

Efficient Induction of TH17 Cells With Authentic TGFβ I^{HuXp} Expressed in Human Cells



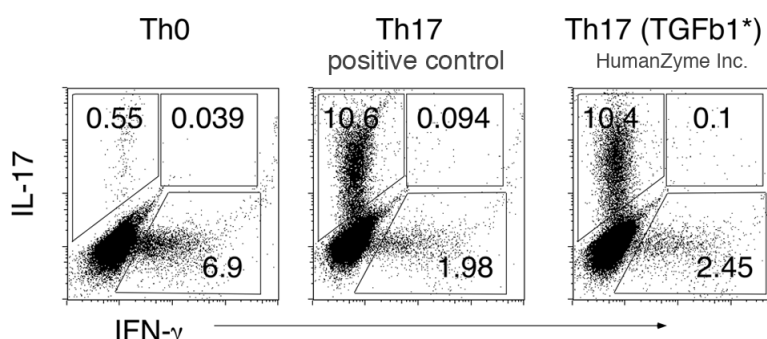
INTRODUCTION

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. Cytokines generally alter the gene expression pattern of the target cell which can lead 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 do not occur in the non-human cell expression systems. HumanZyme has developed an efficient human-cell based technology, HumaXpress™, for scalable production of human cytokines.

Recombinant TGFβ I^{HuXp}

Transforming growth factor-beta (TGF-β) are a group of highly pleiotropic cytokines that act as cellular switches and regulate immune function, proliferation and epithelial-mesenchymal transition. These proteins are produced as precursors. A furin-like convertase processes the proprotein to generate an N-terminal latency-associated peptide (LAP) and a C-terminal mature TGF-β. Disulfide-linked homodimers of LAP and TGF-β remain non-covalently associated after secretion, forming the small latent TGF-β complex. Covalent linkage of LAP to latent TGF-β binding proteins create large latent complex that may interact with the extracellular

matrix. Currently, commercially available TGFβ proteins are produced as a recombinant protein expressed in CHO cells or as native protein in human platelets. Due to the complex post-proteolytic modification, the yield is low and bulk volume is not readily available. HumanZyme has produced TGF-β I^{HuXp} in a stable proprietary human 293 cell expression system. The protein



is disulfide-linked dimer of 25 kD that can be cost-effectively produced in large scale.

The bioactivity of TGF-β I^{HuXp} was determined by the dose-dependent inhibition of IL5 induced proliferation of human TF-1 cells. The results indicate that human cell expressed TGF-β I^{HuXp} is 3-fold more active than the CHO expressed protein. Moreover, it is apparent that TGF-β I^{HuXp} and native platelet TGF-β I are equally effective to induce Th17 cell differentiation.

This product adds to the rapidly expanding range of cytokines available from HumanZyme Inc., manufactured to high quality standards and providing high biological activity, lot-to-lot consistency and low endotoxin levels. See product numbers (HZ-1010, HZ-1011, HZ-1012, HZ-1087) TGF-β I^{HuXp} is available in trial size and in bulk.