Blood collection to study and modulate dendritic cell-driven T cell responses

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Gain a better fundamental understanding of the functioning of the human immune system.Our research focuses on the mechanisms involved in 2 aspects: 1. The induction of Tregs (and inhibition of Th2 cell polarization) by exposing DCs to certain...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON54980

Source
ToetsingOnline

Brief title
Influencing DCs to control T cells / Ctrl-TbyDC

Condition

- Other condition
- Allergic conditions

Synonym
allergy, Autoimmunity

Health condition

met name gezonde vrijwilligers worden geincludeerd. Donoren met een allergie of auto-immuunziekte worden niet uitgesloten

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC, locatie AMC
Source(s) of monetary or material Support: Ministerie van OC&W,Citeq BV,DC4U,Dutch Arthritis Foundation; Health Holland,NanoPass Technologies Ltd.,Trajectum Pharma BV,U-Needle BV

Intervention

Keyword: Blood cells, Dendritic cells, Immunomodulation, T-lymphocytes

Outcome measures

Primary outcome

This is not directly applicable within our research. Important aspects that we

investigate in vitro are:

- T cell polarization towards Th1, Th2, Th17, and Treg phenotype.

- DC function/activation

- neutrophil function/activation

Secondary outcome

not applicable

Study description

Background summary

An effective and balanced immune system is crucial for sustaining and promoting health and longevity of people, and forms the basis for an effective fight against infectious diseases. Aberrant immune responses are a major health problem, as they cause chronic immune diseases. On the one hand, chronic immune diseases can be the result of too strong inflammatory reactions (allergies and autoimmune diseases such as arthritis and diabetes), but on the other hand the result of too weak immune responses (cancer and uncontrolled infections).

Adaptive immune responses induced during infections and chronic immune diseases are generally characterized by (over)activation of specific T helper cell subsets, mainly Th1 and Th17 cells for autoimmunity, and Th2 cells for

allergies. The undisputed paradigm is that the development of these antigen-specific effector T cells is directly controlled by dendritic cells (DCs).

DCs are the gatekeepers of the human body. These cells are located on border areas with the outside world, such as the skin, lungs and intestines, and are constantly searching for danger. When these cells come into contact with invading pathogens, they will initiate defensive reactions to eliminate the intruder as quickly as possible. This is done by activating antigen-specific adaptive immune responses that are characterized by the activation of T helper cells. Depending on the pathogen, the DC will direct a T cell towards a Th1, 2, or 17 phenotype.
However, endogenous molecules and some foreign substances (e.g. small particles of plants, pets or microorganisms floating in the air) are not dangerous. In that case, DCs should actually inhibit immune responses by not activating T cells, or by inducing so-called regulatory T cells (Tregs). These Tregs can then inhibit the activation of other T helper cells. The inhibition of immune reactions against these innocent substances is called tolerance.

Study objective

Gain a better fundamental understanding of the functioning of the human immune system.

Our research focuses on the mechanisms involved in 2 aspects:
1. The induction of Tregs (and inhibition of Th2 cell polarization) by exposing DCs to certain adjuvants, such as Vitamin D3.
2. The induction of Th17 cells that depends on an interaction between DCs and cells of the innate immune system, the neutrophils.

The ultimate goal of our research is to develop disease modulating therapies by directing DC-mediated immune responses. This is in contrast to many current therapies, which are aimed at combating symptoms but do not address the disease process. More fundamental knowledge of the underlying mechanisms involved in establishing effective, tailor-made immune responses against specific pathogens is essential for our research. In addition, we are developing strategies to safely and effectively target immune modulators and allergens/antigens towards DCs, with the aim of directing T cell responses in the body in the right direction to inhibit disease activity.

Study design

Blood will be taken from healthy volunteers weekly. This blood will be used to obtain the cells needed for our research: T cells, neutrophils, and monocytes. Monocytes will be cultured in the laboratory into differentiated towards DCs, which will then be used for our experiments.

These cells will be used in the lab to perform in vitro experiments. Depending on the planned experiments, the experiments will take between 1 day (e.g. neutrophil function study) up to a maximum of 3 weeks (study of DC-mediated T cell polarization towards different T cell phenotypes).

At the end of these experiments, all these cells are discarded. Cells that have been isolated from the blood, but cannot be used immediately in the experiments (often more cells can be isolated than we can immediately use) will be stored in liquid nitrogen. At a later stage, these cells can still be used.

Study burden and risks

Blood collection can sometimes cause mild pain or bruising. For each participation, blood is taken once or twice, in the latter case with an interval of 6 to 7 days. During each participation, we take a maximum of 100 mL of blood, which will not cause any problems for adults. For comparison: the blood bank takes 500 mL of blood at a time. In case of 2 blood samplings, we will not take more than 20 mL during the second collection.
We estimate the load and the risks to be very limited.

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

- age between 18 and 65 year

Exclusion criteria

- ongoing inflammation or infection at time of blood collection
- use of immunosuppressive or biological medication within the last 6 month prior to blood collection
- active malignancies
- subjects who are employees or students at our department

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2021
Enrollment:	150
Type:	Anticipated

Ethics review

Approved WMO Date:	09-07-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL73819.018.21