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Title: Role of nociceptin orphanin FQ peptide - receptor system in mast cell migration

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Body: Asthma is characterised by airway inflammation, airflow obstruction and bronchial hyper-responsiveness. Mast cells play a key role in the pathophysiology of asthma. The heptadecapeptide nociceptin/orphanin FQ (N/OFQ) is the endogenous ligand for N/OFQ peptide (NOP) receptor. Animal studies suggest that N/OFQ-NOP system modulates airway inflammation. Whether mast cells express functional N/OFQ-NOP is unknown. We investigated NOP and ppN/OFQ mRNA expression in human lung mast cells (HLMC) relative to GAPDH mRNA (housekeeping gene) by qRT-PCR and the findings were expressed as Δ CT. NOP protein expression was determined by [125I]N/OFQ saturation binding assays and expressed as receptor density (Bmax) in terms of fmol bound/mg protein. The role of N/OFQ on HLMC migration and proliferation was investigated. No ppN/OFQ mRNA expression was detected. HLMC and HMC-1 cells expressed NOP mRNA with mean Δ CT values of 6.99 ± 0.64 (n=5) and 6.58 ± 1.14 (n=5) respectively. Saturation binding assays detected low NOP protein expression in HMC-1 cells (mean Bmax = 16.99 ± 5.92, n=3) relative to a cell line expressing recombinant human NOP (mean Bmax = 1321.38 ± 60.26, n=4). Transwell migration assays demonstrated that stem cell factor (SCF) induced a 2.29 ± 0.4 (n=5) fold increase in HLMC migration over the control and this was significantly inhibited by N/OFQ (0.98 ± 0.08, n=5, $p< 0.05$). However N/OFQ had no effect on HMC-1 proliferation (n=6). Our findings demonstrated that HLMC express NOP. N/OFQ significantly inhibited SCF-induced HLMC migration suggesting a potential role for N/OFQ in regulating airway inflammation.