



HAL
open science

Epigenome-wide association study (EWAS) with HIV infection status

Abel Garnier, Kevin Hoang, George Nelson, Nicolas Vince, Pierre-Antoine Gourraud, Cheryl Winkler, Sophie Limou

► **To cite this version:**

Abel Garnier, Kevin Hoang, George Nelson, Nicolas Vince, Pierre-Antoine Gourraud, et al.. Epigenome-wide association study (EWAS) with HIV infection status. Labex IGO meeting 2018, Apr 2018, Nantes, France. inserm-02161806

HAL Id: inserm-02161806

<https://inserm.hal.science/inserm-02161806>

Submitted on 21 Jun 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Epigenome-wide association study (EWAS) with HIV infection status

Abel Garnier¹, Kevin Hoang¹, George Nelson², Nicolas Vince¹, Pierre-Antoine Gourraud¹, Cheryl Winkler², Sophie Limou^{1,2,3}

¹ ATIP-Avenir team, Centre de Recherche en Transplantation et Immunologie UMR 1064, INSERM, Université de Nantes, Nantes, France,

² Basic Research Laboratory, NIH/NCI, Frederick National Laboratory, Leidos Biomedical Research, Inc., Frederick MD, USA,

³ Ecole Centrale de Nantes, Nantes, France.



Background and subjects

Genetic and genomic studies have led to the discovery of host factors involved in HIV-1 control and disease development (*CCR5* and *HLA* loci).

However, those factors only account for ~20% of the observed phenotypic variance (McLaren *et al.*, 2015).

⇒ The goal of this study is to investigate the impact of HIV-1 infection on the host epigenome DNA methylation patterns.

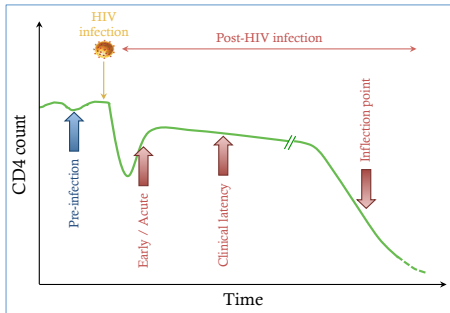


Figure 1: 80 PBMC samples from 19 untreated DC Gay individuals at pre-infection, early post-infection (<12 months), post-infection during clinical latency and post-infection at or near the infection point.

Quality control steps and Methods

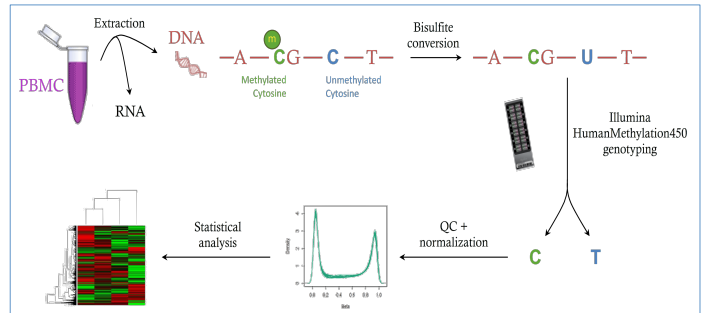


Figure 2: Experimental and analysis pipeline. Following DNA and RNA extraction, bisulfite-converted DNA was genotyped with the Illumina Infinium HumanMethylation450 arrays, covering over 485,000 methylation sites across the genome. After quality control (minfi R package) and normalization (lumi R package), we compared the DNA methylation profiles of pre-infection vs. post-infection samples in an adjusted regression model (limma, Combat R packages).

Results

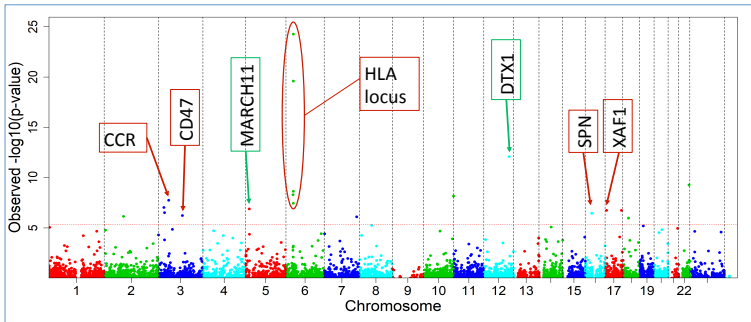


Figure 3: Manhattan plot of the differentially methylated regions (DMR) between before and after HIV infection. The red line corresponds to the Bonferroni significance threshold.

- 19 significant DMRs found
⇒ **powerful strategy** to reveal new factors associated with HIV
- *HLA* and *CCR* loci are confirmed to impact HIV replication control
- 12/18 significant DMRs (67%) are located in genes **directly interacting with HIV proteins**
- 14/18 significant DMRs (78%) are located in genes **playing a role in the immune system**

Conclusions and perspectives

- First EWAS in a **unique cohort** with repeated samples within each individual (limit the inter-individual variability).
- 1 DMP and 19 DMRs significantly associated with HIV infection with an enrichment for biologically relevant genes.
- EWAS is a **promising strategy** to discover new host factors linked with HIV-1 infection.
- The next steps are to confirm our results in an independent cohort and to further explore DNA methylation differences according to AIDS progression profiles (fast, slow and medium).

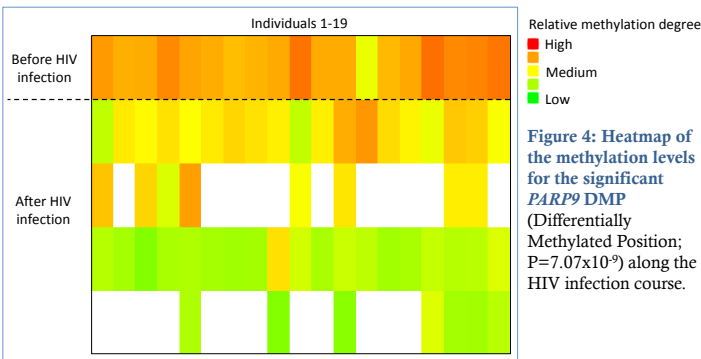


Figure 4: Heatmap of the methylation levels for the significant *PARP9* DMP (Differentially Methylated Position; $P=7.07 \times 10^{-9}$) along the HIV infection course.

PARP9 is a polymerase previously associated with the early HIV-1 replication stages (König *et al.* 2008). Here, we show a decrease of *PARP9* DNA methylation after the HIV infection, indicating a possible **progressive gene expression activation**.