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Title: LSC 2013 abstract - Sphingosine-1-phosphate administration in vivo induces airway inflammation and hypereactivity in a IgE-dependent manner

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Body: Introduction: S1P systemic administration leads to an increased airway hyper-reactivity. Aim: To address the mechanism(s) involved in S1P-induced airway hyper-reactivity. Methods/Results: Balb/c mice receiving s.c. injection of S1P (10ng) display a dose- and time-dependent increase in airway reactivity. Airway hyper-reactivity was coupled to an enhanced inflammatory response. In particular, lungs harvested from S1P-treated animals showed an increased cell infiltration, loss of the alveolar structure and mucous cell metaplasia. We also found a significant increase in serum levels of both PGD_2 and IgE. FACS analysis on lung-derived cells evidenced that mast cells were prominent cell type. Proliferation assay of peripheral lymph nodes-derived cells showed that lymphocytes (CD4+) obtained from S1P-sensitized mice displayed a higher proliferation rate compared to cells from vehicle group. In order to address mast cells or T cells contribution in S1P effect mast cell knock-out mice (MCKO) and nude athymic mice were used. In MCKO mice S1P-induced hyper-reactivity was lost, while, still displayed an ongoing inflammatory response. Furthermore IgE serum levels were still increased in MCKO. Conversely, the absence of T cells first dampened S1P-induced hyper-responsiveness and, more interestingly, abrogated inflammatory response. Conclusions. Our data demonstrate that S1P alters lung morphology leading towards an asthma-like environment in which mucus and prostaglandins together with IgE are highly produced. Mast cells are mainly responsible for the airway increased reactivity but do not play a key role in the inflammatory effect elicited by S1P and driven by T cells.