

IL-32, a Negative Regulator of Angiogenesis in Chronic Airway Diseases

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Chronic asthmatic inflammation in the airways induces angiogenesis demonstrated by several studies in murine models [1] and in human airways [2]. Among the many pro-angiogenic factors involved in asthmatic inflammation in the airways, VEGF-A seems to be the most important one. VEGF-A is mainly produced and secreted by many tissue and immune cells like alveolar epithelial cells, bronchial epithelial cells, smooth muscle cells, fibroblasts, and basophils [3,4]. VEGF-A plays an important role during asthma inflammation: Increased VEGF-A levels are found during asthma attacks already in children [5] and VEGF levels in induced sputum from asthma patients correlate with asthma severity and airflow obstruction [6]. Most importantly, VEGF-A is up regulated by Th2 cytokines like IL-4, IL-5 and IL-13 involved in the pathogenesis of asthma [7]. In addition, the VEGF release by human primary bronchial epithelial cells is increased by rhinovirus infection [7]. In this context, we demonstrated that IL-32 is induced by rhinovirus infection in bronchial epithelial cells and decreases VEGF production and secretion [8]. IL-32 knockdown leads to an up-regulation of VEGF secretion by primary bronchial epithelial cells suggesting that IL-32 might have an inhibitory role in angiogenesis and might be an important factor counter-regulating angiogenesis in rhinovirus-triggered asthma. In addition, IL-32 is also present in sinus epithelial cells after stimulation with TNF- α and IFN- γ [9]. However, the role of IL-32 in angiogenesis during chronic rhinitis has not yet been investigated. Interestingly, IL-32 could be detected in the sera of asthma patients and correlates with significant lung function improvement after 3 weeks of intensive asthma treatment suggesting that IL-32 may distinguish between asthma subtypes with or without fixed airflow limitations. Although the IL-32-mediated decrease in VEGF production during asthmatic airway inflammation suggests an anti-inflammatory function of IL-32, other studies could demonstrate that IL-32 acts as a pro-inflammatory cytokine inducing

TNF- α , IL-8, and macrophage inflammatory protein 2 in monocytes and macrophages [10]. Therefore, more studies investigating IL-32 and its significance for angiogenesis in chronic inflammatory diseases are necessary in the future.

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