

DESCRIPTION

Source	Mouse myeloma cell line, NS0-derived human Noggin protein Gln28-Cys232 Accession # Q13253 Manufactured and tested under current Good Manufacturing Practice (GMP) guidelines.
N-terminal Sequence Analysis	Amino acid sequencing was blocked, suggesting it is consistent with Gln28 as the first N-terminal amino acid. Predicted N-terminal sequence: Gln-His-Tyr-Leu-His-Ile-Arg-Pro-Ala-Pro
Structure / Form	Disulfide-linked homodimer
Predicted Molecular Mass	23 kDa (monomer)

SPECIFICATIONS

SDS-PAGE	30-33 kDa, reducing conditions
Activity	Measured by its ability to inhibit BMP-4-induced alkaline phosphatase production by ATDC5 mouse chondrogenic cells. The ED ₅₀ for this effect is 0.02-0.16 µg/mL in the presence of 50 ng/mL of Recombinant Human BMP-4 (Catalog # 314-BP).
Endotoxin Level	<0.10 EU per 1 µg of the protein by the LAL method.
Purity	>95%, by SDS-PAGE with silver staining, under reducing conditions.
Host Cell Protein	< 1.0 ng per µg of protein when tested by ELISA.
Formulation	Lyophilized from a 0.2 µm filtered solution in PBS. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Reconstitution	Reconstitute at 100 µg/mL in PBS.
Shipping	The product is shipped with polar packs. Upon receipt, store it immediately at the temperature recommended below.
Stability & Storage	<p>Use a manual defrost freezer and avoid repeated freeze-thaw cycles.</p> <ul style="list-style-type: none"> • A minimum of 12 months when stored at ≤ -20 °C as supplied. Refer to lot specific COA for the Use by Date. • 1 month, 2 to 8 °C under sterile conditions after reconstitution. • 3 months, ≤ -20 °C under sterile conditions after reconstitution.

DATA

<p>Bioactivity</p> <p>GMP-grade Recombinant Human Noggin (Catalog # 6057-GMP) inhibits BMP-4-induced alkaline phosphatase production in the ATDC5 mouse chondrogenic cell line. The ED₅₀ for this effect is 0.04-0.2 µg/mL in the presence of 50 ng/mL of Recombinant Human BMP-4 (Catalog # 314-BP).</p>	<p>SDS-PAGE</p> <p>1 µg/lane of GMP-grade Recombinant Human Noggin (Catalog # 6057-GMP) was resolved with SDS-PAGE under reducing (R) and non-reducing (NR) conditions and visualized by silver staining, showing bands at 31 kDa and 57 kDa, respectively.</p>
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BACKGROUND

Noggin is a secreted homodimeric glycoprotein that is an antagonist of bone morphogenetic proteins (BMPs) (1, 2). Human Noggin cDNA encodes a 232 amino acid (aa) precursor protein; cleavage of a 19 aa signal peptide generates the 213 aa mature protein which contains an N-terminal acidic region, a central basic heparin-binding segment and a C-terminal cysteine-knot structure (2). Secreted Noggin probably remains close to the cell surface due to its binding of heparin-containing proteoglycans (3). Noggin is very highly conserved among vertebrates, such that mature human Noggin shares 99%, 99%, 98%, 97% and 89% aa sequence identity with mouse, rat, bovine, equine and chicken Noggin, respectively. Noggin binds some BMPs such as BMP-4 with high affinity and others such as BMP-7 with lower affinity. It antagonizes BMP bioactivities by blocking epitopes on BMPs that are needed for binding to both type I and type II receptors (2, 4). During embryogenesis, Noggin antagonizes specific BMPs at defined times, for example, during neural tube, somite and cardiomyocyte growth and patterning (5-7). During skeletal development, Noggin prevents chondrocyte hyperplasia, thus allowing proper formation of joints (4). Mutations within the cysteine-knot region of human Noggin are linked to multiple types of skeletal dysplasias that result in apical joint fusions (8). Noggin is expressed in defined areas of the adult central nervous system and peripheral tissues such as lung, skeletal muscle and skin (1). During culture of human embryonic stem cells (hESC) or neural stem cells under certain conditions, addition of Noggin to antagonize BMP activity may allow stem cells to proliferate while maintaining their undifferentiated state, or alternatively, to differentiate into dopaminergic neurons (6, 9 - 13). Noggin also appears to maintain adult stem cell populations *in-vivo*, for example, maintaining neural stem cells within the hippocampus (13).

References:

1. Valenzuela, D.M. *et al.* (1995) *J. Neurosci.* **15**:6077.
2. Groppe, J. *et al.* (2002) *Nature* **420**:636.
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4. Brunet, L. J. *et al.* (1998) *Science* **280**:1455.
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6. Itsykson, P. *et al.* (2005) *Mol. Cell. Neurosci.* **30**:24.
7. Yuasa, S. *et al.* (2005) *Nat. Biotechnol.* **23**:607.
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MANUFACTURING SPECIFICATIONS

GMP Proteins

R&D Systems, a Bio-Techne Brand's GMP proteins are produced according to relevant sections of the following documents: WHO TRS, No. 822, 1992 Annex 1, Good Manufacturing Practices for Biological Products; USP Chapter 1043, Ancillary Materials for Cell, Gene and Tissue-Engineered Products and USP Chapter 92, Growth Factors and Cytokines Used in Cell Therapy Manufacturing.

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- Post-bottling lot-specific bioassay results (compliance with an established range) and results of microbial testing according to USP
- Host Cell Protein testing performed by ELISA

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