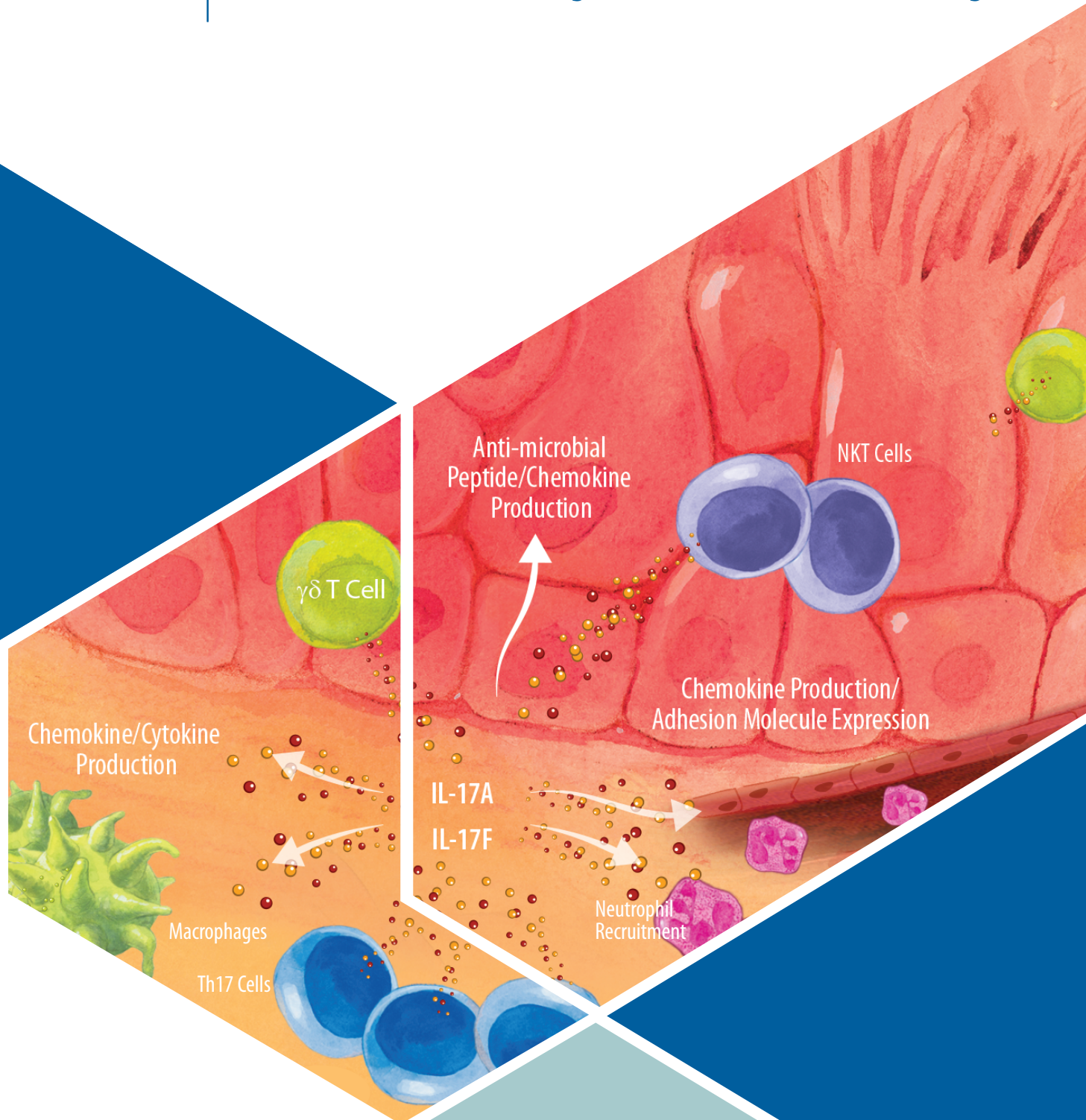


# The IL-17 Cytokine Family



# The IL-17 Cytokine Family

The IL-17 cytokine family consists of six proteins (IL-17A, IL-17B, IL-17C, IL-17D, IL-17E/IL-25, and IL-17F) that are secreted by multiple cell types and primarily promote pro-inflammatory immune responses. IL-17A was the first member of the IL-17 family of cytokines to be cloned, followed by homology-based cloning of the five other IL-17 family members, which share 16–50% amino acid sequence identity with IL-17A.<sup>1,2</sup> Members of this cytokine family contain five spatially conserved cysteine residues at their C-terminal ends and form a cysteine-knot fold structure.<sup>2</sup> They are secreted as disulfide-linked dimers with the exception of IL-17B, which is secreted as a non-covalent homodimer. Signaling by IL-17 family cytokines is mediated by members of the IL-17 receptor family (IL-17 RA – IL-17 RE). All five of these receptors are type I transmembrane proteins that oligomerize to form functional receptor complexes.

Within the IL-17 cytokine family, IL-17A and IL-17F have been the most widely studied because they are secreted by Th17 cells. Th17 cells are of great interest due to their involvement in the pathogenesis of a number of inflammatory and autoimmune diseases.<sup>2,4</sup>

Both IL-17A and IL-17F, as well as IL-17A/F, signal through a receptor complex consisting of IL-17 RA and IL-17 RC. Receptor binding activates a series of intracellular kinases that drive the NFκB-, AP-1-, and C/EBP-dependent expression of pro-inflammatory cytokines, chemokines, and anti-microbial peptides. These molecules promote immunity, but they can also have tissue destructive effects that drive disease development.

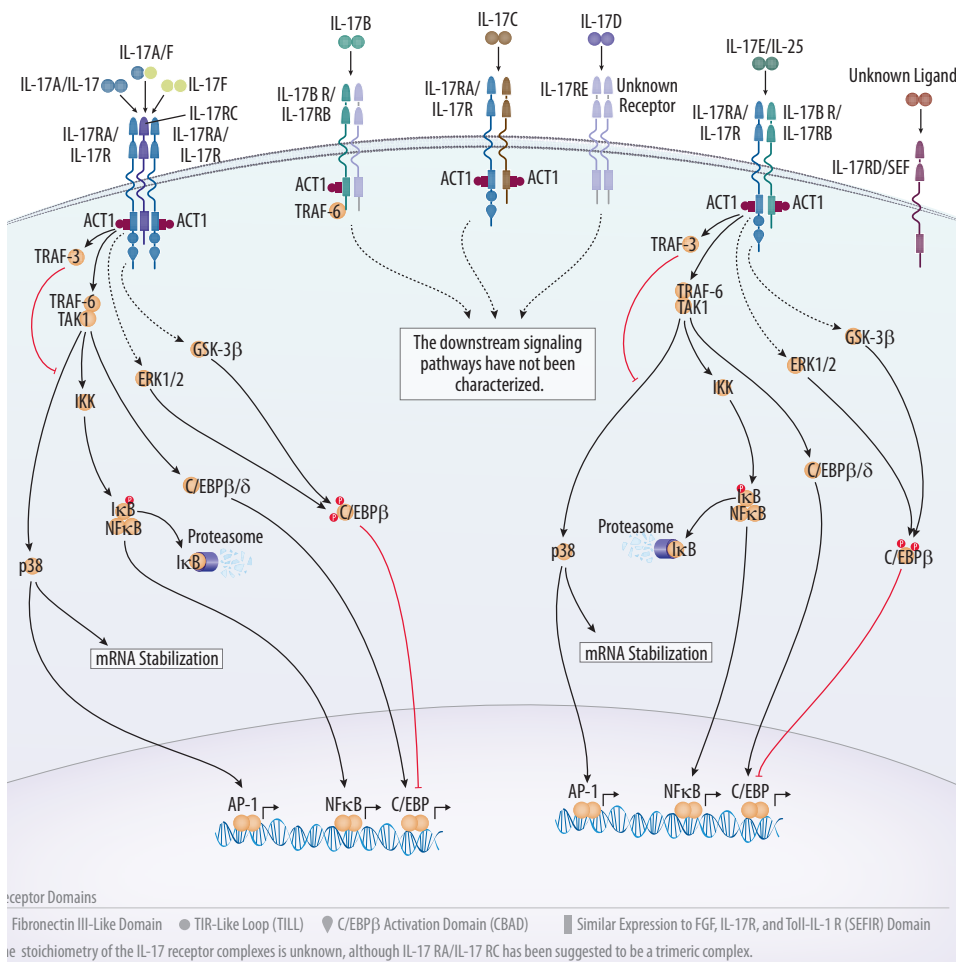
In contrast to IL-17A and IL-17F, IL-17E/IL-25 acts through a receptor complex formed by IL-17 RA and IL-17 RB. It activates similar intracellular signaling pathways but primarily induces the expression of IL-4, IL-5, and IL-13, and promotes eosinophil recruitment.<sup>2,5</sup> As a result, IL-17E/IL-25 stimulates Th2- and Th9-type immune responses and may contribute to the pathogenesis of allergen-induced airway inflammation.<sup>2,5</sup> Less is known about the signaling pathways activated by other IL-17 family cytokines. Recent studies suggest that autocrine signaling by IL-17C in epithelial cells stimulates the production of anti-microbial peptides and pro-inflammatory cytokines, which may contribute to the development of autoimmune diseases.<sup>6,7</sup> IL-17B is known to

bind to IL-17 RB, but the major target cells and effects of IL-17B signaling have not been reported.<sup>4</sup> In addition, the receptor for IL-17D and the ligand for IL-17 RD are currently unknown.

R&D Systems offers a wide selection of products for IL-17 family research including bioactive recombinant human and mouse proteins for most of the IL-17 family ligands and receptors. In addition, we offer antibodies for blocking/neutralization, Western blotting, flow cytometry, and immunohistochemistry, and ELISAs for cytokine and receptor quantification. For more information, please visit our website at [rndsystems.com/IL-17Family](http://rndsystems.com/IL-17Family).

## References

1. Kolls, J.K. & A. Linden (2004) *Immunity* **21**:467.
2. Iwakura, Y. et al. (2011) *Immunity* **34**:149.
3. Gaffen, S.L. (2011) *Curr. Opin. Immunol.* **23**:613.
4. Gaffen, S.L. (2009) *Nat. Rev. Immunol.* **9**:556.
5. Monteleone, G. et al. (2010) *Cytokine Growth Factor Rev.* **21**:471.
6. Song, X. et al. (2011) *Nat. Immunol.* **12**:1151.
7. Ramirez-Carrozzi, V. et al. (2011) *Nat. Immunol.* **12**:1159.



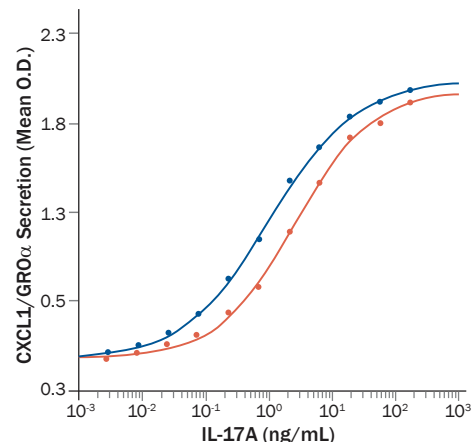
# Products for IL-17 Cytokine Family Research

## Ligands & Receptors

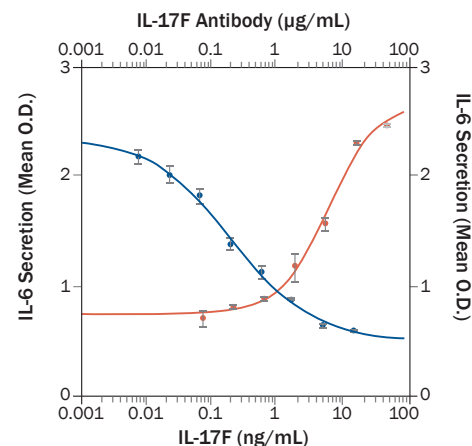
Molecules	Proteins	Antibodies	ELISAs
IL-17/IL-17A	H M R Ca	H (B/N, FC, ICC, IP, WB) M (B/N, FC, WB) Ca (B/N)	H M Ca
IL-17A/F Heterodimer	H M		H M
IL-17B	H M	H (FC, WB) M (B/N, FC, WB)	H M
IL-17C	H M	H (FC, IHC, WB) M (FC, WB)	H
IL-17D	H M	H (B/N, FC, IHC, WB) M (FC, WB)	M
IL-17E/IL-25	H M	H (B/N, FC, WB) M (FC, WB)	M
IL-17F	H M R	H (B/N, FC, ICC, WB) M (FC, ICC, WB)	H M R
IL-17 RA/IL-17 R	H M	H (B/N, FC, WB) M (B/N, FC, WB)	H
IL-17B R/IL-17 RB	H M	H (FC, IHC, WB) M (FC, IHC, WB)	H M
IL-17 RC	H M	H (FC, WB) M (B/N, FC, WB)	H
IL-17 RD/SEF	H M	H (FC, IHC, WB) M (FC, IHC, WB)	
IL-17 RE	H M		

## Intracellular Signaling Molecules

Molecules	Proteins	Antibodies	ELISAs	Activators/Inhibitors
ERK1	H	H (IHC, WB) M (IHC, WB) R (IHC, WB)	H	✓
Phospho-ERK1 (T202/Y204)			H M R	
ERK1/ERK2		H (IHC, WB) M (IHC, WB) R (IHC, WB)		✓
Phospho-ERK1 (T202/Y204)/ERK2 (T185/Y187)		H (FC, ICC/IHC, WB) M (FC, ICC/IHC, WB) R (FC, ICC/IHC, WB)	H M R	
ERK2	H	H (IHC, WB) M (IHC, WB) R (IHC, WB)	H M R	✓
Phospho-ERK2 (T185/Y187)			H M R	
c-Fos		H (WB)		✓
FosB/GOS3		H (IHC, WB) M (WB)		✓
FRA-1		H (IHC, WB)		✓
GSK-3 $\alpha$ / $\beta$		H (FC, ICC, WB) M (FC, ICC, WB) R (FC, ICC, WB)	H M R	✓
Phospho-GSK-3 $\alpha$ / $\beta$ (S21/S9)		H (FC, ICC, WB) M (FC, ICC, WB) R (FC, ICC, WB)	H M R	
GSK-3 $\beta$	H	H (FC, ICC, WB) M (FC, WB) R (FC, WB)		✓
Phospho-GSK-3 $\beta$ (S9)		H (FC, ICC, WB)	H M R	
I $\kappa$ B- $\alpha$		H (WB) M (WB)	H	✓
Phospho-I $\kappa$ B- $\alpha$ (S32/S36)		H (WB)	H M R	
I $\kappa$ B- $\beta$		H (WB) M (WB) R (WB)		✓
I $\kappa$ B- $\epsilon$		H (IHC, WB) M (WB)		
IKK- $\alpha$		H (ICC, WB) M (ICC, WB) R (ICC, WB)		✓
Phospho-IKK- $\alpha$ (S176/S180)		H (WB)		
IKK- $\beta$		H (WB) M (WB)		✓
IKK- $\gamma$		H (ICC, WB) M (ICC, WB) R (ICC, WB)		✓
IKK- $\epsilon$		H (ICC, WB) M (ICC, WB) R (ICC, WB)		✓
c-Jun		H (ICC, WB) M (ICC, WB)		✓
Phospho-c-Jun (S63)			H M R	
JunB		H (WB)		✓
JunD		H (WB) M (WB)		✓
NF $\kappa$ B1		H (ChIP, WB) M (ChIP, WB)		✓
NF $\kappa$ B2		H (ChIP, ICC, WB)		✓
Phospho-p38 (T180/Y182)		H (IHC, WB) M (IHC, WB) R (IHC, WB)	H M	
p38 $\alpha$	H	H (IHC, WB) M (IHC, WB) R (IHC, WB)	H M R	✓
Phospho-p38 $\alpha$ (T180/Y182)		H (WB)	H M R	
p38 $\beta$		H (ICC, WB) M (WB) R (WB)		✓
p38 $\gamma$		H (IHC, WB) M (IHC, WB) R (IHC, WB)	H M R	✓
Phospho-p38 $\gamma$ (T183/Y185)			H M	
p38 $\delta$		H (IHC, WB)		✓
Phospho-p38 $\delta$ (T180/Y182)			H	
c-Rel		H (ChIP, ICC, WB) M (ChIP, ICC, WB)		✓
RelA/NF $\kappa$ B p65		H (ChIP, FC, ICC, WB) M (ChIP, FC, ICC, WB)		✓
Phospho-RelA/NF $\kappa$ B p65 (S529)		H (WB)		
Phospho-RelA/NF $\kappa$ B p65 (S536)		H (WB)	H M R	
RelB		H (ICC/IHC, WB)		✓
TAK1		H (WB)		✓
TRAF-3		H (WB) M (WB) R (WB)		
TRAF-6		H (WB)		



**Activity Comparison Data for Human Cell-Expressed Recombinant Human IL-17A.** The HT-29 human colon adenocarcinoma cell line was treated with increasing concentrations of R&D Systems<sup>®</sup> Human Cell-expressed Recombinant Human IL-17A (Catalog # 7955-IL; blue line) or with human cell-derived recombinant human IL-17A from another company (red line). The bioactivity of the recombinant proteins was assessed by measuring CXCL1/GRO $\alpha$  secretion using the Human CXCL1/GRO $\alpha$  DuoSet<sup>®</sup> ELISA Development Kit (Catalog # DY275). The R&D Systems<sup>®</sup> protein demonstrated 2.5-fold greater activity compared to the other commercially available protein.



**IL-17F-induced IL-6 Secretion and Antibody Neutralization.** The NIH-3T3 mouse embryonic fibroblast cell line was treated with the indicated concentrations of Recombinant Human IL-17F (Catalog # 1335-INS) and IL-6 secretion was measured using the Mouse IL-6 Quantikine<sup>®</sup> ELISA Kit (Catalog # M6000B; orange line). The stimulatory effect induced by 25 ng/mL Recombinant Human IL-17F was neutralized by treating the cells with increasing concentrations of a Mouse Anti-Human IL-17F Monoclonal Antibody (Catalog # MAB13352; blue line).

**R&D** SYSTEMS

 **NOVUS**  
BIOLOGICALS

**TOCRIS**

protein  simple

**bio-techne**<sup>®</sup>

Global [info@bio-techne.com](mailto:info@bio-techne.com) [bio-techne.com/find-us/distributors](http://bio-techne.com/find-us/distributors) TEL +1 612 379 2956  
North America TEL 800 343 7475 Europe | Middle East | Africa TEL +44 (0)1235 529449  
China [info.cn@bio-techne.com](mailto:info.cn@bio-techne.com) TEL +86 (21) 52380373

[bio-techne.com](http://bio-techne.com)

