

Human mast cells developed in NSG-Tg(hu-mSCF) mice degranulate upon challenge with Bet v 1

N. Berg¹, G. Sabatino¹, A. Gentile¹, E. Untersmayr¹, A. Farr², B. Bohle¹, C. Vizzardelli¹

¹Medical University of Vienna, Department of Pathophysiology and Allergy Research, Vienna, Austria, ²Medical University of Vienna, Clinical Department of Obstetrics and Feto-Maternal Medicine, Vienna, Austria

Type selection

Choose your preferred presentation format: Oral presentation

General data

Track: Innate Immunity

Topic: Allergy

Abstract text

Text: Purpose: Mast cells (MC) play a key role in IgE-mediated allergies as they bind allergen-specific IgE antibodies through the high-affinity Fc epsilon receptor (FcεRI) on their surface. Cross-linking of the receptor by IgE-binding to allergen induces their degranulation and the release of different factors, e.g. histamine, that cause allergic reactions. We are in the process of establishing an *in vivo* model of IgE-mediated allergy by engrafting non-obese diabetic severely immunodeficient γc-/- mice transgenic for human membrane-bound stem cell factor [NSG-Tg(hu-mSCF)] with human stem cells (HSC) to develop human MC.

Methods: CD34⁺ HSC were isolated from cord blood mononuclear cells (CBMC), and intravenously (i.v.) injected in NSG-Tg(hu-mSCF) mice. After 16 weeks, huCD45⁺FcεRI⁺CD117⁺ cells were detected in different organs. Mice were subcutaneously sensitized with serum from birch pollen (BP)-allergic donors (100μl/mouse) containing 10 kU_A/ml Betv1-specific IgE. The next day, mice received intracutaneous injections of 20μl PBS containing recombinant (r) Betv1 in the belly skin and ears. Allergic reactions were detected by i.v. injection of Evans Blue (0.5%) and local visualization. Moreover, MC were isolated from the bone marrow, sensitized with BP-serum, and degranulation was detected using Lamp3.

Results: >95% pure CD34⁺ HSC were injected (0.5-1x10⁵) in NSG-Tg(hu-mSCF) mice. After 16 weeks, 55±4% (SEM) huCD45⁺ cells and 19±4% huCD45⁺FcεRI⁺CD117⁺ cells were detected in bone marrow. Mice passively sensitized with BP-specific IgE reacted locally in skin and ears as well as anaphylactic to 1μg rBetv1. In vitro cultured MC showed 53% of hulgE on their surface and degranulation upon Betv1 stimulation.

Conclusion: NSG-Tg(hu-mSCF) mice engrafted with HSC developed human MC that responded to allergen after sensitization with human allergen-specific IgE. This *in vivo* model of IgE-mediated allergy will now be used to study agents that block anaphylactic reactions. This work is supported by the Austrian Science Fund (FWF) project P35791.

Conflict of Interest statement

Do you have any conflict of interest to declare?: No

Affirmation

- 1. Consent to participate and present onsite:** Yes
- 2. Consent to publication publication:** Yes
- 3. Consent on treatment of contact details saved in this system:** Yes