

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

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## ► 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

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

**Results** 

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### Quality control steps and Methods

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- •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 postinfection at or near the inflection point.



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).



Background and subjects

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.



*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**.

#### • 19 significant DMRs found

- $\Rightarrow$  **powerful strategy** to reveal new factors associated with HIV
- $\bullet$  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).