**DESCRIPTION**

**Source**
Mouse myeloma cell line, NS0-derived human Noggin protein

Human Noggin
(Gln28-Cys232)
Accession # Q13253.1

IEGRMD

Human IgG1
(Pro100-Lys330)

N-terminus
C-terminus

Manufactured and tested under cGMP 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:
Gln28-His-Tyr-Leu-His-Ile-Arg-Pro-Ala-Pro

**Structure / Form**
Disulfide-linked homodimer

**Predicted Molecular Mass**
49.6 kDa (monomer)

**SPECIFICATIONS**

**SDS-PAGE**
58-62 kDa, reducing conditions
110-130 kDa, non-reducing conditions

**Activity**
Measured by its ability to inhibit BMP-4-induced alkaline phosphatase production by ATDC5 mouse chondrogenic cells.
The ED50 for this effect is 0.1-0.4 μg/mL in the presence of 30 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**
>90%, by SDS-PAGE with silver staining, under reducing conditions.

**Host Cell Protein**
< 5.0 ng per μg of protein when tested by ELISA.

**Mycoplasma**
Negative when tested in a ribosomal RNA hybridization assay.

**Adventitious Virus**
Master Cell Bank tested for adventitious viruses

**Formulation**
Lyophilized from a 0.2 μm filtered solution in PBS. See Certificate of Analysis for details.

**PREPARED 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**
Use a manual defrost freezer and avoid repeated freeze thaw cycles.
- 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**

**Bioactivity**
Recombinant Human Noggin Fc Chimera GMP Protein
Bioactivity GMP-grade Recombinant Human Noggin Fc Chimera (Catalog # 3344-GMP) inhibits BMP-4-induced alkaline phosphatase production in the ATDC5 mouse chondrogenic cell line. The ED50 for this effect is 0.1-0.4 μg/mL in the presence of 30 ng/mL of Recombinant Human BMP-4 (Catalog # 314-BP).

**SDS-PAGE**
Recombinant Human Noggin Fc Chimera GMP Protein SDS-PAGE 1 μg lane of GMP-grade Recombinant Human Noggin Fc Chimera (Catalog # 3344-GMP) was resolved with SDS-PAGE under reducing (R) and non-reducing (NR) conditions and visualized by silver staining, showing major bands at 60 kDa (R) and 120 kDa (NR).
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, antagonizing 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 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) without feeder layers or conditioned medium, but with addition of FGF basic, addition of Noggin to antagonize BMP activity allows hESC to maintain their undifferentiated, pluripotent state (9, 10). In differentiation protocols, Noggin has been used to create neural crest stem cells from induced pluripotent stem cells (11).

Because of its importance in the development of tissues, regenerative medicine utilizes Noggin to generate cells for intestinal tissues or organoids in vitro (12). Noggin is also an important factor for stimulating bone development and has neuroprotective effects in early stages of spinal cord injury (13, 14). Expression of Noggin can help contain or reduce metastatic lesions by limiting BMP signaling, making it a therapeutic option for cancer treatment (15). Noggin has been used to create bladder cancer organoids that can serve as a tissue model in preclinical testing of chimeric antigen receptor (CAR)-T-cell immunotherapy (16).

References:

R&D Systems, a Bio-Techne Brand’s GMP proteins are produced according to relevant sections of the following documents: USP Chapter 1043, Ancillary Materials for Cell, Gene and Tissue-Engineered Products and Eu. Ph. 5.2.12, Raw Materials of Biological Origin for the Production of Cell-based and Gene Therapy Medicinal Products.

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- Raw material testing and vendor qualification/monitoring
- Fully validated equipment, processes and test methods
- Equipment calibration schedules using a computerized calibration program
- Facility maintenance, safety programs and pest control
- Material review process for variances
- Monitoring of stability over product shelf-life

R&D Systems strives to provide our customers with the analytical characteristics of each product so that customers may determine whether our products are appropriate for their research. The Certificate of Analysis provided contains the following lot specific information:

- N-terminal amino acid analysis, SDS-PAGE analysis, and endotoxin level (as determined by LAL assay) performed on each bulk QC lot, not on individual bottlings of each QC lot
- 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
- Mycoplasma testing by ribosomal RNA hybridization assay

Additional testing and documentation requested by the customer can be arranged at an additional cost.

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