Host restriction factors that determine susceptibility for in vitro HIV-1 infection

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Ethical review	Approved WMO
Status	Pending
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON31377

Source
ToetsingOnline

Brief title
in vitro HIV-1 susceptibility

Condition

- Viral infectious disorders

Synonym
AIDS, HIV infection

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: LSBR (Landsteiner Stichting voor Bloedtransfusie Research)

Intervention

Keyword: HIV, host genetics, macrophages, SNP

Outcome measures

Primary outcome

The difference in genetic profile between various donors ("susceptible" group and "resistant" group). We expect to identify new host factors relevant to the clinical course and treatment of HIV infection.

Secondary outcome

Not applicable

Study description

Background summary

The natural course of HIV-1 infection is widely varialbe with extremes of disease progression within 2 years (rapid progressors) or continious asymptomatic infection for more than 15 years (long term non progressors). Moreover, certain people are relatively resistant to HIV-1 infection despite high levels of sexual risk behavior (high risk seronegatives). In vitro, the ability of HIV-1 to replicate on CD4+ T cells and macrophages also varies considerably from donor to donor. In the majority of cases, the underlying mechanism responsible for the variable outcome of exposure to HIV-1 is not known.

Study objective

The overall goal of our research is to identify host factors responsible for the variability in HIV-1 susceptibility. We hypothesize that host factors that either restrict or enable HIV-1 replication will be additional targets for therapeutic intervention. The host factors involved might directly mediate or interfere with HIV-1 replication or might influence activation levels and immune response to the infection. We will focus on the following research questions:

1. how much of the variation in in vitro HIV-1 susceptibility is explained by known host gene polymorphisms?

2. which novel candidate host genes are correlated with in vitro HIV-1 susceptibility patterns?
3. which host genes explain in vitro and in vivo HIV-1 susceptibility?

Study design

We will collect blood samples from 600 healthy donors. CD4+ T cells and macrophages will be isolated, cultured and subsequently infected with HIV-1. For each donor, susceptibility to HIV-1 will be scored based on virus production at day 14 after infection. Donors will be classified into groups of high and low susceptibility based on the number of virus strains that can replicate in their cells. Polymorphisms in host genes known to influence HIV-1 infection will be determined in the stored DNA samples (isolated from the same blood samples) for the top 100 ("susceptible" group) and bottom 100 ("resistant" group), using existing assays that have previously been used. Donors whose susceptibility pattern can be explained by their genotype for these known polymorphisms will be excluded from further analysis. To identify additional host cell factors that may explain the susceptibility patterns in the groups without known HIV-1 related polymorphisms, we will perform genome-wide Single Nucleotide Polymorphism (SNP) genotyping of the remaining individuals.

Study burden and risks

An additional ~14 ml of blood will be collected from each participant. Since the venapunction will be performed at the blood bank, where the donors will have to be for their regular blood donation, the burden to the participant will be limited, or almost negligible. No specific or additional venapunction will be required for our blood sample.

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

Signed informed consent
Age 18 years or older
Willingness to give a single donation of 14 ml of blood for DNA and white blood cells isolation and subsequent genetic analysis

Exclusion criteria

HIV infected

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending

Start date (anticipated):	15-05-2007
Enrollment:	600
Type:	Anticipated

Ethics review

Approved WMO 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	NL17585.018.07