# ROLE OF TGF-β ON MAP KINASE PHOSPHORYLATION AND CELL PROLIFERATION IN PRIMARY CULTURES OF HUMAN LUNG FIBROBLAST

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Transforming growth factor-β1 (TGF- β 1) is crucially involved in the fibrotic events characterizing interstitial lung diseases, as well as in the airway remodelling process typical of asthma. Within such a context, the aim of our study was to investigate, in primary cultures of normal human lung fibroblasts, the effects of TGF- β 1 on mitogen-activated protein kinase (MAPK) phosphorylation, cell proliferation and production of interleukins 6 (IL-6) and 11 (IL-11), in the presence or absence of a pretreatment with budesonide. MAPK phosphorylation was detected by Western blotting, cell count was performed using Trypan blue staining, and the release of IL-6 and IL-11 into cell culture supernatants was assessed by ELISA. TGF- β 1 (10 ng/mL) significantly stimulated MAPK phosphorylation ($p<0.01$), and also enhanced cell numbers as well as the secretion of both IL-6 and IL-11, which reached the highest increases at the $72^{nd}$ hour of cell exposure to this growth factor. All such effects were prevented by budesonide ($10^{-8}$ M) and, with the exception of IL-6 release, also by a mixture of MAPK inhibitors. Therefore, our findings suggest that the fibrotic action exerted by TGF- β 1 in the lung is mediated at least in part by MAPK activation and by an increased synthesis of the profibrogenic cytokines IL-6 and IL-11; all these effects appear to be prevented by corticosteroids via inhibition of MAPK phosphorylation.