

IL-12^{HuXp} and IL-23^{HuXp} Authentic Hetero-dimer Human Cell Expressed

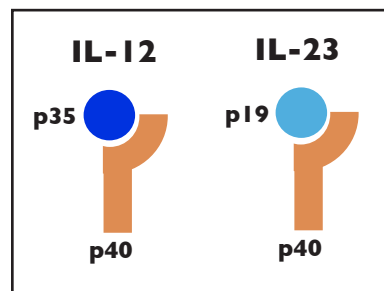


INTRODUCTION

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, HumaXpress[™], for scalable production of human cytokines.

Heterodimeric IL-12 IL-23

IL-12 and IL-23 are heterodimeric cytokines composed of two glycosylated and disulfide-linked subunits. Both cytokines share a common subunit of p40 which are cystine linked to p35 and p19 respectively. Both cytokines induce proliferation and IFN-gamma production by human T cells. While IL-12 acts on both native and memory human T cells, the effects of IL-23 is restricted to memory T cells. Currently, commercially available proteins are produced as heterodimeric or fusion proteins from insect SF9 or SF21 cells. Cytokines produced in SF9 or FF21 cells have post-translational modifications which are not human-like. HumanZyme has produced IL-12^{HuXp} and IL-23^{HuXp} in an engineered human



293 cell with a scalable suspension cell culture system. The protein is a highly stable, authentically glycosylated, disulfide-linked hetero-dimer. These proteins can be cost-effectively produced in large scale.

HumanZyme 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.

