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LIFE SCIENCES

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Interleukin-36γ

An Important Biomarker for Psoriasis

The proinflammatory cytokine IL-36γ is highly expressed in skin epithelial cells and in several myeloid-derived cell types. IL-36γ is a pivotal mediator of epithelial inflammation and is strongly associated with the inflammatory skin disease psoriasis. IL-36γ promotes wound healing after skin injury by regulating keratinocyte proliferation. IL-36γ also assumes a role in the lung innate mucosal immunity during bacterial pneumonia by driving protective type-1 responses and classical macrophage activation, suggesting a potential key role in host defense. As with other IL-1 cytokines, IL-36γ is expressed as an inactive precursor and must be processed by specific proteases (Cathepsin S) to become bioactive. IL-36γ works by directly stimulating type-1 cytokine induction from dendritic cells *in vitro* in a MyD88-dependent manner. IL-36γ has been shown to be an important biomarker for psoriasis and might provide a future drug target, because of its potential amplifier role in TNF-α and IL-17 pathways in psoriatic skin inflammation.

LIT: IL-36γ (IL-1F9) is a biomarker for psoriasis skin lesions: A.M. D'Erme, et al.; J. Invest. Dermatol. **135,** 1025 (2015) • Role of interleukin 36γ in host defense against tuberculosis: F. Ahsan, et al.; J. Infect. Dis. **214,** 464 (2016) • Cathepsin S is the major activator of the psoriasis-associated proinflammatory cytokine IL-36γ: J.S. Ainscough, et al.; PNAS **114,** E2748 (2017) • IL-36γ is a crucial proximal component of protective type-1-mediated lung mucosal immunity in Gram-positive and -negative bacterial pneumonia: M.A. Kovach, et al.; Muc. Immunol. **(Epub ahead of print)** (2017)

NEW

IL-36γ ELISA Kit

NEW IL-36γ (human) ELISA Kit

AG-45B-0008 96 wells

This assay is highly specific for human IL-36γ.
Does not cross-react with human IL-36α and IL-36β.

Sensitivity: 3 pg/ml
Range: 3.9 to 250 pg/ml
Sample: Serum, Cell Culture Supernatant

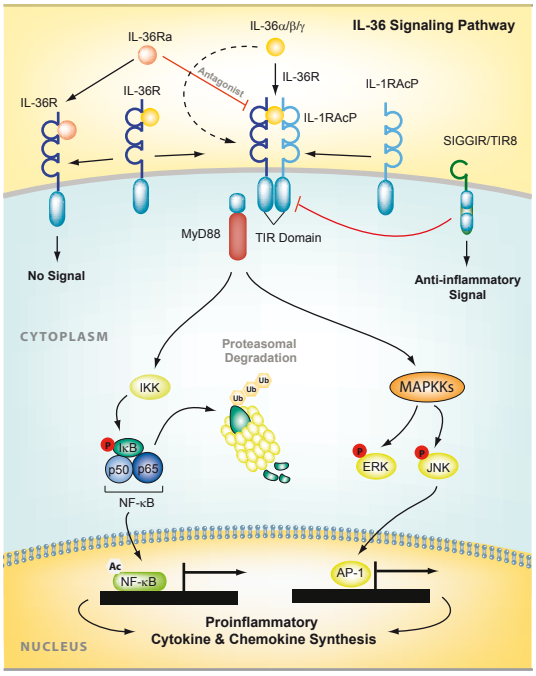
IL-36 Detection Sets

PRODUCT NAME	PID	SIZE
IL-36Ra (human) Matched Pair Detection Set	AG-46B-0006	5 x 96 wells
IL-36β (human) Matched Pair Detection Set	AG-46B-0009	5 x 96 wells
IL-36γ (human) Matched Pair Detection Set	AG-46B-0010	5 x 96 wells

IL-36 Antibodies

PRODUCT NAME	PID	SIZE
anti-IL-36β (human), mAb (Jacky-1)	AG-20B-0069	100 µg
anti-IL-36β (human), pAb (IN107)	AG-25B-0032	100 µg
anti-IL-36γ (human), mAb (Jussy-1)	AG-20B-0072	100 µg

IL-36 Family – Importance in Inflammation



The interleukin (IL)-36 family belongs to the broader IL-1 family. Its members are emerging as important mediators of inflammatory disease. The IL-36 subfamily consists of three ligands, IL-36α, IL-36β and IL-36γ [IL-1F6, IL-1F8 and IL-1F9], which have similar biological effects and the natural antagonist IL-36Ra [IL-1F5]. IL-36 family members are abundantly expressed in skin (keratinocytes), but also found in dendritic cells (DCs), T cell subsets, Langerhans cells and mucosal epithelium. Primary human macrophages express IL-36β and IL-36Ra constitutively, while IL-36α and IL-36γ expression is significantly induced upon TLR stimulation. The IL-36 family members exert their effects through a specific IL-36 receptor consisting of IL-36R (IL-1RL2 or IL-1Rrp2) and IL-1RAcP (co-receptor) chains, which results in signal transduction via MyD88 and consequently NF-κB or MAPK, activating similar intracellular signals as IL-1 and inducing the release of proinflammatory cytokines, such as IL-6, IL-8, IL-17, IL-22 and IL-23. IL-36 cytokines are expressed as inactive precursors and require proteolytic processing for activation. Recently, it has been shown that IL-36α, IL-36β and IL-36γ are activated differentially by the neutrophil granule-derived proteases cathepsin G & S, elastase and proteinase-3, increasing their biological activity. Active IL-36 cytokines can direct both, innate and adaptive immune responses by acting on parenchymal, stromal and specific immune cell subsets. Dendritic cells and naïve CD4$^+$ T cells are targets of the different forms of IL-36 leading to a Th1 response. IL-36 members seem to play important roles in immune responses against microbes. These IL-36 family members are important in psoriatic skin inflammation. Additionally, they can also play important roles in inflammatory disorders in other organs, such as the gastrointestinal tract, joints (arthritis) and the lungs. Targeting the expression and activity of the IL-36 family has the potential to uncover novel therapeutic approaches aimed at treating inflammatory diseases in humans.

IL-36Ra is a highly and specific IL-36 antagonist that binds to IL-36R, competing with IL-36 for the binding site, but does not recruit the co-receptor and consequently fails to transmit the signal. IL-36Ra inhibits the production of proinflammatory cytokines, including IL-12, IL-1β, IL-6, TNF-α and IL-23. IL-36Ra is a key regulator of skin inflammation and is linked to psoriatic inflammation.

SELECTED REVIEWS: Neutrophil-derived proteases escalate inflammation through activation of IL-36 family cytokines: C.M. Henry, et al.; Cell Rep. **14,** 708 (2016) • The emergence of the IL-36 cytokine family as novel targets for inflammatory diseases: P.T. Walsh & P.G. Fallon; Ann. N.Y. Acad. Sci. **(Epub ahead of print)** (2016) • The novel interleukin-1 cytokine family members in inflammatory diseases: M. Hahn, et al; Curr. Opin. Rheumatol. **29,** 208 (2017) • Interleukin-36 cytokines may overcome microbial immune evasion strategies that inhibit interleukin-1 family signaling: L.E. Jensen; Sci. Signal. **10,** 492 (2017)

Biologically Active IL-36 Proteins

PRODUCT NAME	PID	SIZE
IL-36Ra (aa 2-155) (human) (rec.) (untagged)	AG-40B-0097	10 µg | 3 x 10 µg
IL-36Ra (aa 3-156) (mouse) (rec.) (untagged)	AG-40B-0096	10 µg | 3 x 10 µg
IL-36α (aa 6-158) (human) (rec.) (untagged)	AG-40B-0165	10 µg | 3 x 10 µg
IL-36α (aa 8-160) (mouse) (rec.) (untagged)	AG-40B-0098	10 µg
IL-36β (aa 5-157) (human) (rec.) (untagged)	AG-40B-0117	10 µg
IL-36β (aa 31-183) (mouse) (rec.) (untagged)	AG-40B-0099	10 µg
IL-36γ (aa 13-164) (mouse) (rec.) (FLAG)	AG-40B-0105	10 µg
IL-36γ (aa 13-164) (mouse) (rec.) (untagged)	AG-40B-0100	10 µg
IL-36γ (aa 18-169) (human) (rec.) (untagged)	AG-40B-0166	10 µg | 3 x 10 µg

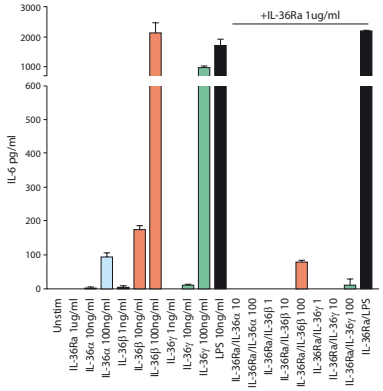


FIGURE: IL-36Ra (aa 3-156) (mouse) (rec.) (AG-40B-0096) inhibits IL-36α, IL-36β, IL-36γ-dependent expression of IL-6 in mouse BMDCs.

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