Deuterated water labelling of specialized T cell subsets

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Primary Objective:1. Turnover rate of antigen-specific cells (group I)2. Turnover rate of functional T-cell subsets (group II)Secondary Objective(s):• Determining absolute numbers of antigen (poliovirus, measles, Hepatitis A and Hepatitis B)...

Ethical review	Approved WMO
Status	Pending
Health condition type	Immune disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON56738

Source
ToetsingOnline

Brief title
DANCE

Condition

- Immune disorders NEC

Synonym
Healthy immune system, immunological memory

Research involving
Human

Sponsors and support

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

Intervention

Keyword: antigen specific T cell memory, heterogeneity, lifespan, T cell subsets

Outcome measures

Primary outcome

1. Turnover rate of antigen-specific cells (group I)

2. Turnover rate of functional T-cell subsets (group II)

Secondary outcome

Determining absolute numbers of antigen (polio, measles, HepA and HepB)

specific T cells during the study

Monitoring cytokine profile and IgG antibody levels in blood in response to the

vaccine

Study description

Background summary

Our immune system is invaluable. It not only gets rid of infectious pathogens and dysfunctional cells upon encounter but also provides (life)long protection via the formation of antigen experienced memory leukocytes. Vaccination and the more recent application of memory leukocytes in cancer treatment are exemplary for the potential of the function of these memory cells, but these application also show that the system performs differently in specific applications. Time for booster vaccination differs widely for different pathogens and efficacy of T cell therapy differs between tumor type. While general process of adaptive immunity are quite well defined, the presence and influence of heterogeneity in the system has become more apparent but is less defined. We will investigate how heterogeneity based on cell functionality and antigen interaction with T cells affects the dynamic characteristics of these subsets. Quantification of the lifespan, turnover and death rates of the different subtypes of memory cells is off essential fundamental value and might steer targeting specific subtypes for specific applications.
We plan to investigate memory subpopulation based on (1) antigen specificity, (2) antigen/ TCR affinity (CD5hi/lo), (3) antigen overstimulation (β-galactosidase+/-), and (4) absence of antigen stimulation, i.e. virtual memory

T cells.

The kinetics of the memory T cell population has been studied extensively. However in humans, the predicted lifespan of yellow fever specific memory T cells (485 days) showed disparity with that of total memory cells (150 days). This difference in the expected lifespan was suggested to be due to the fact that the memory T cell pool is composed of different specialized subpopulations that have different kinetics.

Thus, in this study we will examine if different cell functionalities of different T cell subsets correlate with different turnover rates.

Study objective

Primary Objective:
1. Turnover rate of antigen-specific cells (group I)
2. Turnover rate of functional T-cell subsets (group II)

Secondary Objective(s):
• Determining absolute numbers of antigen (poliovirus, measles, Hepatitis A and Hepatitis B) specific T cells during the study
• Monitoring cytokine profile and IgG antibody levels in blood in response to the vaccine

Study design

The study has a longitudinal character and involves invasive procedures, i.e. administration of the Hepatitis A and B vaccine **TWINRIX**, or polio vaccine **Boostrix-IPV**, or the measles vaccine **M-M-RVaxPro** as well as the temporary drinking of heavy water and the collection of multiple blood and urine-or-saliva samples. The above mentioned vaccines are childhood vaccines in the Netherlands except for TWINRIX which is given preventative to medical students and travelers. All used vaccines are regarded as safe and efficacious. Since not all analyzed cell subsets require a booster vaccination we divided the participants of the study in two groups. Study group II will not receive a booster vaccination and will have a lower study burden.

(I) Study group I will include participants who to take a booster vaccine of either TWINRIX-Adult, M-M-RVaxPro or Boostrix-IVP as well as to follow the drinking schedule and blood and urine-or-saliva donation.
(II) Study group II will include participants who will not take a booster and only follow the drinking schedule and blood and urine-or-saliva donation.

Both groups are required to drink deuterated water and will donate multiple blood and urine/saliva samples. Participants of study group I and II will be self-reported healthy participants without a history of immune altering disease

or treatment. Participants of study group I will have a history of either of the above mentioned vaccines.

Study burden and risks

Participants of group I of this study will get a booster dose of either Boostrix-IPV, M-M-RVaxPro or TWINRIX vaccine and will have to drink 35 ml of 100% enriched deuterated water 3 times a week for 5 days followed by a daily intake of 42 ml for a maximum of 9 weeks during the up-labelling phase. During the study (up and down-labelling) the participants donate urine/saliva once a week and blood (venipuncture) 2-6 times. Even though the physical burden and risks of this study are minimal, the personal burden is higher: participants will have to invest time and energy to visit the hospital, donate blood and urine/saliva, and drink heavy water at home. There are no direct benefits for the participants and the risks are minimal. Participants who participate in group II will not receive any vaccines but will drink heavy water and donate saliva/urine with the same schedule and donate blood maximum 8 times.

Contacts

Public
Universitair Medisch Centrum Utrecht

Lundlaan 6
Utrecht 3584 EA
NL
Scientific
Universitair Medisch Centrum Utrecht

Lundlaan 6
Utrecht 3584 EA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

For study group I
To be eligible for inclusion in study group I cohort of this study, a subject must meet all of the following criteria:
Participants
- Are healthy
- Have vaccination history with either TWINRIX, MMR or IPV and being seropositive for one of the vaccines.
- Are above the age of 18
- Are able to understand a written informed consent form
- Are able to follow the protocol of the study during the study period
- Willing to undergo pregnancy testing (3 tests) before and during the deuterated water consumption phase.

For study group II
To be eligible for inclusion in study group II cohort of this study, a subject must meet all of the following criteria:
Participants
-Are healthy
- Are between the age of 18-40 years
- Are able to understand a written informed consent form
- Are able to follow the protocol of the study during the study period
- Willing to undergo pregnancy testing (3 tests) before and during the deuterated water consumption phase.

Exclusion criteria

Pregnant, uncertain about pregnancy status, currently breastfeeding, chronic infection or autoimmune disease, immunocompromised, use of immunomodulatory drugs, use of immunosuppressant medications, self-reported anemia (group I).
For more detailed criteria see C1 Onderzoeksprotocol section 4.4.

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):	01-05-2024
Enrollment:	26
Type:	Anticipated

Ethics review

Approved WMO

Date:	02-05-2024
Application type:	First submission
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	NL83973.041.23