2000HIV Trained Innate Immunity in HIV elite controllers

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Primary objective:Investigate if a trained immunity profile in innate immune cells might be a mechanism of HIV elite control.Secondary objectives:1. Determine the immune phenotypes that distinguishes family members of HIV elite controllers from...

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

Summary

ID

NL-OMON50913

Source
ToetsingOnline

Brief title
2000HIV-Trained

Condition

- Immune disorders NEC
- Viral infectious disorders

Synonym
HIV

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: ViiV Healthcare Inc.

Intervention

Keyword: Cytokines, Elite controllers, HIV, Immune system

Outcome measures

Primary outcome

Main study endpoints

1. Innate immune training indices:

o Direct cytokine responses to a range of stimuli

o Cytokine responses after 6-day training with Beta-glucan

Secondary outcome

Secundary study parameters:

1. Transcriptome signatures of innate immune training (including long

non-coding RNA patterns)

2. Epigenetic signatures of innate immune training

3. Differentially expressed genes on a transcriptomic level that are associated

with HIV elite controller phenotype or their family members.

4. Specific populations of circulating cells, identified by immune phenotyping,

that can differentiate between HIV elite controller phenotype and

ART-suppressed people with HIV, or their respective family members.

Study description

Background summary

It remains unknown how some individuals spontaneously control HIV in the absence of antiretroviral medication, called HIV *elite controllers* (ECs). Since the beginning, ECs have been absolutely crucial to our current understanding of HIV and they continue to be to this day. While numerous

research focused on the adaptive immune system, there is a vast amount of evidence prompting that the innate immune system is essential to HIV elite control.
Trained innate immunity can be expressed in terms of enhanced responsiveness of innate immune cells to a repeated trigger. This occurs through epigenetic remodeling after exposure to a certain stimulus such as beta-glucan, lipopolysaccharide (LPS) or the bacillus Calmette-Guérin (BCG) vaccine. This results in an altered expression and metabolism on a cellular level, resulting in greater resistance against subsequent infection.

Both the impact of trained immunity of HIV infections as vice versa, specifically the impact of HIV on trained immunity, are unknown. Our hypothesis is that ECs are natural hyperresponders to innate immune training triggers and that this results in the HIV elite control phenotype.

Study objective

Primary objective:
Investigate if a trained immunity profile in innate immune cells might be a mechanism of HIV elite control.

Secondary objectives:
1. Determine the immune phenotypes that distinguishes family members of HIV elite controllers from family members of people living with HIV who have never been controllers.
2. Determine whether HIV can induce a long-term functional and transcriptional program in innate immune cells similar to trained immunity.

Study design

Study design: cross-sectional case-control study.
For the primary objective, HIV elite controllers will be compared to ART-suppressed HIV patients that never have been elite controllers and first degree relatives of HIV elite controllers will be compared to first degree relatives of ART-suppressed HIV patients.
For the secondary objectives, first, a system biology approach will be used in the comparison above. To determine the role of HIV in trained innate immunity we will compare people with HIV (both controllers as non-controllers) to their respective family members.

Study burden and risks

Burden: a single venipuncture, a total amount of 100 mL blood will be collected. There are no risks other than a small chance of a local hematoma related to a single venous puncture. There will be no direct benefits for the

subjects enrolled in this study.

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

All participants/first degree relatives:
1. All participants must be *18 years of age.

HIV elite controllers:
1. Participation in 2000HIV study
2. Available first-degree relative
3. Meet criteria of elite controller (see protocol page 7 for elaborate definition)

ART-suppressed people with HIV:
1. On cART *6 months with an HIV-RNA load <200 copies/mL
2. Never applied to controller definition.
3. At least one documented HIV RNA load >100.000 copies/mL
4. No documentation of recent HIV acquisition combined with ART initiation in less than 6 months
5. Available first-degree relative

Exclusion criteria

All participants:
1. Active hepatitis B/C or signs of acute infections
2. Active or recent malignant condition (i.e. <12 months ago treated)
3. Active systemic auto-immune or auto-inflammatory conditions (such as rheumatoid arthritis, inflammatory bowel disease).
4. Use of immunosuppressive medication
5. Pregnant

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):	02-08-2021
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO Date:	09-06-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-08-2021
Application type:	Amendment
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
ClinicalTrials.gov	NCTnummervolgtnog
CCMO	NL76999.091.21