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Title: Airway reactivity and neuroimmune relationships in animal model of air born irritants induced symptoms – Role of trigeminal TRPA1 channels

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Body: Air born pollutants modulate functions of airways. Many experimental models use inhalation of air born irritants containing aerosols to mimic environmental exposure however, most exposed part is the nose. The aim of our study was to assess the general effects and modulation of airway defensive reflexes in animal model by selective nasal challenges with TRPA1 agonist AITC – allylisothiocyanate. TRPA1 is known to be relevant for most air born irritants. 15 male Dunkin Hartly guinea pigs were repeatedly exposed to 10mM AITC, 15µl administered into both nostrils and nasal symptoms, cough, specific airway resistance (Saw) and bronchoalveolar lavages (BAL) were analyzed afterwards. Nasal administration of 10 mM AITC induces reproducible nasal symptoms, sneezing, discharge, crackles and conjunctival reaction. Also, nasal application of 10mM AITC induces spontaneous rise of Saw measured by Pennock's method in vivo and increases Saw after inhalation of methacholin (p<0.05) rather than histamine, suggesting for nasobronchial reflex. Saw after oxymetazoline (1%) and salbutamol pretreatment suggesting for combined mechanisms. Citric acid induced cough after nasal AITC challenge was significantly suppressed (p<0.05) and it was prevented by pretreatment with TRPA1 antagonist AP18. Nasal AITC challenges in experimental animals for a week induced rise of the count of eosinophils in BAL when comparing to controls confirming the concept of upper and lower airways neuro – immune relationships. Results document the role of TRPA1 in onset of environmental and occupational airway symptoms making it target for clinical applications. VEGA 1/0031/11.