ACTIVATION OF PROTEASE-ACTIVATED RECEPTOR-2 REDUCES AIRWAYS INFLAMMATION IN EXPERIMENTAL ALLERGIC ASTHMA

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Background. Proteinase-activated receptors (PAR)-2 are members of the family of G-protein coupled receptors activated by proteases. These receptors are widely expressed in several tissues and in virtually all cells involved in rhinitis and asthma. In particular, proteinases activating PAR-2 may affect airway functions and play a role in human diseases.
Objective: Assessment of the role of PAR-2 in bronchoconstriction, airway responsiveness**,** and immune response after allergic challenge, in rabbits sensitized to Par j1, the major allergen of *Parietaria judaica* pollen.
Methods: Evaluation of antigen challenge in rabbits treated with PAR-2 activating peptide (PAR-2AP) (SLIGRL) or the scrambled peptide LSIGRL or vehicle immediately before allergen exposure measuring airway responsiveness. Characterization of bronchoalveolar lavage following histamine challenge and phenotype analysis of cells by flow cytometry and analysis of Cytokine production by quantitative PCR.
Results: PAR-2AP pre-treatment, but not the scrambled peptide, was able to significantly inhibits bronchoconstriction, airway hyperresponsiveness, and to modulate the immune response induced by allergic challenge in sensitized rabbits. Western blot analysis showed a clear up-regulation of PAR-2 in rabbit lungs challenged with Par j1. The phenotype analysis of the cells recovered from BAL showed an increase in RLA-DR positive cells while RTLA positive cells were unchanged. IFNγ and IL-2 production were inhibited with a concomitant increase in IL-10 of about 10 fold over the control values.
Conclusions: in this experimental model, PAR-2 modulates bronchoconstriction interfering with antigen challenge-induced immune response, in rabbits sensitized and challenged to Par j1.