

**DESCRIPTION**

<b>Source</b>	Mouse myeloma cell line, NS0-derived human Noggin protein Gln28-Cys232 Accession # Q13253
<b>N-terminal Sequence Analysis</b>	No results obtained: Gln28 predicted
<b>Structure / Form</b>	Disulfide-linked homodimer
<b>Predicted Molecular Mass</b>	23 kDa (monomer)

**SPECIFICATIONS**

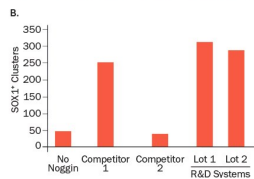
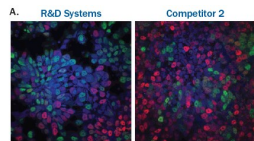
<b>SDS-PAGE</b>	30-33 kDa, reducing conditions
<b>Activity</b>	Measured by its ability to inhibit BMP-4-induced alkaline phosphatase production by ATDC5 mouse chondrogenic cells. The ED <sub>50</sub> for this effect is 0.0200-0.160 µg/mL in the presence of 50 ng/mL of Recombinant Human BMP-4 (Catalog # 314-BP).
<b>Endotoxin Level</b>	<0.10 EU per 1 µg of the protein by the LAL method.
<b>Purity</b>	>95%, by SDS-PAGE visualized with Silver Staining and quantitative densitometry by Coomassie® Blue Staining.
<b>Formulation</b>	Lyophilized from a 0.2 µm filtered solution in PBS. See Certificate of Analysis for details.

**PREPARATION AND STORAGE**

<b>Reconstitution</b>	Reconstitute at 250 µg/mL in PBS.
<b>Shipping</b>	The product is shipped at ambient temperature. Upon receipt, store it immediately at the temperature recommended below.
<b>Stability &amp; Storage</b>	<p><b>Use a manual defrost freezer and avoid repeated freeze-thaw cycles.</b></p> <ul style="list-style-type: none"> <li>• 12 months from date of receipt, -20 to -70 °C as supplied.</li> <li>• 1 month, 2 to 8 °C under sterile conditions after reconstitution.</li> <li>• 3 months, -20 to -70 °C under sterile conditions after reconstitution.</li> </ul>

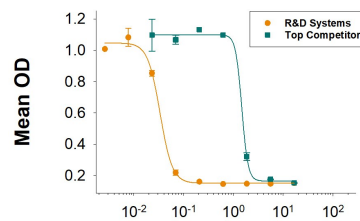
DATA

Bioactivity



**Superior and Consistent Pluripotent Stem Cell Differentiation with R&D Systems Recombinant Human Noggin.** BG01V human embryonic stem cells were cultured in Mouse Embryonic Fibroblast Conditioned Media supplemented with FGF basic (5 ng/mL). Stem cells were driven into early cells of the neuroectoderm using a 3 day incubation in recombinant human Noggin (25 µg/mL) from either R&D Systems (Lot 1, Lot 2; Catalog # 6057-NG) or from two separate competitors (Competitor 1, Competitor 2). Control cells were not incubated in Noggin (No Noggin). The cells were stained for the early ectoderm marker, Otx2, and the neuroectoderm marker, SOX1. (A) Representative images of SOX1 (green), Otx2 (red), and DAPI (blue) staining in embryonic stem cells differentiated with Noggin from R&D Systems or Noggin from Competitor 2. (B) SOX1+ clusters were quantified under each of the indicated culture conditions. Cells treated with R&D Systems Noggin showed an increase in SOX1+ cells compared to both untreated and competitor-treated cells. R&D Systems Noggin showed consistent differentiation across the lots tested. BG01V human embryonic stem cells are licensed from ViaCyte, Inc.

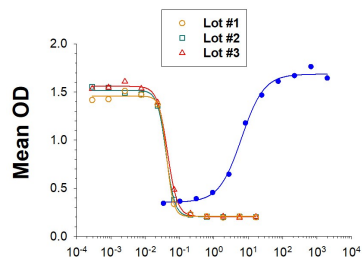
Bioactivity



**Superior and Consistent Pluripotent Stem Cell Differentiation with R&D Systems Recombinant Human Noggin.** Recombinant Human Noggin (Catalog # 6057-NG/CF) inhibits BMP-4 induced alkaline phosphatase production in the ATDC5 mouse chondrogenic cell line. The activity is approximately 30-fold greater than the top competitor's Noggin.

Recombinant Human Noggin (µg/mL)

Bioactivity



Recombinant Human Noggin (µg/mL)

**Recombinant Human Noggin Protein, CF Lot-to-Lot Consistency** The lot-to-lot consistency of Recombinant Human Noggin (Catalog # 6057-NG/CF) was assessed by testing the ability of three independent lots of the protein to inhibit BMP-4-induced alkaline phosphatase production in the ATDC5 mouse chondrogenic cell line (orange, green, red lines). Each trace on the graph represents data obtained from Recombinant Human Noggin from a different manufacturing run. The ED<sub>50</sub> for this effect is 0.020-0.160 µg/mL in the presence of 50 ng/mL Recombinant Human BMP-4 (Catalog # 314-BP/CF). The dark blue line on the graph is showing the ability of Recombinant Human BMP-4 (ng/mL) to induce alkaline phosphatase production in the ATDC5 mouse chondrogenic cell line.

**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.
3. Paine-Saunders, S *et al.* (2002) *J. Biol. Chem.* **277**:2089.
4. Brunet, L. J. *et al.* (1998) *Science* **280**:1455.
5. McMahon, J. A. *et al.* (1998) *Genes Dev.* **12**:1438.
6. Itsykson, P. *et al.* (2005) *Mol. Cell. Neurosci.* **30**:24.
7. Yuasa, S. *et al.* (2005) *Nat. Biotechnol.* **23**:607.
8. Gong, Y. *et al.* (1999) *Nat. Genet.* **21**:302.
9. Xu, R.-H. *et al.* (2005) *Nat. Methods* **2**:185.
10. Wang, G. *et al.* (2005) *Biochem. Biophys. Res. Commun.* **330**:934.
11. Chaturvedi, G. *et al.* (2009) *Cell Prolif.* **42**:425.
12. Chiba, S. *et al.* (2008) *Stem Cells* **26**:2810.
13. Bonaguidi, M.A. *et al.* (2008) *J. Neurosci.* **28**:9194.