

Preface

The IL-17 cytokines represent a novel family of cytokines, which extends the Th1-Th2 paradigm and defines a new effector T cell, the Th17 cell. Th17 cells may co-express at least IL-17A and IL-17F and IL-22. IL-17A and IL-17F can be produced by CD4⁺ T cells (Th17 cells), CD8⁺ T cells (Tc17), $\gamma\delta$ T cells, iNKT, NK cells, lymphoid tissue inducers cells, innate lymphoid cells, mast cells, neutrophils and Paneth cells. IL-17F can be expressed also by epithelial cells. IL-22 can be produced by CD4⁺ T cells (Th22) as well as other cell types. The regulation of IL-17 family members and the effector cells and mechanisms are an area of intense current research, and include as an example the nuclear receptors ROR γ t and proinflammatory cytokines such as IL-1, IL-6, TGF β , IL-21 and IL-23. Some experimental data suggest that IL-17A may have a dual function – proinflammatory and anti-inflammatory – suggesting that IL-17A may also terminate inflammation. Further, the reciprocal regulation of Th17 and regulatory T cells including the role retinoic acid is highlighted.

The discovery that patients with rheumatoid arthritis, allergic disorders and inflammatory bowel disease express IL-17A generated tremendous interest in the medical community and instigated a flurry of experimental research on the potential role of Th17 cells in inflammatory diseases.

Experimental studies confirmed that IL-17A is induced and is critical for the development of allergic lung inflammation, arthritis, inflammatory bowel disease, experimental allergic encephalomyelitis and other inflammatory conditions and organ transplantation. Recent investigation revealed a dual role of IL-22 in inflammation, and IL-22 can be considered as an important protecting factor at the mucosal and cutaneous barriers. A newly defined innate lymphoid cell type emerged as an important source of IL-22 which activates STAT3-dependent protecting peptides at the barrier sites. IL-17A neutralization inhibited experimental arthritis opening a new therapeutic possibility to treat rheumatoid arthritis.

Neutralization of IL-17A, however, might alter host defense to microbial pathogens, such as mycobacteria and opportunistic extracellular pathogens including fungi, and tumor host responses. Therefore the introduction of neutralizing therapies

may require special cautions. However, even if safety data in clinical studies are limited, they have been favorable to date.

Tools for experimental investigations such as recombinant proteins, neutralizing antibodies and gene deficient mice have been developed and are discussed in more detail.

Clinical studies in psoriasis, rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis suggest that IL-17 antibody neutralization may be an interesting addition for the treatment of these diseases. However studies in Crohn's diseases have not kept the promise. Clinical studies in other autoimmune diseases and in asthma are ongoing and new insights in the pathogenesis of these diseases are expected.

The fully revised multi-author contribution with experts in the field will be very useful for scientists and medical doctors exploring novel mechanisms of inflammation and therapy. This comprehensive review on IL-17, IL-22 and Th17 cells is an updated summary by experts and a digest of the literature, which exploded in the last years. Finally, we wish to thank the authors who dedicated their precious time with expert contributions which make this an outstanding volume in Inflammation Research.

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IL-17, IL-22 and Their Producing Cells: Role in
Inflammation and Autoimmunity

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2013, X, 354 p., Hardcover

ISBN: 978-3-0348-0521-6