Modification of allergenic proteins with glycans for oral tolerance induction

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Allergic conditions
Study type	Observational invasive

Summary

ID

NL-OMON54808

Source
ToetsingOnline

Brief title
Modification of allergenic proteins ('GoAllergy')

Condition

- Allergic conditions

Synonym
acute inflammation, Food allergy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: NWO,Nutricia,Nutricia Research BV

Intervention

Keyword: Food allergy, immunotherapy, oral tolerance, Siglec

Outcome measures

Primary outcome

This study has several exploratory parameters:

1. The phenotype and function of cow*s milk/peanut specific T cell lines/clones (Th1, Th2, Th17 and Tregs) determined by extracellular/intracellular T cell markers and cytokines.

2. IgE binding to unmodified and glycan-modified cow*s milk/peanut proteins/peptides.

3. Antibody production and antibody type of allergen-specific B cells

4. The degranulation of basophils (CD63)

5. The degranulation and maturation of mast cells (beta-hexosaminidase and/or cytokines).

Secondary outcome

not applicable

Study description

Background summary

Food allergy is defined as an unwanted response of the immune system to harmless food proteins. For years it has been thought that the best way to prevent the development of food allergy, is to avoid exposure to food proteins. However, recent studies have shown that exposure is necessary to (re)train the immune system to induce tolerance. This is an active process in which food proteins are taken up, processed and presented by antigen presenting cells to naïve T cells. Instead of induction of Th2 cells (allergic response), naïve CD4+ T cells develop a regulatory or anergic phenotype (tolerogenic response).

The form in which the allergens are encountered by a subject may play a key role for the development of oral tolerance. Previous studies have indicated that glycans can induce immunosuppressive responses. Moreover, key cells involved in oral tolerance development and in allergic responses express glycan-binding proteins. In this study we would like to investigate whether modification of allergens with glycans may support oral tolerance induction and/or inhibit the allergic response.

Study objective

This is an exploratory study with two objectives:
1. To investigate whether modification of allergenic milk and peanut proteins or peptides thereof with glycans can support oral tolerance induction by altering the antigen-specific T cell response from a Th2-dominant response towards a more tolerogenic response directly or indirectly via antigen presenting cells.
2. To investigate whether modification of allergenic milk and peanut proteins or peptides thereof with glycans can diminish IgE-mediated responses by inhibiting IgE production by B cells, interfering with IgE binding/cross-linking and/or maturation of effector cells.

Study design

Cow*s milk and peanut allergic patients will be asked to donate 100 ml blood twice. The first blood sample will be used to isolate plasma and peripheral blood mononuclear cells (PBMCs) for the generation of cow*s milk- or peanut-specific T cell lines/clones and autologous Epstein-Barr virus (EBV)-transformed B cells. These cells will be used to investigate the effect of glycans on T cell phenotype (Objective 1). Plasma will be used to study the effect of glycans on IgE binding (Objective 2). The second blood sample will be used for the basophil activation test (IgE cross linking), and for isolation of allergen-specific B cells (antibody production), CD34+ progenitor cells for the generation of mast cells (maturation effector cells) (all three Objective 2), and monocytes for the generation of monocyte-derived DCs (MoDCs). The MoDCs will be used as antigen-presenting cells for the T cell lines/clones (indirect effects on T cell lines/clones) (Objective 1).

Study burden and risks

The subjects are requested to make two visits to the UMC Utrecht for a blood withdrawal of 100 mL. The risk of blood withdrawal consists of slight pain and possible bruising. The risk is considered negligible.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- At least 18 years of age - Cow*s milk or peanut allergy based on either 1) positive food challenge, or 2) IgE-sensitization to cow*s milk or peanut (sIgE>0.35 kU/l or positive skin prick test) in combination with a convincing history (reaction with symptoms suggestive of allergy within 2 hours of ingestion of cow*s milk)

Exclusion criteria

- Use of immunosuppressive drugs
- Previous or current participation in an allergy immunotherapy trial

- Pregnancy

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-09-2023
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	28-09-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	24-07-2023
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL69345.041.21