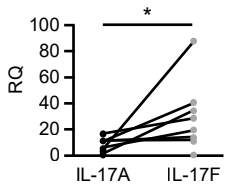
Pathologic Activities of IL-17A and IL-17F Cytokine Signaling and Therapeutic Targets

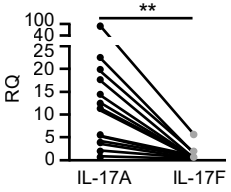
The Expression of IL-17A and IL-17F in Joints and Skin Differs

Psoriasis Skin



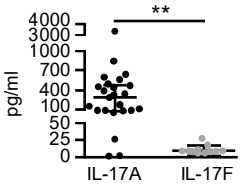
IL-17F mRNA expression was 2.7-fold higher than IL-17A.[1]

SpA Synovial Tissue



IL-17A mRNA expression was 17.3-fold higher than IL-17F.[1]

SpA Synovial Fluid



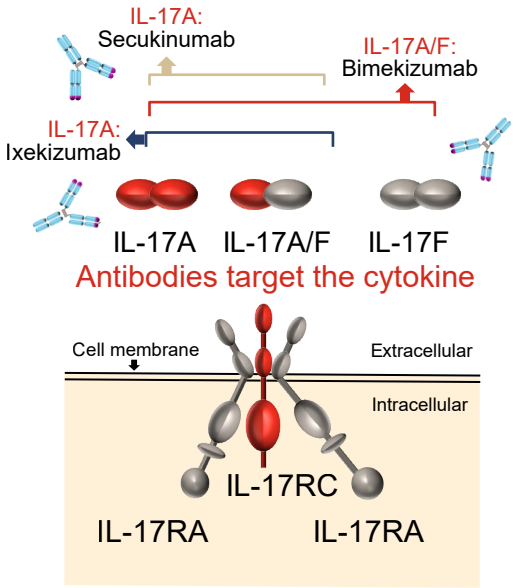
IL-17A protein levels were 37.4-fold higher than IL-17F levels.[1]

IL-17A response is **10 to 30-fold more potent** than IL-17F in terms of downstream gene activation.[2]

IL-17A has a **more dominant role in pathologic changes** than IL-17F in PsO[3] and SpA.[1]

IL-17F contributes to inflammatory responses and protection at barrier surfaces.[4]

The Binding Affinity of IL-17 Inhibitor Antibodies to IL-17 Cytokines Differs



Cytokine	Secukinumab	Ixekizumab	Bimekizumab
IL-17 A/A	129	1.8	3.2
IL-17 A/F	2400	1.8	26
IL-17 F/F	NB	NB	23

A lower number indicates higher binding affinity. Binding affinities (pM) were obtained from published sources using different methodologies and cannot be directly compared.[5]

This data reflects known information about the drug mechanism of action and does not represent a safety or efficacy comparison.[5]

*P <0.01, **P <0.0001.
NB=No Binding; pM=Picomolar; PsO=Psoriasis; RQ=Relative Quantification; SF=Synovial Fluid; SpA=Spondyloarthritis.
1. Chen S, et al. *J Rheumatol.* 2020;47(11):1606-1613. 2. Gaffen SL. *Nat Rev Immunol.* 2009;9(8):556-67. 3. Kolbinger F, et al. *J Allergy Clin Immunol.* 2017;139(3):923-932.e8. 4. McGeachy MJ, et al. *Immunity.* 2019;50(4):892-906.
5. Adams R, et al. *Front Immunol.* 2020;11:1894.
The association between the binding affinity of ixekizumab and efficacy and safety has not been studied by Lilly. No comparisons can be made regarding the binding affinity of IL-17A to ixekizumab and the binding affinity of other products to their targets. This has not been studied by Lilly.