

## **Role of A1 Adenosine Receptors in an Allergic Murine Model of Asthma**

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Role of A1 Adenosine Receptors in an Allergic Murine Model of Asthma. Ernest J. Young, A. Nadeem and S. Jamal Mustafa: Dept. of Physiology and Pharmacology, Center for Cardiovascular and Respiratory Sciences, West Virginia University, Morgantown, WV Asthma is an inflammatory disease in which adenosine is known to play an important role through cell surface adenosine receptors (AR). A1AR has already been shown to be involved in airway inflammation and bronchoconstriction in a rabbit model of asthma (Adenosine A1 receptor antagonist versus montelukast on airway reactivity and inflammation, Nadeem, A, et al. 2006, Eur J Pharmacol, 551, 116-24). However, the role of A1AR in airway inflammation and bronchoconstriction has not been explored in a murine model of asthma using A1AR knock out (KO) mice. Therefore, the present study was designed to explore the role of A1AR on bronchoconstriction and inflammation using A1KO and corresponding wild-type mice (WT). Mice were sensitized with two i.p. injections of ovalbumin (30 ug) on days 1 and 6, followed by 5% ovalbumin aerosol challenge on days 11, 12 and 13. On day 14 and 15, airway hyperresponsiveness (Penh) to aerosolized methacholine (MCh) and CCPA (A1AR agonist) respectively were assessed by whole body plethysmography. BAL analysis was performed immediately after CCPA dose response curve. Methacholine as well as CCPA induced bronchoconstriction was greater in WT sensitized and challenged mice as compared to WT controls ( $p < 0.05$ ). KO mice showed no response to CCPA ( $p > 0.05$ ). WT sensitized and challenged mice also had greater numbers of macrophages, lymphocytes, neutrophils, and eosinophils as compared to WT control mice ( $p < 0.05$ ); whereas KO mice showed attenuation of all cell types as compared to WT sensitized mice ( $p < 0.05$ ). These data suggest that A1AR plays an important role in bronchoconstriction and inflammation in this mouse model of asthma. Our future experiments will explore the role of neuronal involvement in A1AR-mediated inflammation and bronchoconstriction.