

## **Mast cell hyperplasia underlies respiratory syncytial virus infection-induced predisposition for asthma**

Ashley L St. John, Jozef Balla *Duke-NUS Medical School*

Asthma is a chronic inflammatory airway disease, which affects approximately 300 million people worldwide. A growing number of epidemiological cohort studies supports an association between pediatric allergic asthma susceptibility and prior respiratory syncytial virus (RSV) infection. In this study, we aimed to experimentally test whether RSV infection promotes the subsequent development of allergic asthma. Either wild type mice or mast cell-deficient congenic KitW-sh mice were infected with RSV or sterile vehicle. After infection clearance, the mice were sensitized to Ragweed (*A. artemisiifolia*) pollen allergens and subsequently challenged intranasally with Ragweed to induce asthma. Disease severity was measured as airway hyperreactivity to inhaled  $\beta$ -methylcholine using a mechanical ventilator. RSV caused an acute and productive infection in mice, which was associated with a rapid cytokine response in the lungs. In our murine allergic asthma model, the wild type animals which had previously cleared the RSV infection developed more severe disease, when compared to mice that have not experienced RSV. We found that there was a sustained increase in the numbers of airway mast cells following the resolution of an acute RSV infection. The induction of allergic asthma disease in our animal model was dependent on mast cells, as it was strongly attenuated in mast cell-deficient KitW-sh mice. Furthermore, there was no potentiation of allergic asthma severity by a previous RSV infection in Sash mice, indicating this process is mast cell-dependent. Thus, RSV induces airway mast cell hyperplasia, which predisposes mice for more severe allergic responses.