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Editorial

IL-17 and its role in psoriasis

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T cells are part of our innate immune system and are involved in pathogenesis of many diseases. Many subsets of T cells are continuously being discovered. Th-17 is one of them and it produces cytokines like IL-17.[1] The family of IL-17 is involved in many inflammatory processes of diseases like psoriasis, inflammatory bowel disease, multiple sclerosis, asthma and rheumatoid arthritis.[1]

There are six known subtypes of IL-17 including A, B, C, D, E and F. Three of them (A, C and F) have a more prominent role in psoriasis. These molecules act after binding with receptors including IL17RA, IL17RB, IL17RC, IL17RD, IL17RE and IL17RF.[2]

IL-17 induces release of many cytokines (e.g. IL-6, G-CSF, GM-CSF, IL-1B, TGF-B, TNF-∞), chemokines (e.g. IL-8, GRO-∞ and MCP-1) and prostaglandins such as PGE2 from fibroblasts, endothelial cells, keratinocytes and macrophages. IL-17 along with IL-22 induces antimicrobial peptide production by keratinocytes.[3] The release of cytokines results in keratinocyte and vascular response along with enhanced cell recruitment.[1] Keratinocytes in response produce chemokines and cytokines, which specifically cause neutrophil recruitment.[1] Il-17 also downregulates filaggrin, leading to disruption of skin barrier. IL-17A, the best-studied member of this family, is composed of 155 amino acids with molecular weight of 15KDa. It forms heterodimers or homodimers with IL-17F, binding with IL-17RA and IL17RC subunits leading to gene activation.[4]

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Role in psoriasis

Research has shown IL23/IL17 pathway to play a central role in pathogenesis of psoriasis. Biopsies taken from active lesions of psoriasis show increased T cells and neutrophils containing IL-17.[5,6]

Il-17 induces inflammatory response in skin that damages the keratinocytes and consequently activates immature dendritic cells.[5] Different cytokines including TNF-∞, IL-1 and IL-6 are released which recruit T cells, NK cells and monocytes. These cells release IL-23 which induces Th-17 cells to produce IL-17 in combination with IL-22.[5] Il-17 interacts with IL-17RA receptors leading to release of IL-6, antimicrobial peptides, IL-8 and CCL-20.[7]

Due to altered immune response in psoriasis, there is unchecked IL-17 production in lesions enhancing IL-17 mediated cellular response. Neutrophils remove the damaged keratinocytes. Recruitment of new immature dendritic cells restarts the inflammatory cycle and causes progression of psoriasis (**Figure 1**).[6]

IL-17 is now considered as the driver cytokine in psoriasis, and therapies targeting this cytokine are being tried. The IL-23 antibody Ustekinumab is also being used to treat psoriasis by reducing IL-17.[8] Newer therapies targeting IL-17 are currently under clinical trials showing good clinical efficacy. The three monoclonal antibodies against IL-17 are brodalumab, ixekizumab and secukinumab.

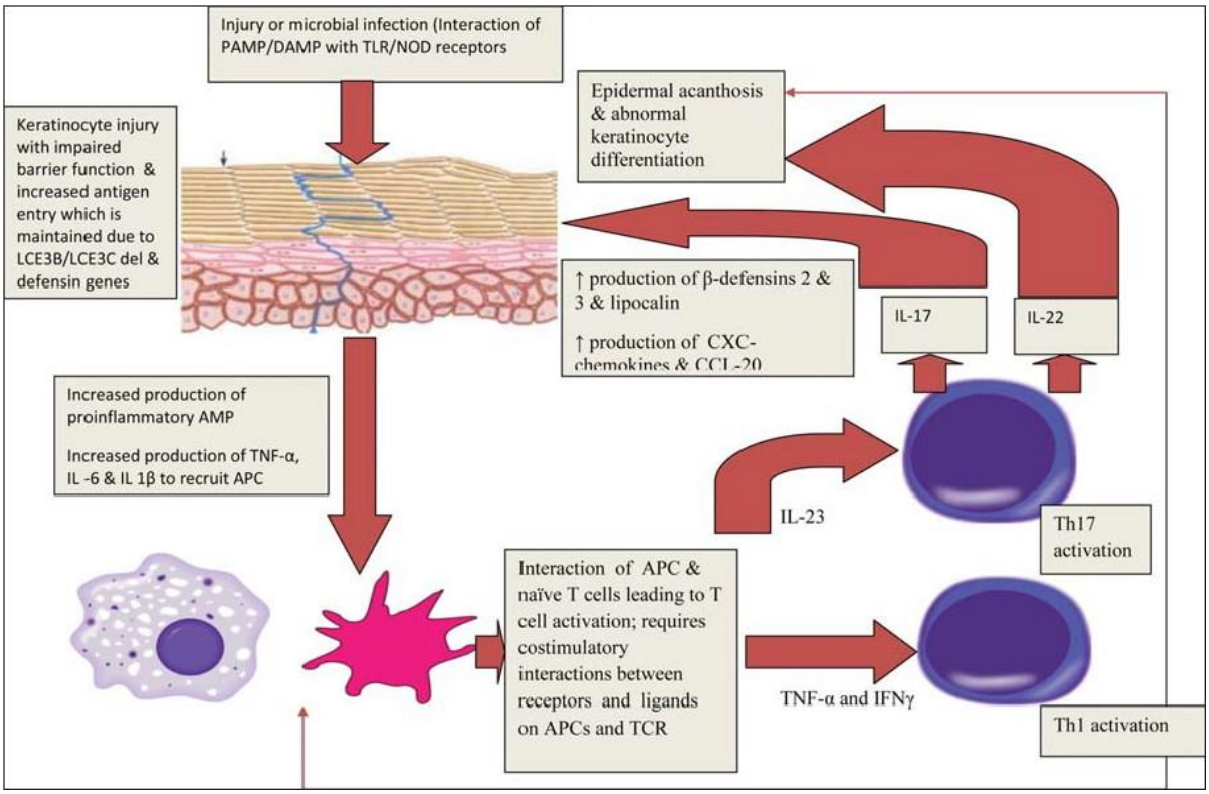

Figure 1 IL-17 pathway in psoriasis.

Brodalumab in a human, anti IL-17 receptor monoclonal antibody that binds with IL-17RA, inhibiting the activity of IL17A, IL17F and IL17A/F heterodimers and IL-17E.[9]

Ixekizumab is humanized immunoglobulin G4 monoclonal antibody and secukinumab is a fully human IgG1k monoclonal antibody that acts against IL-17A.[10,11]

The continued efforts of investigators to find new therapeutic targets in the treatment of psoriasis are validating its theory of pathogenesis. The successful use of biologicals like anti-IL-17 and anti-IL-17R will improve the patient care and will reduce the cardiovascular diseases, arthritis and other co-morbidities associated with psoriasis.

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