



2011

# Polymorphism in HIV-1 dependency factor PDE8A affects gene expression and HIV-1 replication in primary macrophages

Thijs Booiman

*Academic Medical Center of the University of Amsterdam*

Sebastian Bol

*Academic Medical Center of the University of Amsterdam*

Evelien Bunnik

*Academic Medical Center of the University of Amsterdam*

*See next page for additional authors*

Follow this and additional works at: [http://scholarscompass.vcu.edu/obgyn\\_pubs](http://scholarscompass.vcu.edu/obgyn_pubs)

© 2011 Booiman et al; licensee BioMed Central Ltd. This is an open access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Downloaded from

[http://scholarscompass.vcu.edu/obgyn\\_pubs/9](http://scholarscompass.vcu.edu/obgyn_pubs/9)

This Article is brought to you for free and open access by the Dept. of Obstetrics and Gynecology at VCU Scholars Compass. It has been accepted for inclusion in Obstetrics and Gynecology Publications by an authorized administrator of VCU Scholars Compass. For more information, please contact [libcompass@vcu.edu](mailto:libcompass@vcu.edu).

---

**Authors**

Thijs Booiman, Sebastiaan Bol, Evelien Bunnik, Perry Moerland, Karel van Dort, Jerome Strauss, Margit Sieberer, Hanneke Schuitemaker, Neeltje Kootstra, and Angélique van't Wout



ORAL PRESENTATION

Open Access

# Polymorphism in HIV-1 dependency factor *PDE8A* affects gene expression and HIV-1 replication in primary macrophages

Thijs Booiman<sup>1\*</sup>, Sebastiaan Bol<sup>1</sup>, Evelien Bunnik<sup>1</sup>, Perry Moerland<sup>2</sup>, Karel van Dort<sup>1</sup>, Jerome Strauss<sup>3</sup>, Margit Síeberer<sup>1</sup>, Hanneke Schuitemaker<sup>1</sup>, Neeltje Kootstra<sup>1</sup>, Angélique van't Wout<sup>1</sup>

From *Frontiers of Retrovirology* 2011  
Amsterdam, The Netherlands. 3-5 October 2011

## Background

The limited size of the human immunodeficiency virus 1 (HIV-1) genome and the small number of proteins it encodes make the virus highly dependent on host proteins for its replication. Four genome-wide RNAi screens have recently identified a large number of HIV-1 dependency factors (HDFs), with the majority of these proteins never before associated with HIV-1 replication. Recently, we reported more than 3 log variation in the ability of HIV-1 to replicate in monocyte derived macrophages (MDM) derived from >400 healthy seronegative blood donors. In our present study we determined whether single nucleotide polymorphisms (SNPs) in the genes encoding the newly identified HDFs were associated with this variation in HIV-1 replication.

## Materials and methods

DNA from Caucasian donors whose MDM had low (n=96) or high (n=96) viral Gag p24 production, was used for genome-wide SNP genotyping. Linear regression assuming an additive model was used to test for association between the genotype of HDF SNPs and HIV-1 replication in MDM.

## Results

We found a significant association between the minor allele of SNP rs2304418 located in the phosphodiesterase 8a (*PDE8A*) gene and lower HIV-1 replication ( $p=2.4 \times 10^{-6}$ ), even after correction for multiple testing. This finding was independent of the *CCR5*  $\Delta 32$  genotype. The minor allele of SNP rs2304418 was also

significantly associated with lower *PDE8A* mRNA levels in MDM ( $p=8.3 \times 10^{-5}$ ) and *PDE8A* mRNA levels correlated with HIV-1 replication. Resequencing of the promoter and untranslated regions of the *PDE8A* mRNA did not reveal novel SNPs likely to be the causative variant.

## Conclusions

Our finding is in agreement with the reported finding that RNAi knock-down of *PDE8A* resulted in lower HIV-1 replication. *PDE8A* is highly expressed in macrophages and specifically catalyzes the hydrolysis of cAMP to AMP. We are currently investigating at which level of the virus life cycle *PDE8A* affects HIV-1 replication.

## Author details

<sup>1</sup>Department of Experimental Immunology, Academic Medical Center of the University of Amsterdam, Amsterdam, 1105AZ, The Netherlands.

<sup>2</sup>Department Bioinformatics, Academic Medical Center of the University of Amsterdam, Amsterdam, 1105AZ, The Netherlands. <sup>3</sup>Department of Obstetrics and Gynecology, Virginia Commonwealth University, School of Medicine, Richmond, VA, 23298, USA.

Published: 3 October 2011

doi:10.1186/1742-4690-8-S2-O37

**Cite this article as:** Booiman *et al.*: Polymorphism in HIV-1 dependency factor *PDE8A* affects gene expression and HIV-1 replication in primary macrophages. *Retrovirology* 2011 **8**(Suppl 2):O37.

<sup>1</sup>Department of Experimental Immunology, Academic Medical Center of the University of Amsterdam, Amsterdam, 1105AZ, The Netherlands  
Full list of author information is available at the end of the article