

Noggin^{HuXp} Human Cell Expressed Glycosylated Disulfide-linked Homodimer



INTRODUCTION

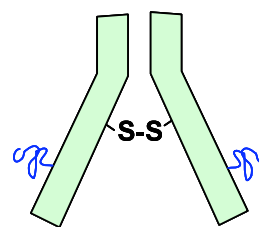
Cytokines are a group of proteins and polypeptides that organisms use as signaling molecules. Most cytokines are glycoproteins less than 30 kDa in size and bind to specific, high-affinity cell surface receptors. Due to their central role in the immune system, cytokines are involved in a variety of immunological, inflammatory and infectious diseases and widely used in research, diagnostics and therapeutics. Cytokines generally alter the gene expression pattern of the target cell which leads to changes in the rate of cell proliferation and/or in the state of cell differentiation. Currently, these proteins are predominantly produced in non-human cells (e.g. *E. coli*, SF9, CHO) and therefore lack authenticity due to the absence of physiologically relevant glycosylation. In addition, a number of important cytokines are not commercially available due to inadequate proteolytic processing, protein folding or other post-translational modifications that occur in the non-human cell expression systems. HumanZyme has developed an efficient human-cell based technology, HumaXpresssm, for scalable production of human cytokines.

Noggin

Noggin is a secreted homodimeric glycoprotein that is an antagonist of bone morphogenetic proteins (BMPs). During culture of human embryonic stem cells without feeder layers or conditioned medium, but with addition of FGF basic, noggin antagonizes the activity of BMPs to allow stem cells to maintain their undifferentiated, pluripotent state.

Currently, commercially available noggin proteins are produced in several forms which approximate, at best, the authentic human noggin. These non-authentic forms are: 1) a non-glycosylated protein expressed in *E. coli*, 2)

an Fc-fusion protein expressed in NS0, and 3) a glycosylated non-disulfide bonded dimer form transiently expressed in mono-layer human cell culture. HumanZyme has produced Noggin^{HuXp} in an engineered human 293 cell with a scalable suspension cell culture system. The protein is a highly stable, authentically glycosylated, disulfide-linked dimer.



Authentic human noggin

The bioactivity of Noggin^{HuXp} was determined by the dose-dependent inhibition of rhBMP4-induced alkaline phosphate production by ATDC5 cells. The results (.005 µg/mL ED₅₀) indicate Noggin^{HuXp} is 10-fold more active than the non-disulfide bonded dimer form expressed in *E. coli*. (typically, .05 µg/mL is the reported ED₅₀) (Please see product number HZ-1026 at www.humanzyme.com. This product is also available in bulk.)

HumanZyme has developed and continues to develop a growing range of tag-free cytokines, including difficult-to-express protein members of the TGFβ1 superfamily. HumanZyme Authentic Cytokines can be used as highly preferred reagents in a wide range of applications for cancer, inflammation, stem cell research, and antibody development.