Local Lung Inflammation Shapes The Respiratory Immune Response To Influenza And Sensitization To Allergen

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Abstract
Natural sensitizations to allergens and the subsequent developments of asthma require many years of exposures. In contrast mouse asthma models for performing objective mechanistic studies take only weeks to develop but may not truly mimic the pathological changes that are seen in clinical asthma. Undoubtedly there are many differences between allergic mice and humans. Most striking among these is that murine sensitizations are normally transitory and mice do not normally show any respiratory symptoms when challenged. The use of real respiratory allergens to sensitize and challenge mice has improved this and with repeated exposures allergic inflammation can be sustained. People inhale a wide range of substances yet become allergic to just a few. This suggests that there is something different about those proteins that cause asthma (allergens). We attempt to understand what is responsible for this and have generated a Blo t 5 CD4 TCR transgenic mouse (BT-II mouse) for this cause. The cells from these mice are specific for a real inhalant antigen and have not ever been used in murine lung models. We have developed a physiological asthma model in which the allergy-provoking effects and recorded asthmatic reactions are afforded using highly polarized T helper cells prepared from the BT-II mouse that are then transferred in vivo and repeated exposures to the recombinant Blo t 5 protein. Blo t 5 is a major epitope of the tropical mite. Histological analyses of the lungs from these animals show evident airway remodelling and bronchus-associated lymphoid tissues. Unlike asthma models that use egg proteins, this model of asthmatic lungs does not turn off the immune response. This model will find clinical significance and be useful in studying asthma chronicity, airway remodelling and other prominent features of asthma and for testing new therapeutics.

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