New Product Highlights

β-Defensins: Peptides that play an important role in innate and adaptive immune responses

The β-defensin peptides are small, cationic members of the defensin family of peptides that were first discovered for their antimicrobial activity. **β-Defensin 1** (Prod. No. **D 9565**), comprising 36 amino acids and **β-defensin 2** (Prod. No. **D 9690**), comprising 41 amino acids, are characterized by a unique disulfide bridge pattern connecting six cysteine residues (C1-C5, C2-C4, C3-C6) [1]. Human β-defensins are expressed primarily by keratinocytes and epithelial cells [1,2]. β-Defensin 1 is expressed constitutively by these cells, while β-defensin 2 expression is induced by **lipopolysaccharide** (LPS, Prod. No. **L 2630**) and inflammatory cytokines such as **tumor necrosis factor-α** (TNF-α; Prod. No. **T 6674**) and **interleukin-1** (IL-1, Prod. Nos. **I 2778** and **I 9401**) [2,3].

β-Defensin 1 exhibits a broad spectrum of antimicrobial activity as well as antiviral activity against adenoviruses. In contrast, β-defensin 2 acts as a more potent antimicrobial peptide with activity primarily against Gram-negative bacteria and yeast (*Candida albicans*) [4]. In this regard, β-defensin 2 is 10 times more potent than β-defensin 1 against *Escherichia coli* and *Pseudomonas aeruginosa* [5]. It has been shown that high salt concentrations inhibit the expression of β-defensin [1,4]. Inhibition of β-defensin 2 may contribute to recurrent airway infections in cystic fibrosis patients [5]. In addition, β-defensins play a regulatory role in the adaptive immune response in that they are chemoattractants for $CD4^+/CD45RO^+$ memory T lymphocytes as well as for immature dendritic cells via signaling through the chemokine receptor CCR6 [1,6].

In summary, β-defensins 1 and 2 are biologically active peptides that play important roles in both innate and adaptive immune responses. Due to the fact that β-defensins are small endogenous peptides, they may prove to be nonimmunogenic adjuvants for treating infections. The related human α-defensin products, **Defensin HNP-1** (Prod. No. **D 2043**) and **Defensin HNP-2** (Prod. No. **D 6790**) are also offered by Sigma-RBI.

References
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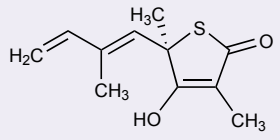
Thiolactomycin: Bacterial fatty acid synthesis inhibitor

Mycolic acid (Prod. No. **M 4537**), one of the structurally largest fatty acids found in nature, is a vital cell wall component of the human tuberculosis strain of *Mycobacterium tuberculosis*. The impermeability of this strain to many antibiotics has spawned much research interest into the biosynthesis of mycolic acid with a view to developing novel antibiotics. Drugs that have resulted from this interest include **isoniazid** (Prod. No. **I 3377**), **ethionamide** (Prod. No. **E 6005**) and **cerulenin** (Prod. No. **C 2389**).

Biosynthesis of fatty acyl chains involves two fatty acid synthetic systems; fatty acid synthase I (FAS I), which catalyzes *de novo* fatty acid synthesis and fatty acid synthase II (FAS II), which consists of monofunctional enzymes that elongate FAS I products into long chain mycolic acid precursors [1]. Three enzymes, β-ketoacyl-acyl carrier protein synthase (Kas) A and B and the condensing enzyme FabH, have all been identified as FAS II enzymes involved in mycolic acid and fatty acid biosynthesis [1,2]. **Thiolactomycin** (Prod. No. **T 9567**), synthesized recently by Sigma-RBI, inhibits fatty acid synthesis by inhibiting FabH, KasA and KasB. Thiolactomycin inhibited KasA and KasB displaying IC_{50} values of 20 μM and 90 μM, respectively [1].

Myristate is the fatty acid moiety in the glycosyl phosphatidylinositol (GPI) anchored surface glycoproteins of *Trypanosoma brunei*, which causes African sleeping sickness. As the host produces little myristate, it was discovered by using thiolactomycin that trypanosomes synthesize fatty acids. Thiolactomycin, which is known to inhibit bacterial myristate synthesis, also selectively inhibits trypanosomal fatty acid synthesis *in vitro*, displaying an IC_{50} value of 150 μM [3]. In contrast, cerulenin, a eukaryotic and bacterial fatty acid synthase inhibitor, is not effective at preventing myristate synthesis in trypanosomes [3].

Thiolactomycin is therefore a useful tool for studying and understanding the mechanisms underlying parasitic infections and infectious diseases.



Thiolactomycin
(Prod. No. T 9567)

References
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