Department of Medicine 3 – Rheumatology and Immunology

Chair of Internal Medicine III

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Research focus
- Activation of synovial fibroblasts by microparticles in rheumatoid arthritis (RA)
- Apoptosis, necrosis, and NETosis as immune modulators
- Activation of neutrophile granulocytes
- National and international clinical trials
- Immunogenetics and transplantimmunology
- Immunodeficiencies and infectious diseases
- Mechanisms for the activation of fibroblasts in systemic sclerosis (SSc)
- Molecular signaling pathways in RA
- Metabolic impact on inflammation
- Pathomechanisms of bone destruction in RA
- Analysis of risk factors and long-term outcome in patients with systemic lupus erythematosus (SLE)
- Immunobiology and molecular mechanisms of inflammation
- Analysis of inflammatory mechanisms in adult onset Still’s disease
- Molecular and cellular immunology in metabolism
- Epidemiology and experimental imaging

Structure of the Chair
Professorships: 6
Personnel: 163
- Doctors (of Medicine): 18
- Scientists: 28 (thereof funded externally: 24)
- Graduate students: 47

Clinical focus areas
- Rheumatology (In- and outpatient department)
- Immunology (In- and outpatient department)

Research
The Department of Medicine 3 focuses on translational and clinical inflammation research to decipher the mechanisms that are responsible for pathogenesis and perpetuation of rheumatic inflammatory and autoimmune diseases. The emphasis of the experimental research is on the interaction between immune cells and cells of affected organs. The main focus of the clinical research is besides drug trial studies on interdisciplinary cooperations to optimize imaging methods.

Activation of synovial fibroblasts by microparticles in rheumatoid arthritis (RA)
PI: Prof. Dr. J. Distler
Microparticles are realized by activated and apoptotic leukocytes and accumulate in the involved joints in patients with RA. We demonstrated that microparticles represent a novel mechanism for inter-cellular communication and that they play a role in the pathogenesis of RA by triggering a vicious circle of inflammation and bone-erosion. The mechanisms by which microparticles activate synovial fibroblasts are currently in focus.

Apoptosis, necrosis, and NETosis as immune modulators
PI: Prof. Dr. Dr. M. Herrmann
We utilize controlled suicide systems to analyze generation and role of ROS (reactive oxygen species) and their intracellular accumulation. We employ the MSU (monosodium urate) driven inflammation to analyze recruitment of granulocytes to sites of inflammation, NET formation, and aggregation.

Activation of neutrophile granulocytes
PI: Dr. M. Hoffmann
Neutrophil granulocytes can either fuel or downregulate inflammation. We investigate the influence of neutrophils on inflammatory diseases and bone metabolism (gout, RA, or SLE). We focus on the formation of neutrophil extracellular traps (NET) and on chemical redox reactions. Finally, we are going to translate data from animal models and in vitro-findings to humans and develop new treatment strategies.

Immunogenetics and transplantimmunology
PI: Prof. Dr. B. Spriewald
One research area is the induction of transplantation tolerance and modulation of transplant arteriosclerosis through the application of donor alloantigen and co-stimulation blockade. An important contribution to clinical research is the detection and differentiation of anti-HLA alloantibodies.

Immunodeficiencies and infectious diseases
PI: Prof. Dr. T. Harrer
The major research interests of this group are aspects of HIV-infection, such as immunology, drug resistance, and research on new therapeutic and diagnostic procedures, like T cell receptor transfer and immunomonitoring using mRNA electroporation. We are developing immunotherapies, like vaccines and immunomodulators, and participate in clinical studies on therapeutics for HIV-infection. Other projects focus on further infectious and immunologic diseases and chronic fatigue syndrome.

Mechanisms for the activation of fibroblasts in systemic sclerosis (SSc)
PI: Prof. Dr. J. Distler
SSc is characterized by organ fibrosis, mediated by an uncontrolled production of ECM by fibroblasts. However, therapies to inhibit selectively the overproduction of ECM are lacking. We investigate novel signaling cascades that activate fibroblasts and study therapeutic approaches to inhibit the overproduction of ECM by SSc fibroblasts.

Molecular signaling pathways in RA
PI: Prof. Dr. G. Schett, PD Dr. M. Stock
RA is characterized by perpetuating synovial inflammation and progressive joint destruction based on cartilage damage and bone erosion as a result of an imbalance of formation and resorption of cartilage and bone. Wnt signals link inflammation to this structural damage in arthritis and may play a major role in the pathogenesis of RA. We focus on regulation of the Wnt signaling network in rheumatic diseases and evaluate the potentials to interfere with cartilage damage caused by dysregulated Wnt signaling.

Metabolic impact on inflammation
PI: Prof. Dr. A. Bozec
Arthritis, adipose, and diabetes appear to form an alliance that has a pro-inflammatory and destructive effect on joints and bones. We investi-
gate central transcription factors and signaling pathways relevant as checkpoints for differentiation and activation in osteoclasts, osteoblasts, and adipocytes.

Pathomechanisms of bone destruction in RA
Pt. Prof. Dr. G. Schett, Dr. U. Steffen
RA is one of the most common inflammatory rheumatic joint diseases with an estimated prevalence of 1%. Chronic arthritis, if poorly controlled, typically provokes extensive joint damage with the emergence of bone destruction associated with significantly decreased functional capacities. Hence, the project group focuses on the pathophysiology of bone destruction by the use of experimental arthritis models. They investigate the mechanisms leading to increased synovial activation of osteoclasts and decreased ability to repair bone destruction with the help of osteoblasts.

Analysis of risk factors and long-term outcome in patients with systemic lupus erythematous (SLE)
Pt: Prof. Dr. B. Manger
In a cohort of 410 SLE patients, genetic, serological, and clinical predictors for long-term outcome are analyzed in retrospective and prospective studies. One focus is on the investigation of premature atherosclerosis and ovarian failure in SLE.

Immunobiology and molecular mechanisms of inflammation
Pt: Prof. Dr. G. Kronke
Insights into basic principles of immunity are a key for the better understanding of autoimmunity and inflammation. Simultaneously, they allow the development of new therapeutic strategies for autoimmune and chronic inflammatory diseases. We investigate molecular mechanisms that link innate and adaptive immunity and thus influence inflammation, tolerance, and autoimmune responses. Our aim is to understand key decisions points that trigger a physiological immune response or cause autoimmunity (e.g. RA and systemic lupus).

Analysis of inflammatory mechanisms in adult onset Still's disease
Pt: PD Dr. J. Rech, Prof. Dr. B. Manger
Inflammatory mechanisms and cytokine profiles in patients with adult onset Still’s disease are analyzed with respect to clinical presentation and outcome to identify therapeutic strategies for this rare disease.

Molecular and cellular immunology in metabolism
Pt: Dr. M. Zaiss
Different types of immune responses require alterations in metabolism – vice versa, are immunomodulators (e.g. cytokines) dictating direct alterations in metabolism, which highlight the interaction between these two aspects? Our aim is the investigation of the interplay of immunology, metabolism, and nutrition in order to prevent or resolve autoimmune diseases.

Epidemiology and experimental imaging
Pt: Dr. A. Kleyer, Dr. D. Simon
Epidemiological research with well-defined patient cohorts is an essential element to understand the course of rheumatic diseases and to provide optimal targeted treatment. Our group is particularly interested in the early stages of RA and psoriatic arthritis (PsA). We are developing and establishing new outcome measures by using experimental imaging to study the transition from silent disease to clinical evident inflammation.

Teaching
The Department of Medicine 3 is embedded into the curriculum-based teaching of the Medicine and Dentistry. In the course of interdisciplinary teaching, the lecture “Dr. House in Erlangen – surgical and internal differential diagnosis for first-year students” is to highlight particularly. Furthermore, Master’s as well as MD and PhD theses are supervised.

Selected publications
Kienhöfer D et al. Experimental lupus is aggravated in mouse strains with impaired induction of neutrophil extracellular traps. JCI Insight. 2017 May 18;2(10): pii: 92920

International cooperations
Prof. L. Klareskog, Karolinska Institute, Stockholm: Sweden
Prof. Dr. S. Kiechl, Medizinische Universität Innsbruck, Innsbruck: Austria
Prof. M. Hansson, Uppsala University, Uppsala: Sweden
Prof. Dr. E. Wagner, Spanish National Cancer Research Centre (CNIO), Madrid: Spain
Prof. I. McIntnees/ Dr. C. Goodyear, University of Glasgow, Glasgow: UK