

Development of a mouse model of food allergy

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Introduction

Definition:

Allergy is defined as an inappropriate immune response toward harmless antigens. In the case of food allergy, symptoms include itching, nausea, vomiting, diarrhea, abdominal pain, and can sometimes lead to strong anaphylactic reactions.

Allergic diseases have dramatically increased in the last 20 years, becoming a major health problem in industrialized countries. The precise understanding of the mechanisms related to allergy will help to find medications and for this purpose animal models are needed.

Goals:

The purpose of this work is to establish a solid model a food allergy in mice, with the aim to understand the underlying mechanism of food hypersensitivity and to test various modulators of allergy, as for example microorganisms.

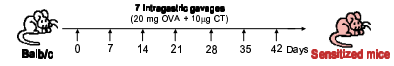
The mouse Balb/c strain is used together with the chicken ovalbumin (OVA) allergen.

Sensitization and Tolerization Protocols

To induce allergic reactions in mice, the allergen OVA is administered intragastrically in presence of the mucosal adjuvant cholera toxin (CT).

Sensitization protocol:

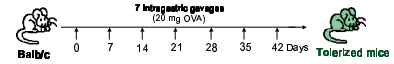
Groups of six to ten mice are sensitized with seven intragastric administrations of OVA mixed with CT.



As negative control, mice were fed with the allergen in order to induce a conventional response toward food antigen. These mice are considered to be tolerized.

Tolerization protocol:

Groups of 8 mice are fed seven times with OVA to induce tolerization.

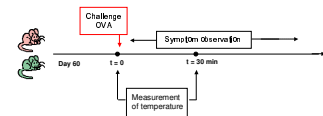


Results

Challenge:

To induce allergic symptoms, both groups of mice were challenged with 100 mg OVA intragastrically. Allergic scores and temperature are examined.

Procedure:

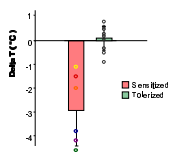


Allergic scores



Allergic scores are given in accordance to a scale which includes symptoms such as pilar erect, scratching, reduced activity, wheezing and diarrhea.

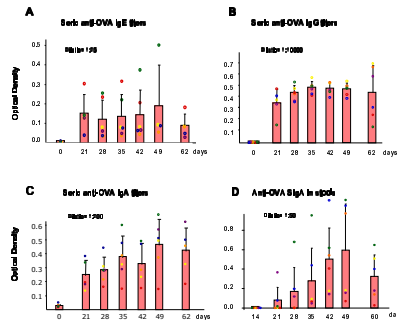
Temperature variation



A prolonged drop in body temperature, together with strong allergic scores are observed in sensitized mice, whereas tolerized mice remain unaffected.

Humoral response:

Antibody titers in sera and stools are analyzed by ELISA during the sensitization protocol and after the challenge.



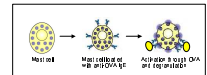
Anti-OVA IgE are detected in low levels in sera from sensitized mice (A). Anti-OVA IgG are very abundant throughout the protocol (B). Anti-OVA IgA in sera (C) and stools (D) are found to increase in sensitized mice throughout the protocol. Tolerized mice have undetectable levels of anti-OVA IgE, anti-OVA IgA, and very low levels of anti-OVA IgG.

The presence of anti-OVA IgE, even at low levels, suggests that the sensitization occurred. On the contrary, tolerized mice have undetectable levels of OVA specific IgE, IgG and IgA throughout the protocol, meaning that oral tolerance took place.

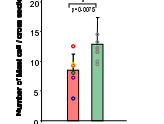
Mast cells in the gastrointestinal mucosa:

Mast cells present in the mucosa can, through activation by IgE cross-linking with the allergen, release numerous inflammatory factors, which will subsequently lead to inflammation.

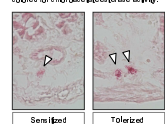
Therefore, mast cells are quantified in jejunum cross sections, as well as inflammatory mediators in sera.



Mast cell number

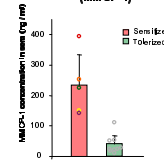


Jejunum cross sections



Mast cells number is significantly decreased in sensitized mice, probably because degranulation occurred, making mast cells difficult to identify. Pictures present a more dispersed coloration when mast cells are degranulated.

Mouse mast cell protease 1 (MMCP-1)



MMCP-1 was quantified in serum of challenged mice. The increase of MMCP-1 in sensitized mice suggests that degranulation occurred.

Mast cell number in mucosa is decreased, and MMCP-1 levels are elevated in sera, meaning that degranulation occurred after challenge in sensitized mice, as expected in the context of allergic reactions.

Conclusions

Using a sensitization procedure restricted to the mucosal compartment, we are able to induce allergic like reactions in mice.

The allergic symptoms include:

- Strong allergic scores
- Drop of body temperature 30 min after challenge
- Detectable levels of allergen-specific IgE in sera
- Degranulation of mucosal mast cells following challenge

These preliminary results are very promising and will lead to the establishment of a solid model of food allergy in mice.

Perspectives

This model will be used to study the potential immunomodulatory function of secretory IgA and microorganisms including acid lactic bacteria.

Acknowledgments

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