Beneficial effects of Nociceptin/OrphaninFQ (N/OFQ) on immunopathology and airway hyperresponsiveness in asthma

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There is evidence supporting a role for Nociceptin/OrphaninFQ (N/OFQ) receptor (NOP) and its endogenous ligand N/OFQ in the modulation of neurogenic inflammation, airway tone and calibre (Corboz et al., 2000; Basso et al., 2005; D'Agostino B. et al., 2010). We hypothesised that NOP activation has beneficial effects upon asthma immunopathology and airway hyper-responsiveness. Therefore, the expression and function of N/OFQ-NOP was examined in healthy and asthmatic human airway tissues. The concept was further addressed in an animal model of allergic asthma (Kumar RK et al, 2008). NOP expression was investigated by qRT-PCR. Sputum N/OFQ was determined by RIA. N/OFQ function was tested using several assays including proliferation, migration, collagen gel contraction and wound healing. The effects of N/OFQ administration *in vivo* were studied in ovalbumin(OVA)-sensitised and challenged mice. Our results showed that NOP is expressed on a wide range of human and mouse immune and airway cells. Moreover, eosinophils express N/OFQ-precursor mRNA and their number correlates with N/OFQ concentration. N/OFQ is found in human sputum and increases in asthma. Additionally, elevated N/OFQ immunoreactivity is seen in asthmatic human lung. We found that NOP activation inhibits migration of immunocyte and increases wound healing in airway structural cells. In addition, N/OFQ relaxes spasmogen-stimulated gel contraction. Remarkably, these findings were mirrored in OVA-mice where N/OFQ treatment before or during sensitisation substantially reduced airway constriction and immunocyte trafficking to the lung; in particular eosinophils. N/OFQ also reduced inflammatory mediators and mucin production. In conclusion, we have demonstrated a novel dual airway immunomodulator/bronchodilator role for N/OFQ and suggest targeting this system as an innovative treatment for asthma.

References:
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