The effect of clonal hematopoiesis on trained immunity; an exploratory study

Published: 11-06-2020
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To investigate the interrelatedness between clonal hematopoiesis of indeterminate potential (CHIP) and trained immunity.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Observational invasive

Summary

ID

NL-OMON49356

Source
ToetsingOnline

Brief title
CHIP in TRIM

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
atherosclerisis, obesity

Research involving
Human

Sponsors and support

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

Intervention

Keyword: atherosclerosis, clonal hematopoiesis, obesity, trained immunity

Outcome measures

Primary outcome

60 ml of blood will be drawn by venepuncture to measure cytokine production

capacity and the susceptibility to develop trained immunity.

Secondary outcome

In addition, within the subjects with the driver mutations, single cell RNA

sequencing will be performed to explore the hypothesis that monocytes with a

mutation are more amenable to trained immunity.

Study description

Background summary

In the past years, two mechanisms of innate immune cell activation have been discovered that both contribute to the development of atherosclerotic cardiovascular disease: clonal hematopoiesis of indeterminate potential (CHIP) and trained immunity. CHIP describes the age related occurrence of somatic DNA mutations in myeloid progenitor cells which confer a survival benefit to the cell, resulting in circulating monocyte clones. These driver mutations most commonly occur in the epigenetic enzymes DNMT3A and TET2. Trained immunity described the phenomenon that monocytes can build a long-term proinflammatory phenotype after brief exposure to inflammatory stimuli. This is also mediated by epigenetic reprogramming.

Study objective

To investigate the interrelatedness between clonal hematopoiesis of indeterminate potential (CHIP) and trained immunity.

Study design

Exploratory observational single centre study

Study burden and risks

The subjects will have no benefit. Sixty mls of blood will be drawn which will

not have any adverse consequences for the participants.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- Participant of the 300OB study
- Mutation in TET2, DNMT3A, or no driver mutation
- Informed consent

Exclusion criteria

- Current use of immunomodulatory drugs.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-05-2021
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO

Date:	11-06-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL72552.091.20