

P001 Local treatment with a pan-neurotrophin binding decoy as a novel approach for asthma therapy

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Neurotrophins, particularly the nerve growth factor (NGF) and the brain derived neurotrophic factor (BDNF), have been implicated in the pathogenesis of allergic inflammation and the development of sensory nerve hyperreactivity within the airways. Sensory hyperreactivity provides the basis for airway hyperreactivity to many unspecific stimuli like cold air or cigarette smoke in patients with allergic asthma. We presume that blocking of Trk mediated signals could be a promising concept for therapeutic intervention in asthma.

To test this hypothesis, we analyzed the effects of REN1826, a soluble neurotrophin receptor fragment, which functions as a pan-Trk receptor decoy, in a mouse model of allergic asthma. Before aerosol challenge with ovalbumin (OVA), REN1826 was delivered topically into the lungs of OVA sensitized mice. Hyperreactivity of sensory nerves was assessed by head-out bodyplethysmography in response to capsaicin, and bronchoalveolar lavage (BAL) was performed. We observed a dose-dependent reduction of sensory nerve hyperreactivity in mice treated with REN1826. In addition, a significant decrease of Th2 cytokine levels in the BAL fluid was detected which was associated with a slightly diminished number of eosinophils.

Our results therefore indicate that antagonization of Trk receptor signalling may represent an exciting novel approach for the treatment of asthma.