P18: MOLECULAR MECHANISM OF UTEROGLOBIN-RELATED PROTEIN 1 (UGRP1) INDUCTION BY INTERLEUKIN-10 IN AIRWAY EPITHELIAL CELLS

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ABSTRACT

Interleukin-10 (IL-10) induction of uteroglobulin-related protein 1 (UGRP1) gene expression was examined using human lung adenocarcinoma NCI-H441 cells. Treatment of the cells with 25 or 50 ng/ml IL-10 induced the expression of h*UGRP1* mRNA as early as 2 hours and the level of expression continued for at least 24 hours. Actinomycin D inhibited IL-10 induction of h*UGRP1* mRNA expression whereas cycloheximide did not have any effect, suggesting that IL-10 regulated h*UGRP1* expression at transcriptional level. Transient transfection analysis with and without IL-10 treatment using several reporter constructs containing up to 324 bp of the h*UGRP1* gene promoter sequence revealed a potential transcriptional control site for IL-10 signal transduction between –179 and –209 bp of the h*UGRP1* gene promoter. Co-transfection analysis using mutant constructs, gel shift analysis and chromatin immunoprecipitation assay demonstrated that the binding of T/EBP to its specific binding sites at both –187 and –68 bp in the h*UGRP1* gene promoter was responsible for IL-10 induction of h*UGRP1* gene expression. Both IL-10R subunits, IL-10R1 and IL-10R2, were expressed in NCI-H441 cells; however, STAT3 was barely activated upon IL-10 treatment as judged by Western blotting for phospho-STAT3. When cells were treated with other members of the IL-10 family such as IL-22 and IFN-β, intense band for phospho-STAT3 was obtained while no *UGRP1* expression was found. Mouse embryo lungs cultured in the presence of IL-10 and lungs obtained from mice intranasally instilled IL-10 exhibited the increase of *Ugrp1* mRNA levels. These results demonstrated that IL-10 induced *UGRP1* gene expression in lung epithelial cells through T/EBP-dependent pathway. Together, these findings suggest that UGRP1 may play a role in airway anti-inflammatory processes by serving as a downstream transcriptional target of IL-10 activation.

Key Words: Uteroglobin related protein 1, Interleukin-10, airway epithelial cells, STAT3