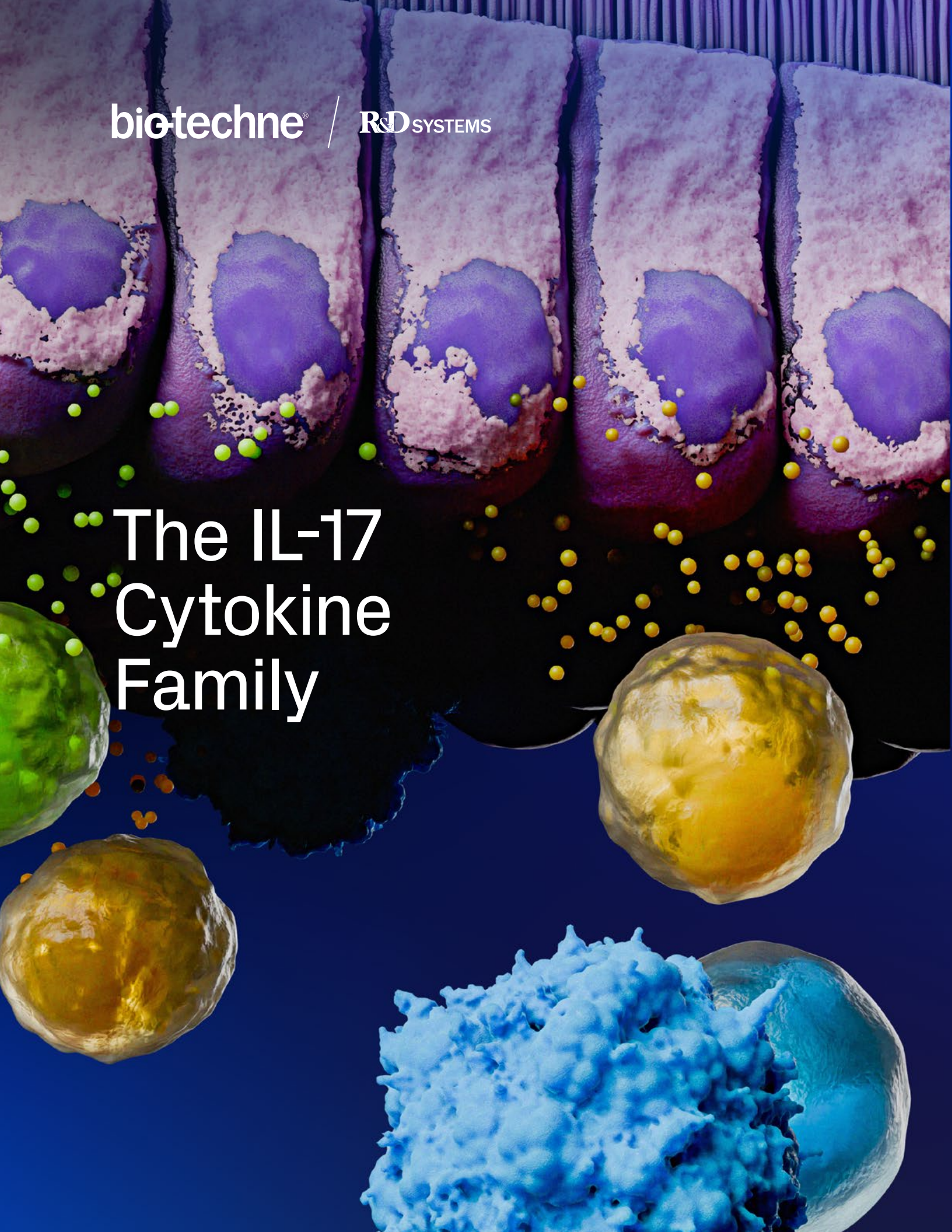


biotechne® / R&D SYSTEMS

# 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.<sup>1,2</sup> 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>3,4</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>4</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>4,6</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 NF- $\kappa$ B-, 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.

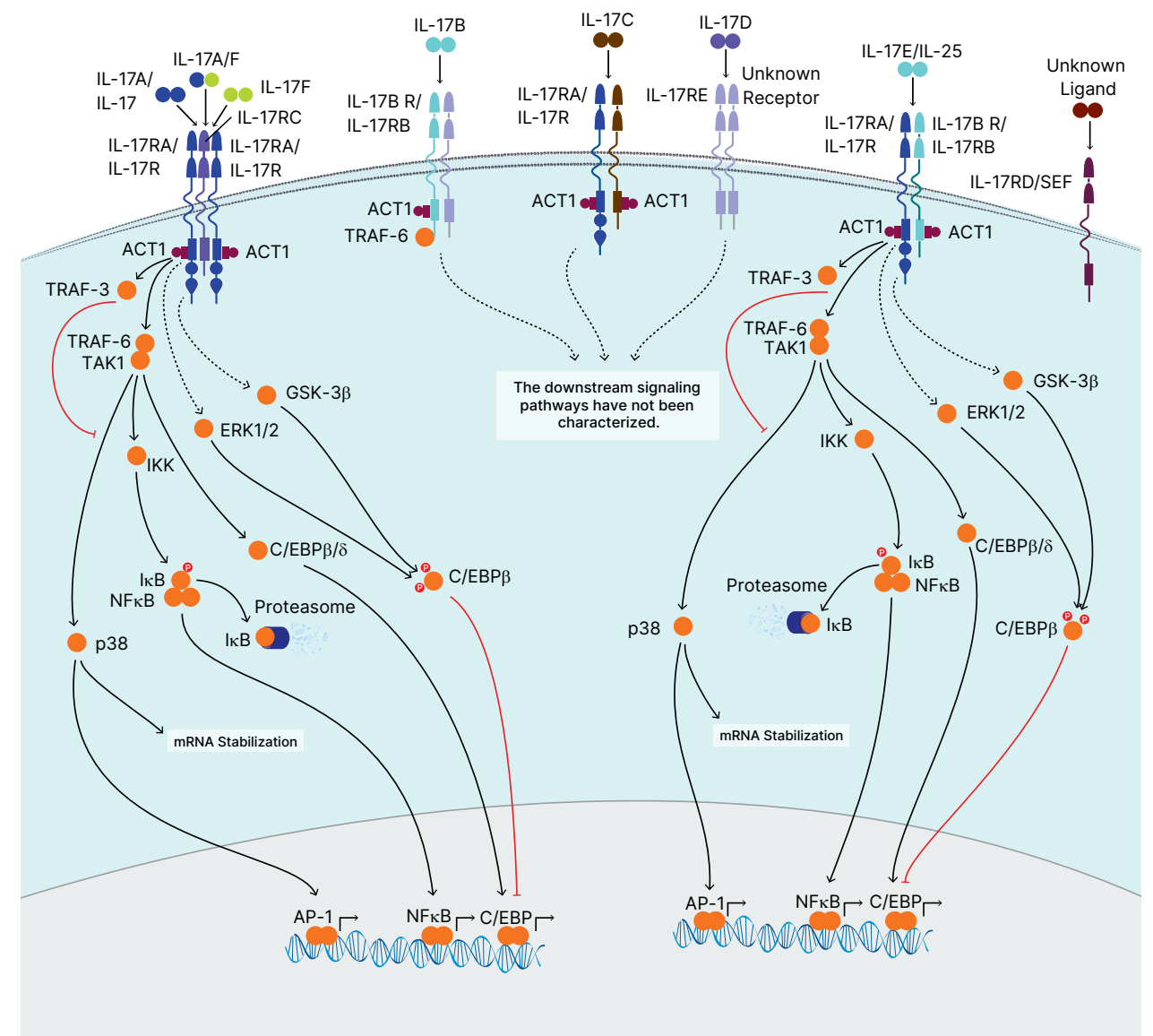
In contrast to IL-17A and IL-17F, IL-17E/IL-25 acts through a receptor complex formed by IL-17 RA and IL-17 RB. It activates similar intracellular signaling pathways but primarily induces the expression of IL-4, IL-5, and IL-13, and promotes eosinophil recruitment.<sup>4,7</sup>

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>4,7</sup> Less is known about the signaling pathways activated by other IL-17 family cytokines. 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>8,9</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>6</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 [bio-techne.com/reagents/proteins/cytokines/il-17-family](https://www.bio-techne.com/reagents/proteins/cytokines/il-17-family).

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## RECEPTOR DOMAINS

▲ Fibronectin III-like Domain ● TIR-Like Loop (TILL) ◆ C/EBP $\beta$  Activation Domain (CBAD) ■ Similar Expression to FGF, IL-17R, and Toll-IL-1R (SEFIR) Domain

The stoichiometry of the IL-17 receptor complexes is unknown, although IL-17 RA/IL-17 RC has been suggested to be a trimeric complex.



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# Products for IL-17 Cytokine Family Research

## Ligands & Receptors

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

## Intracellular Signalling 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	✓
c-Fos		H (ICC, 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)		✓
Phospho-GSK-3 $\alpha/\beta$ (S21/S9)		H (ICC, WB) M (ICC, WB) R (ICC, WB)	H M R	
GSK-3 $\beta$	H	H (FC, ICC, WB) M (FC, ICC, WB) R (FC, ICC, WB)		✓
Phospho-GSK-3 $\beta$ (S9)		H (FC, ICC, WB)		
I $\kappa$ B- $\alpha$		H (ICC, WB) M (ICC, WB)	H	✓
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 (ICC, WB)		
JunB		H (WB)		✓
JunD		H (WB) M (WB)		✓
NF $\kappa$ B1		H (ChIP, WB) M (ChIP, WB)		✓
NF $\kappa$ B2		H (ChIP, ICC, WB)		✓

### SPECIES KEY

H Human M Mouse R Rat Ca Canine CM Cynomolgus Monkey

### APPLICATION KEY

B/N Blocking/Neutralization ChIP Chromatin Immunoprecipitation FC Flow Cytometry ICC Immunocytochemistry IHC Immunohistochemistry WB Western Blot

Intracellular Signalling Molecules Continued

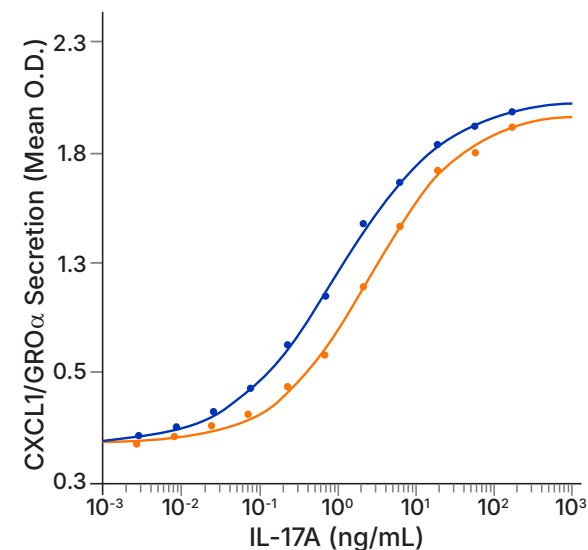
Molecules	Proteins	Antibodies	ELISAs	Activators/ Inhibitors
<b>Phospho-p38 (T180/Y182)</b>		<b>H</b> (IHC, WB) <b>M</b> (IHC, WB) <b>R</b> (IHC, WB)	<b>H M</b>	
<b>p38<math>\alpha</math></b>	<b>H</b>	<b>H</b> (IHC, WB) <b>M</b> (IHC, WB) <b>R</b> (IHC, WB)	<b>H M R</b>	✓
<b>Phospho-p38<math>\alpha</math> (T180/Y182)</b>		<b>H</b> (ICC, WB)	<b>H M R</b>	
<b>p38<math>\beta</math></b>		<b>H</b> (ICC, WB)		✓
<b>p38<math>\gamma</math></b>		<b>H</b> (IHC, WB) <b>M</b> (IHC, WB) <b>R</b> (IHC, WB)		✓
<b>p38<math>\delta</math></b>		<b>H</b> (IHC, WB)		✓
<b>c-Rel</b>		<b>H</b> (ICC, WB) <b>M</b> (ICC, WB)		✓
<b>RelA/NF<math>\kappa</math>B p65</b>		<b>H</b> (ChIP, FC, ICC, WB) <b>M</b> (ChIP, FC, ICC, WB) <b>R</b> (ChIP, FC, ICC, WB)		✓
<b>Phospho-RelA/NF<math>\kappa</math>B p65 (S529)</b>		<b>H</b> (WB)		
<b>Phospho-RelA/NF<math>\kappa</math>B p65 (S536)</b>		<b>H</b> (ICC, WB)		
<b>RelB</b>		<b>H</b> (ICC/IHC, WB)		✓
<b>TAK1</b>		<b>H</b> (WB)		✓
<b>TRAF-3</b>		<b>H</b> (WB) <b>M</b> (WB) <b>R</b> (WB)		
<b>TRAF-6</b>		<b>H</b> (FC, WB)		

**SPECIES KEY**

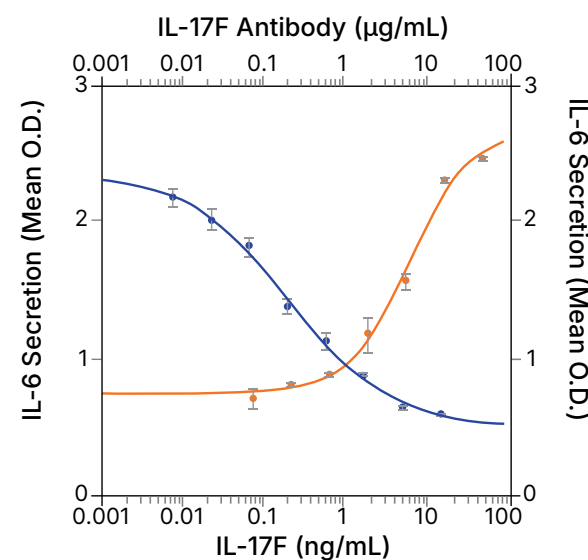
**H** Human **M** Mouse **R** Rat **Ca** Canine **CM** Cynomolgus Monkey

**APPLICATION KEY**

**B/N** Blocking/Neutralization **ChIP** Chromatin Immunoprecipitation **FC** Flow Cytometry **ICC** Immunocytochemistry  
**IHC** Immunohistochemistry **WB** Western Blot



**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™ human cell-expressed Recombinant Human IL-17A (Catalog # 7955-IL; blue line) or with human cell-derived recombinant human IL-17A from another company (orange line). The bioactivity of the recombinant proteins was assessed by measuring CXCL1/GRO $\alpha$  secretion using the Human CXCL1/GRO $\alpha$  DuoSet™ ELISA Development Kit (Catalog # DY275). The R&D Systems™ 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™ 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).

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