A novel class of regulators: the potential of IL-10 producing B cells in decreasing allergic inflammation in asthmatic patients.

Published: 06-11-2009
Last updated: 10-08-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Allergic conditions
Study type	Observational non invasive

Summary

ID

NL-OMON43781

Source
ToetsingOnline

Brief title
Breg cells reduce allergic inflammation.

Condition

- Allergic conditions
- Bronchial disorders (excl neoplasms)

Synonym
allergy, asthma

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Nederlands Astma Fonds

Intervention

Keyword: asthma, B cells, IL-10, immunotherapy

Outcome measures

Primary outcome

IL-10 producing B cells in PBMC

IL-4 producing T cells (Th2 cells) in reaction to relevant allergens

Secondary outcome

Total IgE and allergen-specific IgE, IgG1, IgG2a, IgG4, IgA in plasma and nose

washings.

Affinity of allergen-specific IgE molecules

TNFalpha and IL-10 in plasma and nose washings.

Molecular profiling of B cell populations with ATACseq

Study description

Background summary

In the last few decades, the incidence of childhood allergic asthma and rhinitis has strongly increased. A possible explanation is the decreased exposure to microbial molecules due to a decreased frequencies of childhood infections. The hypothesis is that some of these microbial substances are able to avoid immunity by active induction of tolerance. Simultaneously also tolerance is raised against bystanders antigens, such as allergens. New therapies could benefit from the use of microbial molecules to induce tolerance.

One example of a protective pathogen is the infection by parasitc worm infections, associated with reduced frequencies in allergy and asthma. Parasitic worms can suppress the immune system of the host for their own

survival. The hypothesis is that they not onlysuppress immune responses to their own antigens, but also to bystander antigens such as allergens. Knowlegde on how parasitic worm infections suppress the immune system can help to desing new therapies and drugs to prevent or suppress allergic asthma or rhinitis.

Recently, our laboratory has found evidence for a new regulatory cell for suppression of experimental allergic airway inflammation. These new findings point towards an emerging role for IL-10 producing B cells in protection against allergic asthma and rhinitis.

Study objective

Conditions that promote IL-10 producing B cells in humans are still ill defined. In this project our aim is to investigate the frequnecy of IL-10 producing B cells in healthy volunteers. Next, we aim to compare this to the frequency of IL-10 producing B cells in peripheral blood of allergic asthma or rhinitis patients before and at different time points after the start of immunotherapy, and at the same time investigate their inhibitory potential of allergen-specific immune responses. Finally, we aim to investigate whether worm-derived molecules are able to increase the frequency and activity of IL-10 producing B cells in peripheral blood cells from allergic asthma or rhinitis patients in vitro, with the ultimate goal to suppress asthmatic and/or allergic symptoms in vivo.

Study design

Healthy controls, allergic rhinitis and allergic asthma patients are cross-sectional compared. Subsequently, allergic asthma and rhinitis patients will be studied during a longitudinal follow-up at several time points after the start of immunotherapy.

Study burden and risks

Standardized lung function tests are applied worldwide for the examination of patients with asthma and are proven to be save. Nose washings are routinely taken, are save and non-invasive. Venous blood for the laboratory assessment will be collected by professionals.

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

General inclusion criteria:
- Written informed consent
- Male and female persons, aged >= 18 years and <= 55 years;Specific inclusion criteria:
Group 1 (allergic rhinitis):
- moderate/severe allergic rhinitis (ARIA guidelines)
- PC20 of histamine > 16 mg/ml
- specific IgE >= 0.7 kU/l for tree or grass pollen and/or house dust mite (HDM)
- positive skin prick test response (wheal > 5 mm) for tree or grass pollen and/or HDM
- total IgE >30 < 700 Iu/ml;Group 2 (allergic asthma):
- Clinical controlled asthma for at least 6 months according GINA guidelines, without severe exacerbations in the previous 6 months
- FEV1> 70% (short-acting β2-agonists if needed)
- History of episodic symptoms of wheezing, breathlessness, cough or chest tightness (>12 months)
- PC20 of histamine < 8 mg/ml
- a positive skin prick test response (wheal > 5 mm) for tree or grass pollen and/or HDM
- specific IgE >= 0.7 kU/l for tree or grass pollen and/or house dust mite (HDM)
- total IgE >30 < 700 IU/ml;Group 3(healthy control group):
- negative SPT

- PC20 of histamine > 16 mg/ml
- Specific IgE < 0.7 kU/l for tree or grass pollen and/or house dust mite (HDM)
- Total IgE <100 IU/ml

Exclusion criteria

age < 18 yrs
smoking
pregnancy
airway infection
Severe/ instable chronic asthma
Specific IgE >= 0.7 kU/l for animals to which the patients has daily contact with
Immunotherapy for the last 5 years
Anatomical abnormalities of the nose
Contraindications for immunotherapy according to international guidelines
anti-IgE treatment previously
systemic steroids or suffered exacerbations in the last year

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-10-2010
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	06-11-2009
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	31-01-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	17-04-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	28-04-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL28786.058.09