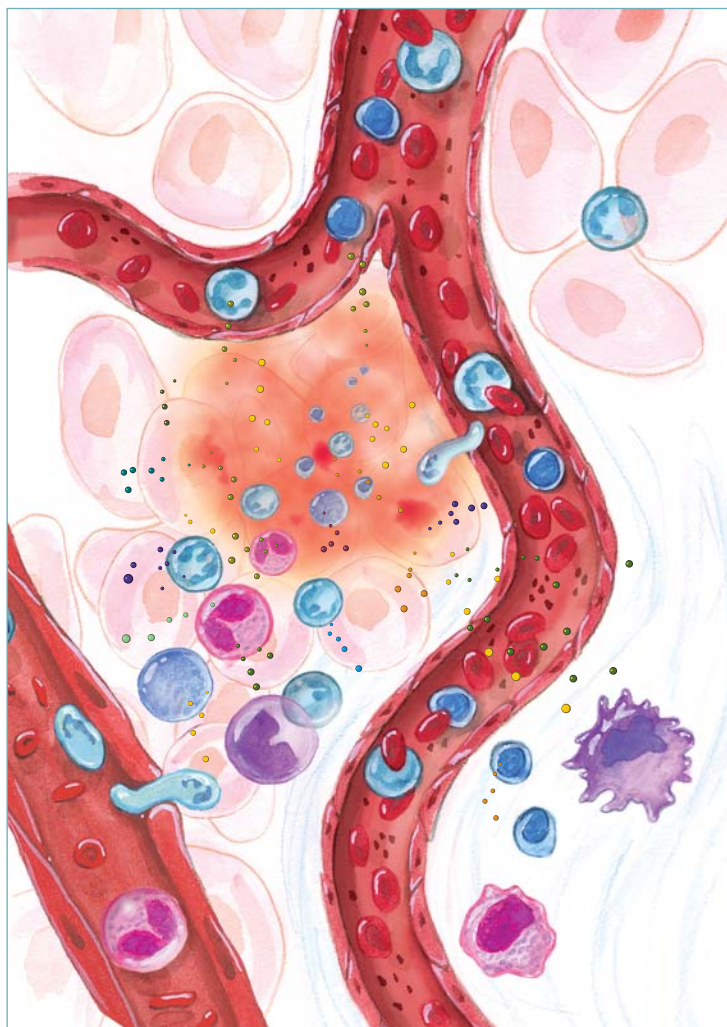


Products for IL-1 Family Research



The IL-1 Family of Cytokines

The IL-1 family of cytokines consists of eleven members (IL-1F1-IL-1F11) that share a conserved β -trefoil structure and bind to receptors belonging to the IL-1 receptor family (IL-1 R1-IL-1 R9). With the exception of IL-1ra/IL-1F3, IL-1 family cytokines lack a signal peptide and therefore are not thought to be secreted by the conventional endoplasmic reticulum/Golgi-dependent secretory pathway used by other cytokines.¹ IL-1 β /IL-1F2 and IL-18/IL-1F4 are synthesized as inactive precursor proteins that are activated and secreted following cleavage by Caspase-1.² Other IL-1 family cytokines are biologically active as full-length molecules, including IL-1 α /IL-1F1, IL-33/IL-1F11, IL-36Ra/IL-1F5, IL-36 α /IL-1F6, IL-36 β /IL-1F8, and IL-36 γ /IL-1F9, although N-terminal processing of many of these cytokines generates more potent forms, suggesting that the truncated forms may also be relevant *in vivo*.^{1,3}

IL-1 family cytokines activate intracellular signaling pathways by binding to a primary receptor subunit, such as IL-1 RI/IL-1 R1, IL-18 R α /IL-1 R5, IL-1 Rrp2/IL-1 R6, or ST2/IL-1 R4, which then recruits an accessory receptor to form the active receptor complex. IL-1 family receptors have three extracellular immunoglobulin-like domains, and with the exception of IL-1 RII/IL-1 R2, possess a cytoplasmic Toll/IL-1 receptor (TIR) domain. This domain is also conserved in Toll-like receptors (TLRs) and a number of intracellular adaptor proteins that mediate IL-1 R/TLR signaling. Signaling cascades triggered by IL-1 α , IL-1 β , IL-18, IL-33, IL-36 α , IL-36 β , or IL-36 γ activate MAPKs and NF κ B, leading to the expression of pro-inflammatory cytokines, chemokines, and secondary mediators of the inflammatory response.⁴⁻⁶ In addition, several of these cytokines have been shown to regulate the differentiation and function of T helper cells.^{1,7,8} Other members of the IL-1 family inhibit inflammation by functioning as antagonists of IL-1 or IL-36 signaling.^{1,9} IL-1ra negatively regulates IL-1 signaling by binding to IL-1 RI, which inhibits its ability to interact with IL-1 α and IL-1 β . Similarly, IL-36Ra binds to IL-1 Rrp2 and inhibits IL-36 signaling. Both the IL-1 and IL-36 receptor antagonists are incapable of initiating downstream signaling on their own due to an inability to recruit the accessory receptor, IL-1 RACp.

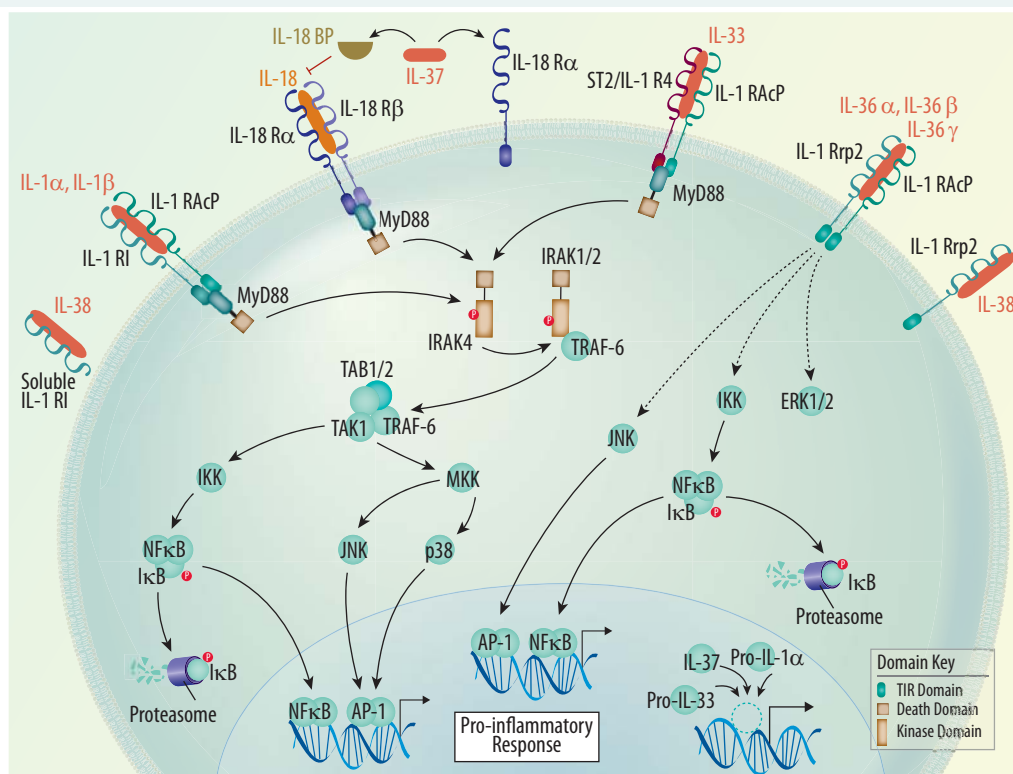
Although less is currently known about IL-37/IL-1F7 and IL-38/IL-1F10, both are also thought to have anti-inflammatory effects.⁹⁻¹¹ Five splice variants of IL-37/IL-1F7 exist, with four containing a putative Caspase-1 cleavage site.⁹ Both the immature and the mature forms of the longest isoform, IL-37b, bind to IL-18 BP and enhance its ability to inhibit IL-18 activity. Additionally, IL-37b binds to IL-18 R α , but does not act as a direct agonist or antagonist of IL-18 signaling. Like the precursor forms of IL-1 α and IL-33, the mature form of IL-37b can also translocate to the nucleus where it may act as a transcriptional regulator.⁹ IL-38/IL-1F10 binds to soluble IL-1 RI and the IL-36 receptor, IL-1 Rrp2.¹¹ Initial data suggests that the interaction between IL-38/IL-1F10 and IL-1 Rrp2 has anti-inflammatory effects similar to those induced by IL-36Ra.¹¹

R&D Systems offers a wide selection of bioactive proteins for IL-1 family research, including the recently developed N-terminally truncated forms of Recombinant Human and Mouse IL-36 β /IL-1F8 and IL-36 γ /IL-1F9, and Recombinant Human IL-37b/IL-1F7b. In addition, we offer ELISAs for cytokine and receptor quantification, and antibodies suitable for multiple applications, including blocking/neutralization, flow cytometry, immunocytochemistry/immunohistochemistry, and Western blot. For additional information, please visit our website at www.RnDSystems.com/IL-1Family.

References

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5. Dinarello, C.A. (2009) Annu. Rev. Immunol. 27:519.
6. Towne, J.E. (2004) J. Biol. Chem. 279:13677.
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IL-1 FAMILY CYTOKINES			
Systematic Name	Alternate Name	Receptor Subunits	Function
IL-1F1	IL-1 α	IL-1 RI, IL-1 RACp	Agonist; pro-inflammatory
IL-1F2	IL-1 β	IL-1 RI, IL-1 RACp	Agonist; pro-inflammatory
IL-1F3	IL-1ra	IL-1 RI	Receptor antagonist; Anti-inflammatory
IL-1F4	IL-18	IL-18 R α , IL-18 R β	Agonist; pro-inflammatory
IL-1F5	IL-36Ra	IL-1 Rrp2	Receptor antagonist; Anti-inflammatory
IL-1F6	IL-36 α	IL-1 Rrp2, IL-1 RACp	Agonist; pro-inflammatory
IL-1F7	IL-37	IL-18 R α	Anti-inflammatory
IL-1F8	IL-36 β	IL-1 Rrp2, IL-1 RACp	Agonist; pro-inflammatory
IL-1F9	IL-36 γ	IL-1 Rrp2, IL-1 RACp	Agonist; pro-inflammatory
IL-1F10	IL-38; IL-1HY2	IL-1 RI; IL-1 Rrp2	Anti-inflammatory
IL-1F11	IL-33	ST2, IL-1 RACp	Agonist; pro-inflammatory



R&D Systems Products for IL-1 Family Research

IL-1 FAMILY LIGANDS & RECEPTORS									
Ligands	Proteins	Antibodies	ELISAs		Ligands	Proteins	Antibodies	ELISAs	
IL-1α/IL-1F1	H M R C R P	H (B/N, E, FC, IHC, WB) M (B/N, E, FC, IHC, IP, WB) R (B/N, E, WB) CR (B/N, WB) P (B/N, WB)	H M R		IL-37/IL-1F7	H	H (B/N, WB)		
IL-1β/IL-1F2	H M R C a C R E F G P P Pr Rb	H (B/N, E, FC, IHC, WB) M (B/N, FC, IHC, WB) R (B/N, E, IHC, WB) Ca (B/N, FC, WB) CR (B/N, WB) E (B/N, IHC, WB) F (B/N, E, IHC, WB) P (B/N, E, WB)	H M R F G P P		IL-37b/IL-1F7b	H			
IL-1ra/IL-1F3	H M R E P	H (B/N, E, IHC, WB) M (B/N, E, WB) E (E, IHC, WB) P (B/N, IHC, WB)	H M E		IL-38/IL-1F10		H (WB)		
IL-18/IL-1F4	H M R F P Pr	H (B/N, E, IP, WB) M (B/N, E, IP, WB) R (B/N, WB) Ca (IHC, WB) F (B/N, WB) P (IHC, WB) Pr (B/N, IHC, WB)	H M		Receptors	Proteins	Antibodies	ELISAs	
IL-33/IL-1F11	H M	H (B/N, E, FC, IHC, WB) M (E, FC, IHC, WB)	H M		IL-1 RI	H M R	H (B/N, E, FC, WB) M (B/N, FC, IHC, WB)	H	
IL-36α/IL-1F6	H M	H (IHC, WB) M (B/N, FC, WB)			IL-1 RII	H M	H (B/N, E, FC, IHC, WB) M (FC, IHC, WB)	H	
IL-36β/IL-1F8	H M	H (B/N, IHC, WB) M (B/N, WB)			IL-1 RAcP/IL-1 R3	H	H (FC, WB)		
IL-36γ/IL-1F9	H M	H (B/N, WB)			IL-1 RAPL1/IL-1 R8		H (WB)		
IL-36Ra/IL-1F5	H M	H (B/N, IHC, WB)			IL-1 RAPL2/IL-1 R9	H	H (FC, IHC, WB) M (WB)		
					IL-1 Rrp2/IL-1 R6	H M R	H (WB) M (WB) R (WB)		
					IL-18 Rα/IL-1 R5	H	H (B/N, FC, IHC, WB) M (B/N, FC, WB)		
					IL-18 Rβ/IL-1 R7	H	H (B/N, FC, WB) M (WB)		
					SIGIRR	H M	H (FC, WB) M (WB)		
					ST2/IL-1 R4	H M	H (B/N, E, FC, WB) M (B/N, E, FC, WB)	H M	

INTRACELLULAR SIGNALING MOLECULES/REGULATORS OF SIGNALING BY IL-1 FAMILY MEMBERS									
Molecules	Proteins	Antibodies	ELISAs	Activators/ Inhibitors	Molecules	Proteins	Antibodies	ELISAs	Activators/ Inhibitors
ERK1	H	H (IHC, WB) M (IHC, WB) R (IHC, WB)	H	✓	Phospho-MKK3 (S218/T222)			H	
Phospho-ERK1 (T202/Y204)			H M R		MKK3/MKK6		H (WB) M (WB) R (WB)		✓
ERK1/2		H (IHC, WB) M (IHC, WB) R (IHC, WB)		✓	Phospho-MKK3 (S218/T222)/ MKK6(S207/T211)		H (WB)		
Phospho-ERK1 (T202/Y204) / ERK2 (T185/Y187)		H (FC, IHC, WB) M (FC, IHC, WB) R (FC, IHC, WB)	H M R		MKK4		H (ICC)		✓
ERK2	H	H (IHC, WB) M (IHC, WB) R (IHC, WB)	H M R	✓	Phospho-MKK4 (S257/T261)		H (ICC, WB) M (ICC, WB) R (ICC, WB)		
Phospho-ERK2 (T185/Y187)			H M R		MKK6		H (ICC, WB) M (ICC, WB) R (ICC, WB)		✓
c-Fos		H (WB)		✓	Phospho-MKK6 (S207/T211)			H	
IκB-α		H (WB) M (WB)	H	✓	MKK7		H (IHC, WB)		✓
Phospho-IκB-α (S32/S36)		H (WB)	H M R		NFκB1		H (ChIP, WB) M (ChIP, WB)		✓
IκB-β		H (WB) M (WB) R (WB)			NFκB2		H (ChIP, ICC, WB)		✓
IκB-ε		H (IHC, WB) M (WB)			Phospho-p38 (T180/Y182)		H (IHC, WB) M (IHC, WB) R (IHC, WB)	H M	
IKK-α		H (ICC, WB) M (ICC, WB) R (ICC, WB)		✓	p38α	H	H (IHC, WB) M (IHC, WB) R (IHC, WB)	H M R	✓
IKK-β		H (WB) M (WB)		✓	Phospho-p38α (T180/Y182)		H (WB)	H M R	
IKK-γ		H (ICC, WB) M (ICC, WB) R (ICC, WB)		✓	p38β		H (ICC, WB) M (WB) R (WB)		✓
IKK-ε		H (ICC, WB) M (ICC, WB) R (ICC, WB)		✓	p38γ		H (IHC, WB) M (IHC, WB) R (IHC, WB)	H M R	✓
IL-18 BPa	H	H (B/N, E, WB)	H		Phospho-p38γ (T183/Y185)			H M	
IL-18 BPc		M (WB)			p38δ		H (IHC, WB)		✓
IL-18 BPd	M	M (B/N, WB)			Phospho-p38δ (T180/Y182)			H	
IRAK1		H (WB)			RelA/NFκB p65		H (ChIP, FC, ICC, WB) M (ChIP, FC, ICC, WB)		✓
IRAK2		H (WB)			Phospho-RelA/NFκB p65 (S529)		H (WB)		
IRAK3		H (WB)			Phospho-RelA/NFκB p65 (S536)			H M R	
IRAK4		H (ICC, WB)			TAB1		H (ICC, WB) M (ICC, WB)		
JNK		H (IHC, WB) M (IHC, WB) R (IHC, WB)	H M R	✓	TAK1		H (WB)		✓
Phospho-JNK (T183/Y185)		H (IHC, WB) M (IHC, WB) R (IHC, WB)	H M R		TRAF-6		H (WB)		
JNK1	M	H (ICC, WB) M (ICC, WB) R (ICC, WB)		✓					
JNK1/JNK2		H (ICC, WB) M (ICC, WB) R (ICC, WB)		✓					
JNK2		H (ICC, WB) M (ICC, WB) R (ICC, WB)	H M R	✓					
Phospho-JNK2 (T183/Y185)			H M R						
c-Jun		H (ICC, WB) M (ICC, WB)		✓					
Phospho-c-Jun (S63)			H M R						
JunD		H (WB) M (WB)		✓					
MKK3		H (ICC, WB) M (ICC, WB) R (ICC, WB)		✓					

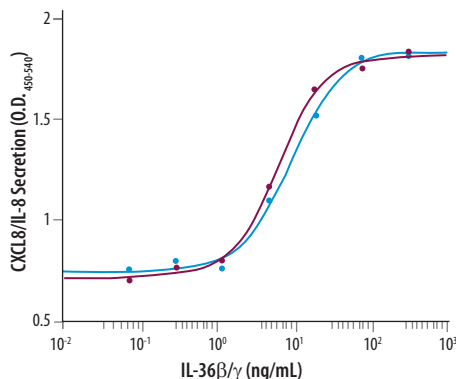
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Application Key: B/N Blocking/Neutralization, ChIP Chromatin Immunoprecipitation, E ELISA, FC Flow Cytometry, ICC/IHC Immunocytochemistry/Immunohistochemistry, IP Immunoprecipitation, WB Western blot

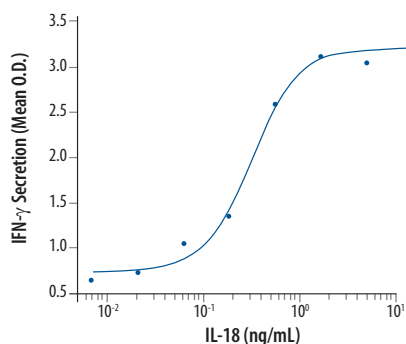
✓ TOCRIS activators and inhibitors targeting these molecules are available from R&D Systems.

Proteins

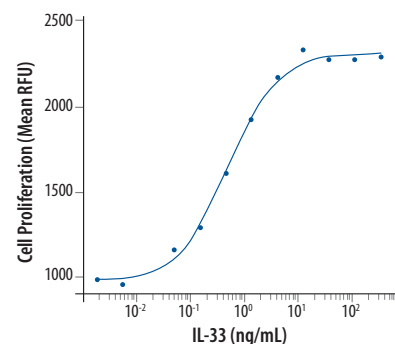
With more than 25 years of experience expressing and purifying proteins, R&D Systems is committed to producing the highest quality natural and recombinant proteins for your research. Today our selection includes more than 1,700 proteins from 16 different species. Most proteins that we offer are tested for a specific biological activity based on observations reported in the scientific literature. Stringent production and purification guidelines, along with rigorous bioassay testing, ensure quality and minimal lot-to-lot variability.



IL-36β- and IL-36γ-induced IL-8 Secretion by Human Pre-adipocytes. Primary human pre-adipocytes were treated with increasing concentrations of Recombinant Human IL-36β/IL-1F8 (aa 5-157; Catalog # 6834-IL; red line) or Recombinant Human IL-36γ/IL-1F9 (aa 18-169; Catalog # 6835-IL; blue line). The levels of CXCL8/IL-8 in the cell culture supernatants were measured using the Human CXCL8/IL-8 DuoSet® ELISA Development System (Catalog # DY208).



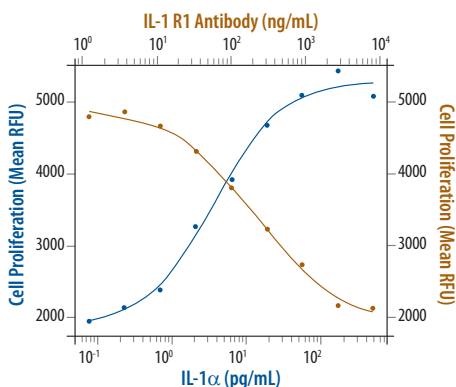
IL-18/IL-1F4-induced IFN-γ Secretion by Activated Mouse T Cells. Activated mouse T cells were treated with increasing concentrations of Recombinant Mouse IL-18/IL-1F4 (Catalog # B004-2) and 0.1 ng/mL Recombinant Mouse IL-12 (Catalog # 419-ML). IFN-γ secretion was measured using the Mouse IFN-γ Quantikine® ELISA Kit (Catalog # MIF00).



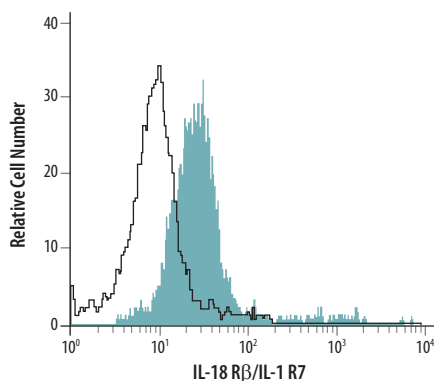
IL-33-induced Proliferation of Mouse Helper T Cells. Proliferation of the D10.G4.1 mouse helper T cell line was assessed following treatment with increasing concentrations of Recombinant Human IL-33 (Catalog # 3625-IL), in the presence of suboptimal amounts of a Hamster Anti-Mouse CD3ε Monoclonal Antibody (Catalog # MAB484).

Antibodies

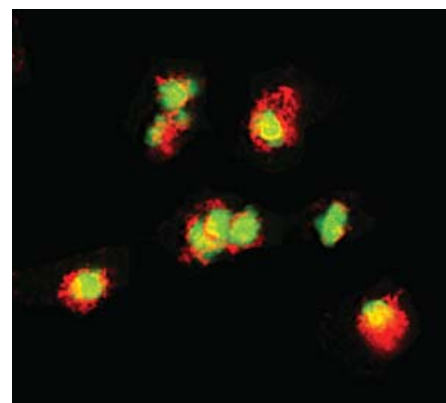
We offer an extensive selection of antigen affinity-purified polyclonal antibodies, monoclonal antibodies, and fluorochrome-conjugated antibodies for the detection of cytokines, cell surface receptors, intracellular signaling molecules, and multiple other proteins. R&D Systems antibodies are generated in several different host species and are quality tested for a broad range of applications, including neutralization, blocking ligand-receptor interactions, flow cytometry, immunocytochemistry/immunohistochemistry, Western blot, and ELISA.



IL-1α/IL-1F1-induced Proliferation and Neutralization using an Anti-Mouse IL-1 R1 Antibody. Proliferation of the D10.G4.1 mouse helper T cell line was assessed following treatment with increasing concentrations of Recombinant Mouse IL-1α/IL-1F1 (Catalog # 400-ML; blue line). The stimulatory effect induced by 50 pg/mL Recombinant Mouse IL-1α/IL-1F1 was neutralized by treating the cells with increasing concentrations of a Hamster Anti-Mouse IL-1 R1 Monoclonal Antibody (Catalog # MAB7711; orange line).



Detection of IL-18 Rβ/IL-1 R7 by Flow Cytometry. KG-1 human myeloid leukemia cells were stained with a PE-conjugated Mouse Anti-Human IL-18 Rβ/IL-1 R7 Monoclonal Antibody (Catalog # FAB118P; filled histogram) or a PE-conjugated Mouse IgG_{2b} Isotype Control (Catalog # IC0041P; open histogram).



Detection of IL-1β in Concanavalin A-activated Mouse Splenocytes. IL-1β was detected in Concanavalin A-activated mouse splenocytes by indirect immunofluorescent staining using a Goat Anti-Mouse IL-1β/IL-1F2 Antigen Affinity-purified Polyclonal Antibody (Catalog # AF-401-NA). The cells were stained using a fluorochrome-conjugated secondary antibody (red) and counterstained (green).

**R&D Systems, Inc.**614 McKinley Place NE
Minneapolis, MN 55413

TEL: (800) 343-7475

(612) 379-2956

FAX: (612) 656-4400

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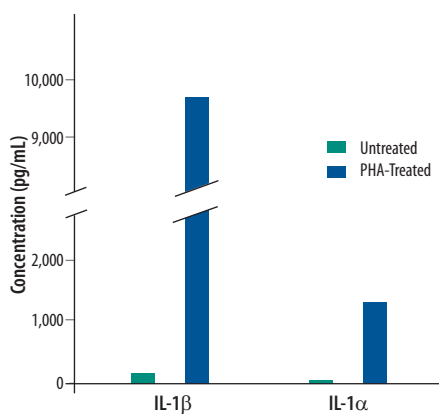
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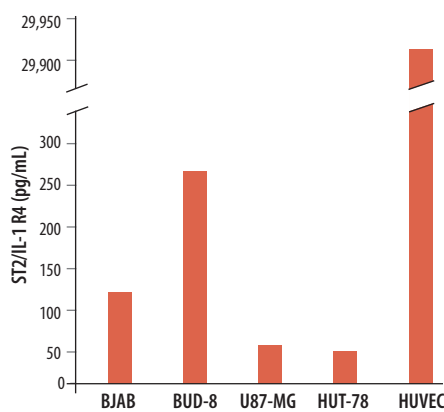
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ELISA Kits

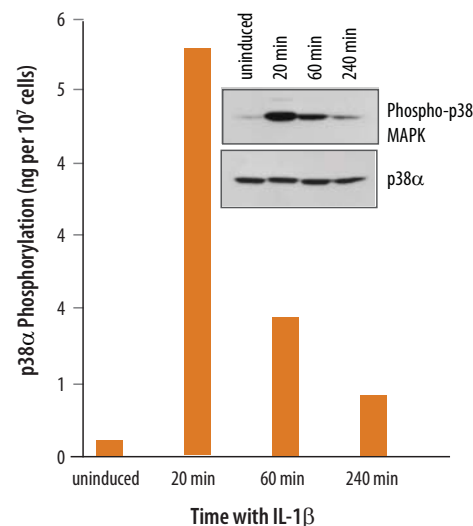
R&D Systems has the most referenced selection of ELISA kits in the world. We currently offer over 300 complete, fully-validated Quantikine ELISA Kits. These kits utilize two highly specific antibodies to quantify a specific target analyte in a designated set of complex sample types. Quantikine Kits undergo rigorous testing during development to ensure that they will provide customers with reliable, consistent results without the need for further assay optimization. In addition to our Quantikine Kits, we offer fully validated Surveyor™ IC ELISA Kits for the quantification of intracellular proteins and more than 750 DuoSet and 180 DuoSet IC ELISA Development Systems to allow researchers flexibility in developing their own working assays. Several multianalyte profiling kits are also available that allow the simultaneous detection of IL-1 α , IL-1 β , IL-1ra or intracellular kinases involved in IL-1 family signaling such as JNK, p38, and MKKs. Please visit our website at www.RnDSystems.com/MultiplexAssays for more information.



Measurement of IL-1 α and IL-1 β in Peripheral Blood Mononuclear Cell Supernatants. Human peripheral blood mononuclear cells were treated with PHA. The levels of IL-1 α and IL-1 β in cell culture supernatants from treated and non-treated cells were assessed using the Human IL-1 α /IL-1F1 Quantikine ELISA Kit (Catalog # DLA50) or the Human IL-1 β /IL-1F2 QuantiGlo® ELISA Kit (Catalog # QLB00).



Measurement of ST2/IL-1 R4 Levels in Cell Culture Supernatants using the Human ST2 Quantikine ELISA Kit. Aliquots of cell culture supernatants removed from the BJAB human Burkitt's lymphoma cell line, BUD-8 human skin fibroblast cell line, U87-MG glioblastoma/astrocytoma cell line, HUT-78 human mature cutaneous T cell lymphoma cell line, and human umbilical vein endothelial cells (HUVEC) were assayed for ST2/IL-1 R4 using the Human ST2/IL-1 R4 Quantikine ELISA Kit (Catalog # DST200).



Detection of IL-1 β -induced p38 α Phosphorylation in HepG2 Cells. The HepG2 human hepatocellular carcinoma cell line was treated with Recombinant Human IL-1 β /IL-1F2 (Catalog # 201-LB) for the indicated times. p38 α phosphorylation was assessed in cell lysates using the Human/Mouse/Rat Phospho-p38 α (T180/Y182) Surveyor IC ELISA Kit (Catalog # SUV869; bar graph). The results obtained from the Surveyor IC ELISA are consistent with the relative levels of phosphorylated p38 detected in the same lysates by Western blot (inset) using a Rabbit Anti-Human/Mouse/Rat Phospho-p38 MAPK (T180/Y182) Antigen Affinity-purified Polyclonal Antibody (Catalog # AF869). Total p38 α was detected using a Mouse Anti-Human/Mouse/Rat p38 α Monoclonal Antibody (Catalog # MAB869).