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## Interleukin-13 impairs barrier function of human airway epithelia by inducing ubiquitination and internalization of tight junction proteins

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The airway epithelium forms the first defense line against airborne pathogens. Its tightness depends on tight junction (TJ) complexes. Disturbances of TJ result in epithelial barrier damage facilitate pathogen invasion and thereby aggravate chronic inflammatory lung diseases. The cytokine interleukin-13 (IL-13) has been shown to play a pivotal role in inflammatory lung diseases as asthma or COPD. Whereas increased mucus production is a well described IL-13 effect, its impact on barrier function is hardly elaborated. Therefore, our study aimed on the effect of IL-13 on barrier function and TJ of airway epithelia. IL-13 exposure of primary human tracheal epithelial cells (hTEpC) cultivated as air-liquid-interface reduced transepithelial electrical resistance and increased permeability for sodium fluorescein. RT-PCR experiments revealed reduced mRNA transcript levels of the TJ proteins claudin 8, 9 and 16 and upregulation of the ubiquitin E2 ligase (UBE2Z). Immunocytochemical experiments revealed reduced apico-lateral localization and an intracellular accumulation of TJ proteins in IL-13 treated hTEpC. By contrast, the lateral localization of the adherens junction protein E-cadherin remained unaffected by IL-13. Janus kinase inhibitors abolished IL-13 effects. Proximity ligation assays demonstrated ubiquitination of TJ proteins as well as interaction of ZO 1 and several claudins with the ubiquitin conjugating enzyme UBE2Z. Our results demonstrate, that IL-13 impairs airway epithelial barrier by internalization of TJ proteins via an ubiquitin dependent mechanism. Therefore, IL-13 signaling could be a promising therapeutic target to prevent epithelial dysfunction in inflammatory lung diseases.

### Biography

Hanna Schmidt is studying medicine since 2010 at Ulm University (Germany). From 2013 to 2016 she did her Doctorate in the Institute of General Physiology. Her thesis is currently under revision. She is working in the field of lung epithelial physiology and her research focuses on water and ion transport and epithelial barrier function.

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