Anti-IL-17A/IL-17F Cross-Reactive Antibodies And Methods Of Use Thereof

RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No. 61/126,465, filed May 5, 2008, and U.S. Provisional Application No. 61/098,369, filed September 19, 2008, the contents of each of which are hereby incorporated by reference in their entirety.

FIELD OF THE INVENTION

This invention relates generally to the generation of monoclonal antibodies, *e.g.*, fully human monoclonal antibodies, that recognize IL-17F, to monoclonal antibodies, *e.g.*, fully human antibodies that recognize the heterodimeric IL-17A/IL-17F complex, and to monoclonal antibodies, *e.g.*, fully human cross-reactive antibodies that recognize both IL-17F and IL-17A when not complexed together, and to methods of using the monoclonal antibodies as therapeutics.

BACKGROUND OF THE INVENTION

IL-17A (originally named CTL-8, and also known as IL-17) is the archetypical/founding member of the IL-17 family of cytokines. In addition to IL-17A, members of the IL-17 cytokine family presently include the proteins IL-17B, IL-17C, IL-17D, IL-17E (also called IL-25) and IL-17F that share a conserved C-terminal region but different N-terminal segments.

IL-17A and IL-17F are the two most closely related members of the family, both in terms of sequence and biological properties. IL-17F shares 55% sequence identity with IL-17A at the amino acid level. Both IL-17A and IL-17F are secreted as disulfide linked homodimers which signal through the receptors IL-17R, IL-17RC, or a multimeric receptor complex composed of the IL-17R and IL-17RC. Both are also co-expressed on the same T cell subsets (principally by the Th17 $CD4^+$ T cells).

Moreover, both have been similarly implicated as contributing agents to progression and pathology of a variety of inflammatory and auto-immune diseases in humans and in mouse models of human diseases. Specifically, IL-17A and IL-17F have been implicated as major effector cytokines that trigger inflammatory responses and thereby contribute to a number of autoinflammatory diseases including multiple sclerosis, rheumatoid arthritis, and inflammatory bowel diseases and cancer.

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