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Cytokines IL-17, TNF and IFN-γ alter the expression of Antimicrobial Peptides and Proteins disparately: a targeted proteomics analysis using SOMAscan technology

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Background:

Antimicrobial or host defence peptides are immunomodulatory molecules required to resolve infections. Antimicrobial peptides and proteins (APPs) are important in the control of infections. We have previously shown that exposure to allergens and air pollution, environmental factors that exacerbate asthma in children, alters the expression of specific APPs in the lungs. Allergens and air pollution also enhance the production of pro-inflammatory cytokines, but the impact of these cytokines on APPs expression in the lungs is not completely defined.

Objective:

To evaluate the effects of pro-inflammatory cytokines IL-17, TNF and IFN-γ on the expression profile of APPs in human bronchial epithelial cells (HBEC).

Methods:

HBEC were stimulated with either IL-17A/F (50 ng/mL), TNF (20 ng/mL) or IFN-γ (30 ng/mL) for 24 hour. Cell lysates (n=5) were probed using Slow Off-rate Modified Aptamer (SOMAmer®)-based proteomic array. Western blots were further used to independently validate APPs selected from the proteomic screen.

Results:

Proteomic analyses showed that the abundance of 13 specific APPs was altered in HBEC following stimulation with either IL-17, TNF or IFN-γ. Independent validations of APPs selected from the proteomic screen i.e. those that were enhanced >2-fold ($p<0.01$) demonstrated that the inflammatory cytokines altered the expression of APPs disparately. For example, abundance of cathepsin S was enhanced by only IFN-γ, whereas lipocalin-2 was increased by IL-17 alone. Abundance of elafin was increased in the presence of IL-17 or TNF, but decreased in response to IFN-γ. Whereas the abundance of cathepsin V decreased following stimulation with either IL-17, TNF or IFN-γ.

Conclusion:

The results of this study demonstrate that inflammatory cytokines alter the expression of APPs disparately. This suggests that the composition of the inflammatory cytokine milieu may influence APPs abundance and thus alter the processes required for infection control and regulation of inflammation in the lungs.