HIV functional cure, what can be learned from HIV-2 infection?

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Primary Objective: Create a complete transcriptome of blood cells from dichotomous HIV-2 infection.Secondary Objective(s): Define host factors and pathways that are implicated in the pathogenesis of HIV infection. Determine of the mechanisms that...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Immunodeficiency syndromes
Study type	Observational invasive

Summary

ID

NL-OMON42172

Source
ToetsingOnline

Brief title
non progressive HIV infection

Condition

- Immunodeficiency syndromes
- Viral infectious disorders

Synonym
AIDS, latent infection

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Virgo;EU project

Intervention

Keyword: HIV-2, immune activation, transcriptome

Outcome measures

Primary outcome

Create a complete transcriptome of blood cells from dichotomous HIV-2

infection.

Secondary outcome

Define host factors and pathways that are implicated in the pathogenesis of HIV

infection.

Determine of the mechanisms that guide the dichotomous course of HIV-2

infection and find opportunities for intervention.

Study description

Background summary

HIV provokes a chronic infection that results in the degradation of the immune system resulting in AIDS, when not treated. In the case of HIV-1 infection this happens in approximately 99% van de patients. For HIV-2 infections the percentage of patients that develop AIDS is only 50%. The difference between progressive and non-progressive HIV-2 infection may be instructional in helping to understand the pathogenesis, also in relation to HIV-1 infection. This may help to identify correlates of protection and biomarkers that may be exploited for treatment and vaccine development.
In a recent review in HIV-1 and HIV-2 chronic infection have been compared (1). Clinical progression (once it happens) is remarkably similar in HIV-1 and HIV-2 infected patients. Innate immune responses comprise a role for NK cells in HIV-2 suppression in early asymptomatic infection, but not in progressive HIV-2 and HIV-1 infection (2). Specific immune responses against HIV-2 are more robust with an important role for polyfunctional Gag-specific CD4 T cell responses (3). More recently CD8 T cells have also been implicated in the control of HIV-2 infection (4). A clear difference between the virus is the presence of the vpx gene in HIV-2 but not HIV-1. Vpx renders myeloid cells permissive for HIV-2 infection via degradation of SAMHD1 (5). Paradoxally,

this, and the broader co-receptor usage of HIV-2 (see below), extend its tropism, but do not enhance its relative pathogenicity.
In HIV-1 infection chronic immune activation is thought to drive deterioration of the host defence (6), which may be the result of microbial translocation. In non-viremic HIV-2 infection immune activation is low, but increases in with higher pvl which correlates with increased LPS levels (7). Other explanation for reduced immune activation in HIV-2 infection have been sought in the action of Nef. Nef of lentiviruses infecting their natural host, downregulates CD3 and CD28, thereby preventing cell activation. In HIV-2 this property of Nef is conserved, but in HIV-1 downregulation has been lost (8).
A cohort of HIV-2 infected patients from Rotterdam has been followed for more than 20 years (9). Up to date more than ten patients have remained clinically well, with high stable CD4 counts and low or undetectable plasma viral load (pvl), without antiretroviral treatment (cART). Other HIV-2 infected patients had to start cART to prevent progression to AIDS. Thus this cohort provides a unique opportunity to compare progressive and non-progressive chronic HIV-2 infection.
Previous research from our lab has mainly focussed on the contribution of HIV-2 variants to differences in disease progression. Biological virus clones have been isolated from both groups (10,11) (METC 2000/221). These viruses have been characterized for replicative capacity (12), co-receptor usage (13,14), beta chemokine sensitivity (15), but these properties did not explain differences in clinical follow-up between these HIV-2 infected patients. Furthermore Nef-mediated down modulation of CD3 and CD28 correlated with high CD4 T cell counts in viremic infection, but did not explain why some patient had low or undetectable viremia (16). In addition we studied Vpx genes from our biological clones and found no clues for in role in the maintenance of non-progressive infection (17)

Study objective

Primary Objective:
Create a complete transcriptome of blood cells from dichotomous HIV-2 infection.

Secondary Objective(s):
Define host factors and pathways that are implicated in the pathogenesis of HIV infection.
Determine of the mechanisms that guide the dichotomous course of HIV-2 infection and find opportunities for intervention.

Study design

This is a research study that uses peripheral blood received through venipuncture from HIV-infected individuals. In vitro experiments are performed on RNA isolated peripheral blood cells. Chronically HIV-infected volunteers will be asked to donate blood either during their scheduled physician visit or

during a scheduled visit for the blood donation. Blood (3 ml) will be collected in a Tempus tube, containing a chaotropic agent for the instant lysis of all blood cells and proteins and the stabilization of DNA and RNA. After cryopreservation RNA will be isolated and hybridized to microarrays for transcriptome profiling. Transcriptome profiles from progressive and non-progressive HIV-2 infection will be compared and distinctive markers will be identified.

Study burden and risks

The only potential risk of participation in this study is the minor risk connected to blood donation through venipuncture. There are no direct benefits for participants in this in vitro research 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

HIV infection, latent or active or actively suppressed

Exclusion criteria

Non-compliance to hospital visits

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-03-2016
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	16-10-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL51994.078.15