

Efficient Induction of Th17 Cells with Humankine[®] TGFβ1

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 do not occur in the non-human cell expression systems.

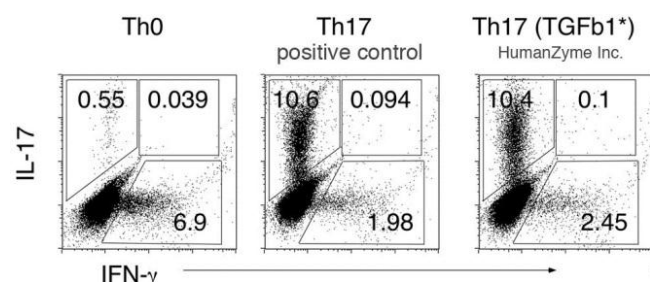
HumanZyme has developed an efficient human-cell based technology, HumaXpress[®], for cost-effective and scalable production of human cytokines.

RECOMBINANT TGFβ1

Transforming growth factors-beta (TGFβ) are highly pleiotropic cytokines that act as cellular switches and regulate immune function, proliferation and epithelial-mesenchymal transition. These proteins are produced as precursors, and then a furin-like convertase processes the proprotein to generate an N-terminal latency-associated peptide (LAP) and a C-terminal mature TGFβ. Disulfide-linked homodimers of LAP and TGFβ remain non-covalently associated after secretion, forming the small latent TGFβ complex.

Covalent linkage of LAP to latent TGFβ binding proteins creates a large latent complex that may interact with the extracellular matrix. Commercially available TGFβ proteins are produced as a recombinant protein expressed in CHO cells or as purified native protein from human platelets. Due to complex post-proteolytic modifications, TGFβ yield is low and the products are not available in economic bulk quantity. HumanZyme has produced HumanKine TGFβ1 in a stable proprietary human 293 cell expression system. The protein is a disulfide-linked dimer of 25 kD that can be cost-effectively produced in large scale.

The bioactivity of HumanKine TGFβ1 was determined by the dose-dependent inhibition of IL5 induced proliferation of human TF-1 cells. The results indicate that human cell expressed HumanKine TGFβ1 is 3-fold more active than the CHO expressed protein. Moreover, it is apparent that HumanKine TGFβ1 and native platelet TGFβ1 (positive control) are equally effective to induce Th17 cell differentiation (see figure).



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. HumanKine TGFβ1 is available at www.humanzyme.com (see product numbers H-1011, HZ-1131 and HZ-1087).