

**EFFECTS OF THE IL-6 RECEPTOR SUPERANTAGONIST SANT7 ON
TGF-B-INDUCED CELL PROLIFERATION AND MAP KINASE
PHOSPHORYLATION IN PRIMARY CULTURES OF FIBROTIC HUMAN LUNG
FIBROBLASTS**

Gallelli Luca, Falcone Daniela, Renda Teresa, Pelaia Girolamo, Maselli Rosario, Savino Rocco,
De Sarro Giovambattista

Department of Experimental and Clinical Medicine, Faculty of Medicine, University Magna
Graecia of Catanzaro, Italy

Both interleukin-6 (IL-6) and transforming growth factor-beta (TGF-beta) are crucially involved in the fibrotic events characterizing interstitial lung diseases (ILDs), as well as the airway remodeling process typical of asthma. Therefore, the aim of this study was to investigate, in primary cultures of fibrotic human lung fibroblasts (HLFs) exposed to either IL-6 or TGF- β 1, the effects on phosphorylation of mitogen-activated protein kinases (MAPK) and cell growth of IL-6 signaling inhibition, performed by the IL-6 receptor superantagonist Sant7. MAPK phosphorylation was detected by Western blotting, HLF viability and proliferation were evaluated using Trypan blue staining and the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay, respectively. Sant7, at a concentration of 1 mcg/ml, was capable of significantly inhibiting HLF proliferation and MAPK phosphorylation induced by cell exposure to IL-6 (100 ng/ml) or TGF- β 1 (10 ng/ml). These results thereby suggest that, in HLFs derived from patients with ILDs, the proliferative mechanisms activated by TGF- β 1 are at least in part mediated by an increased release of IL-6, leading to phosphorylation-dependent MAPK activation. Such preliminary findings may thus open new therapeutic perspectives for fibrogenic ILDs and subepithelial airway fibrosis, based on inhibition of signal transduction pathways stimulated by the IL-6 receptor.