

Construction of a new strain of mice that lack mast cells and set-up of a mouse asthma model

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Asthma is a chronic inflammatory disease of the airways which causes recurrent episodes of coughing, wheezing, chest tightness and shortness of breath in susceptible individuals. Today, asthma is one of the most common chronic diseases affecting approximately 300 million people globally and about 5% of the adult Swedish population. Normally when foreign substances such as pathogens enter the body, the host immune system recognizes them and starts to produce specific proteins so-called immunoglobulins (Ig) or antibodies against them. These are capable of neutralizing foreign substances. However, individuals that are genetically susceptible to allergy, produce immunoglobulins of IgE type against one or more harmless non-infectious environmental substances, termed allergens. These allergen-specific IgE molecules can then bind strongly to their receptors (FcεRI) that are present on the surface of mast cells. This process is called sensitization. In sensitized individuals, re-exposure to the same allergen leads to crosslinking of FcεRI-bound IgE with allergen. This activates mast cells to release proinflammatory substances.

Even though mast cells are well known for their important role in allergic diseases, the exact role of mast cells in pathogenesis of allergic asthma is yet to be understood. Today, the best approach to investigate the contribution of mast cells is to study their roles in a mouse model of allergic asthma using mice that lack mast cells. Currently, the most widely used mast cell-deficient mice are those that have mutation in the gene encoding c-Kit. This cell surface receptor is required for survival and development of mast cells. However, the main disadvantage of these mice with regard to allergic asthma modeling is that they are available on mouse strains that do not have a genetic tendency to react with allergy toward foreign substances. Therefore, one aim of this study was to create mast cell-deficient mice on a mouse strain that have a genetic predetermined tendency to develop allergic reactions. In the present study we created such mast cell-deficient mice and used different techniques to prove that they lacked mast cells.

Moreover, since mice do not spontaneously develop asthma, an artificial asthma-like reaction needs to be induced in the airways. This can be achieved by exposing mice to inhaled allergen which consequently leads to development of lung inflammation as a result of migration of immune cells into the lung. Accordingly, we set-up a model of allergic asthma using a common human allergen, house dust mite, which was exposed to the airways. Using this model, we were able to induce allergic airway inflammation in normal mice characterized by a massive increase of inflammatory cells including eosinophils, lymphocytes and macrophages in the lung. This experimental model if combined with mast cell-deficient mice which have a tendency to react with allergy toward foreign substances provides an excellent tool to study the roles of mast cells in pathogenesis of allergic asthma. Because the type of allergen, the route of exposure and the genetic predisposition of mouse strain resembles the onset of allergic asthma in humans as closely as possible.

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