropathies (SpA). Gut inflammation - histologically present in SpA patients - was directly related to the locomotoric inflammation and could lead to Chron's disease. This relationship was further studied by comparing immunological features of gut biopsy and synovial biopsy, after needle arthroscopy. New insights in the genetic background, especially in relation to the CARD 15 mutations suggest that SpA and Chron's disease should be considered as distinct phenotypes of common immune-mediated inflammatory pathways rather than as separate disease entities.

The department works together with international groups (ASAS, GRAPPA, CASPAR) in order to define assessments, outcome measures and classification criteria in the SpA's. New classification criteria for the diagnosis of psoriatic arthritis were developed during an international study (CASPAR).

Rheumatoid Arthritis (RA) - pathophysiology, diagnostic use of auto-antibodies and long-term follow-up of biological

Both HC gp-39 and citrullinated antigens, like fibrin have intimate relations with the RA-associated HLA-DR shared epitope. HC gp-39 mainly leads to T cell autoreactivity, while citrullinated antigens are more associated with B cell autoimmunity and autoantibodies. We gained important insight into the diagnostic association between anti-citrullinated protein antibodies (ACPA) and RA. Recent research focused on a novel citrullinated autoantigen in RA, namely processed citrullinated vimentin, a protein present in the synovial tissue proteome of patients with RA. We are currently studying the diagnostic potential of this protein. Clinical research in RA has been the long-term follow-up of RA patients under anti-TNF therapy. DAS28 was shown to be the best 'surrogate marker' for good response to therapy in clinical practice for patients under biological treatment.

Orphan inflammatory diseases

Prospective observational studies have been set up in order to contribute to the understanding of uncommon long-lasting disorders. One example is, the Belgian Systemic Sclerosis Cohort (BSSC), created to follow prospectively patients suffering from this affection. This national project, has as purpose, on one hand, to improve and standardize the care of systemic sclerosis patients and, on the other hand, to define the natural history of the disease, to identify prognostic factors and to test pathophysiological hypotheses. Clinical expertise has been acquired in the technique of capillaroscopy.

Selected Publications

1- Nailfold capillaroscopy for day-to-day clinical use: construction of a simple scoring modality as a clinical prognostic index for digital trophic lesions.

Smith V, De Keyser F, Pizzorni C, Van Praet JT, Decuman S, Sulli A, Deschepper E, Cutolo M. *Ann Rheum Dis.* 2011;70:180-3.

IF 8,111

2- Effectiveness of adalimumab in treating patients with active psoriatic arthritis and predictors of good clinical responses for arthritis, skin and nail lesions.

Van den Bosch F, Manger B, Goupille P, McHugh N, Rødevand E, Holck P, van Vollenhoven RF, Leirisalo-Repo M, Fitzgerald O, Kron M, Frank M, Kary S, Kupper H.

Ann Rheum Dis. 2010;69:394-9.

IF 8,111

- 3- Invariant natural killer T cells are natural regulators of murine spondylarthritis.
Jacques P, Venken K, Van Beneden K, Hammad H, Seeuws S, Drennan MB, Deforce D, Verbruggen G, Apostolaki M, Kollias G, Lambrecht BN, De Vos M, Elewaut D.
Arthritis Rheum. 2010;62:988-99.
IF 7,332
- 4- Rituximab in diffuse cutaneous systemic sclerosis: an open-label clinical and histopathological study.
Smith V, Van Praet JT, Vandooren B, Van der Cruyssen B, Naeyaert JM, Decuman S, Elewaut D, De Keyser F.
Ann Rheum Dis. 2010;69:193-7.
IF 8,111
- 5- Systemic levels of IL-23 are strongly associated with disease activity in rheumatoid arthritis but not spondyloarthritis.
Melis L, Vandooren B, Kruithof E, Jacques P, De Vos M, Mielants H, Verbruggen G, De Keyser F, Elewaut D.
Ann Rheum Dis. 2010;69:618-23.
IF 8,111
- 6- The morbid anatomy of "erosive osteoarthritis" of the interphalangeal finger joints. an optimized scoring system to monitor disease progression in affected joints.
Verbruggen G, Wittoek R, Vander Cruyssen B, Elewaut D.
Ann Rheum Dis. 2010;69:862-7.
IF 8,111
- 7- Differential mechanism of NF-kappaB inhibition by two glucocorticoid receptor modulators in rheumatoid arthritis synovial fibroblasts.
Gossye V, Elewaut D, Bougarne N, Bracke D, Van Calenbergh S, Haegeman G, De Bosscher K.
Arthritis Rheum. 2009;60:3241-50.
IF 7,332
- 8- Cutting Edge: The Chemokine Receptor CXCR3 Retains Invariant NK T Cells in the Thymus.
Drennan MB, Franki AS, Dewint P, Van Beneden K, Seeuws S, van de Pavert SA, Reilly EC, Verbruggen G, Lane TE, Mebius RE, Deforce D, Elewaut D.
J Immunol. 2009;183:2213-6.
IF 7,145
- 9- Differential expression of alphaB-crystallin and evidence of its role as a mediator of matrix gene expression in osteoarthritis.
Lambrecht S, Verbruggen G, Elewaut D, Deforce D.
Arthritis Rheum. 2009;60:179-88.
IF 7,332
- 10- Armaka M, Apostolaki M, Jacques P, Kontoyiannis DL, Elewaut D, Kollias G. Mesenchymal cell targeting by TNF as a common pathogenic principle in chronic inflammatory joint and intestinal diseases. *J Exp Med.* 2008;205:331-7.
IF : 15.651

Current Funding

Fund Scientific Research, Flanders
Cancer UK
Marato, Spain
Institute for Science and Innovation (IWT), Flanders
KBVR – Koninklijke Belgische Vereniging voor Reumatologie
Research Council Ghent University
Industry

Training of Fellows in Research

Since 25 years we organize a series of postgraduate training courses for Flanders' rheumatologists, 10 times a year. With the sponsoring of the pharmaceutical industry we organize Clinical Observation Programs (COP) on the treatment of the Spondylarthropathies with TNF-blocking agents for rheumatologists of the different continents.

WebPage

<http://www.uzgent.be/wps/wcm/connect/nl/web/zorg/patienten/diensten/reumatologie/reumatologie>