

**DESCRIPTION**

**Source** *Spodoptera frugiperda*, Sf 21 (baculovirus)-derived  
Asp63-Leu148  
Accession # Q99075

**N-terminal Sequence Analysis** Asp63 (major), Gly32, Glu24

**Predicted Molecular Mass** 9.7 kDa

**SPECIFICATIONS**

**SDS-PAGE** 11-20 kDa, reducing conditions

**Activity** Measured in a cell proliferation assay using Balb/3T3 mouse embryonic fibroblast cells. Rubin, J.S. *et al.* (1991) Proc. Natl. Acad. Sci. USA 88:415.  
The ED<sub>50</sub> for this effect is 0.15-0.75 ng/mL.

**Endotoxin Level** <1.0 EU per 1 µg of the protein by the LAL method.

**Purity** >97%, by SDS-PAGE with silver staining.

**Formulation** Lyophilized from a 0.2 µm filtered solution in PBS with BSA as a carrier protein. See Certificate of Analysis for details.

**PREPARATION AND STORAGE**

**Reconstitution** Reconstitute at 250 µg/mL in sterile PBS containing at least 0.1% human or bovine serum albumin.

**Shipping** The product is shipped at ambient temperature. Upon receipt, store it immediately at the temperature recommended below.

**Stability & Storage** **Use a manual defrost freezer and avoid repeated freeze-thaw cycles.**

- 12 months from date of receipt, -20 to -70 °C as supplied.
- 1 month, 2 to 8 °C under sterile conditions after reconstitution.
- 3 months, -20 to -70 °C under sterile conditions after reconstitution.

**BACKGROUND**

Human HB-EGF (Heparin-Binding EGF-like growth factor) is a 12-16 kDa member of the EGF family of peptide growth factors (1-3). Also known as the DTR (diphtheria toxin receptor), it is further classified as a group 2 ErbB ligand based on its ability to activate both the EGF/ErbB1 and ErbB4 receptors (4, 5). HB-EGF is synthesized as a 208 amino acid (aa) type I transmembrane preproprecursor (1, 6). It contains a 19 aa signal sequence, a 43 aa prosegment, an 86 aa mature region (aa 63-148), an 11 aa juxtamembrane cleavage peptide, a 24 aa transmembrane segment, and a 25 aa cytoplasmic tail (aa 184-208). As an integral membrane protein, HB-EGF is expressed as a 19-27 kDa protein in mammalian cells (7-9). The variability in molecular weight (MW) is attributed to heterogeneity in glycosylation and/or the utilization of multiple proteolytic cleavage sites during maturation. Mature HB-EGF is a soluble peptide that arises from proteolytic processing of the transmembrane form. It possesses an EGF-like domain between aa 104-144, and a heparin-binding motif between aa 93-113. Although the aa range for "mature" HB-EGF is typically stated to be Asp63-Leu148, potential N-terminal start (cleavage) sites also exist at Gly32, Arg73, Val74, Ser77 and Ala82 (8, 10-12). Thus, differential processing (in part) likely accounts for the 16-23 kDa range in MW noted for mammalian-derived mature HB-EGF. Proteases suggested to contribute to HB-EGF processing include TACE, MMP-3 and -7, ADAM-17 and ADAM-12 (11, 13-16). When expressed recombinantly in *E.coli*, HB-EGF (aa 73-148) runs at 14 kDa in SDS-PAGE; when expressed in Baculovirus, HB-EGF (aa 63-148, 77-148 and 32-148) runs at 18 kDa, 15 kDa, and 19 kDa respectively (8, 12, 17). Over aa 63-148, human HB-EGF shares 76% and 73% aa sequence identity with rat and mouse HB-EGF, respectively (1, 18). Cells known to express HB-EGF include bronchial epithelium (19), visceral and vascular smooth muscle (20, 21), CD4+ T cells (22), cardiac muscle (23), glomerular podocytes (24), keratinocytes (13) and IL-10-secreting regulatory macrophages (25). As noted earlier, HB-EGF is known to bind to both 170 kDa EGFR and 180 kDa ErbB4, and through heterodimerization, ErbB2 (13, 26). Activity associated with ErbB4 binding appears to be limited to non-mitogenic actions, while EGFR binding induces both mitogenic and non-mitogenic activity.

**References:**

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