

Authentic Activin A^{HuXp} Expressed in Human Cells



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. 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, **HumaXpress™**, for the scalable production of human cytokines. The company is expanding this range of tag-free produced cytokines, including difficult-to-express members of the TGFβ superfamily. HumanZyme's authentic cytokines are preferred reagents for stem cell, cancer, inflammation research, and antibody development.

Activin A^{HuXp}

Activin A belongs to the TGF-β super-family and exhibits a wide range of biological activities including regulation of cellular proliferation and differentiation, and promotion of neuronal survival. Activin A is a disulfide-linked dimeric protein produced as precursor with an amino-terminal propeptide that is enzymatically cleaved to release the carboxy-terminal bioactive ligand. Due to complex post-proteolytic modification processes, yield from insect cell and CHO cell expression systems is low and as a result bulk volume is uneconomical and not readily available. HumanZyme has produced Activin A^{HuXp} in a stable cell culture of engineered human HEK293 cells. The protein is expressed as a disulfide-linked

dimer of 26 kD and, due to the scalability of the stable culture, can be cost-effectively produced. As shown in Fig. 1, Activin A^{HuXp} is highly purified while a commercially sourced cytokine expressed in CHO exhibits contamination by the precursor and several other proteins.

Activin A^{HuXp} was assayed by its ability to inhibit the proliferation of murine MPC-11 cells. The results indicate the activity of **HumaXpress™** Activin A is comparable to that of the CHO expressed version. HumanZyme cytokines are manufactured to high quality standards and provide high biological activity, lot-to-lot consistency and low endotoxin levels. Activin A^{HuXp} is available in trial size and in bulk. (See product catalog number HZ-1136, HZ-1137 and HZ-1138 at www.humanzyme.com.)

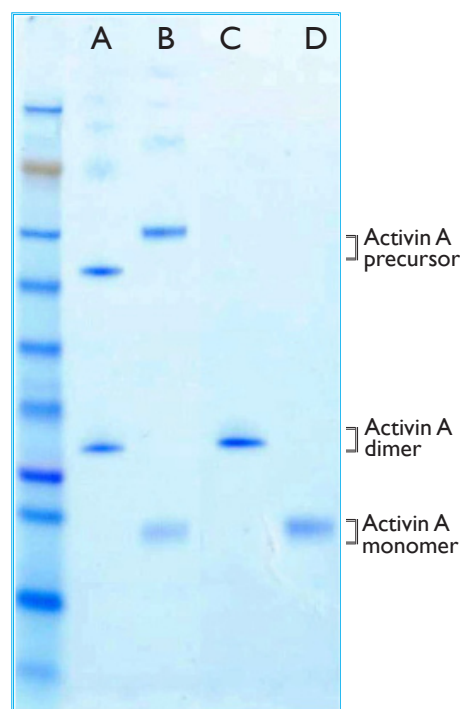


Fig. 1. Purified CHO expressed Activin A from a commercial source (A) without DTT, (B) with DTT and HumanZyme Activin A^{HuXp} (C) without DTT, (D) with DTT.