Chapter 3

ANTI-INTERLEUKIN 17 THERAPY: FOCUS ON SECUKINUMAB

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INTRODUCTION

The (IL-17) /IL-17 receptor (IL-17R) family has recently been discovered to be very important in the pathogenesis of human autoimmune diseases. Particularly IL-17A is considered to be a key driver of chronic inflammatory reactions in immune mediated diseases. Blocking this cytokine seems potentially beneficial for treating these disorders since it allows to preserve key functions of the immune system (Zhu and Qian, 2012). Several antibodies that target IL-17A signaling directly or indirectly are in clinical development for the treatment of autoimmune diseases.

Secukinumab (formerly named AIN-457), the fully human monoclonal antibody (mAb), which selectively targets the IL-17A cytokine, in clinical trials in psoriasis, rheumatoid arthritis (RA), auto-immune uveitis, psoriatic arthritis (PsA), ankylosing spondylitis (AS) and Crohn's disease (CD) will be reviewed.

HISTORY

The differentiation of naive CD4+ T cells into effector T- helper cells is driven by the cytokines of the innate immune system. This process was classified as IL-12 (with IL-18) drives differentiation via the Th1 pathway and IL-4 (with IL-33) drives differentiation via the Th2 pathway previously (Mosmann et all., 1986). These T-helper subsets produce different cytokines that mediate host defenses. Th1 cells primarily produce interferon (IFN)γ to activate macrophages against intracellular pathogens and certain fungi, whereas Th2 cells produce IL-4, IL-5, and IL-13 to activate eosinophils offering protection against parasitic infections (Miossec, Korn and Kuchroo, 2009). Discovery of Th17 cells was impulsed by the finding that a non-Th1, IL-23-regulated population of cells was necessary for induction of autoimmune disease in animal studies (Harrington et all., 2005).

Transforming growth factor TGFβ, IL-6, and IL-1β works together to stimulate the transcription factor retinoid-related orphan receptor (ROR)γt in murine

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results of this study may be explained by the protective function of IL-17A in the intestine, as observed in an animal model of colitis (Ogawa et all., 2004). More research is needed to verify the postulated role of IL-17A in CD pathophysiology.

CONCLUSION

IL-17A participates in the pathogenesis of autoimmune diseases, including psoriasis, RA, PsA and AS. IL-17A-based therapies exert more targeted effects and so less serious adverse events on the immune system than existing biologicals. Secukinumab is one of several antibodies targeting IL-17A signalling that are in clinical development for the treatment of autoimmune diseases. It seems like a promising treatment choice for compelling, life quality decreasing inflammatory diseases such as psoriasis, RA, PsA, and AS.

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