HPV Differently Hijacks Anal Interferon Response in HIV+ and HIV- MSM

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BACKGROUND

- HIV+ MSM show higher rate of HPV persistence, HPV-related anal dysplasia (squamous intraepithelial lesion, SIL) and anal cancer in respect to HIV- MSM.
- Local interferon (IFN) response represents the first line of defense against HPV at the mucosal site.
- HPV has evolved multiple strategies to evade local IFN response, allowing for chronic infection, onset of anal SIL and, ultimately, anal cancer.
- Reduced expression of IFN inducible genes have been described in HPV infected keratinocytes.

METHODS

- 70 HIV+ MSM and 30 HIV- MSM were enrolled.
- Individuals with detectable HIV RNA in plasma, diagnosis of anal cancer or Inflammatory Bowel Disease were excluded.
- Participants underwent anal HPV DNA test, anal cytology and High Resolution Anoscopy.
- An additional anal swab was collected to evaluate the expression of a wide array of IFN inducible genes (IFNAR1, IFNAR2, IFN**β**, MxA, ISG15, ISG56, IRF1, IRF7, TLR3, TLR4, TLR8, TLR9, IFN**λ**1-3)

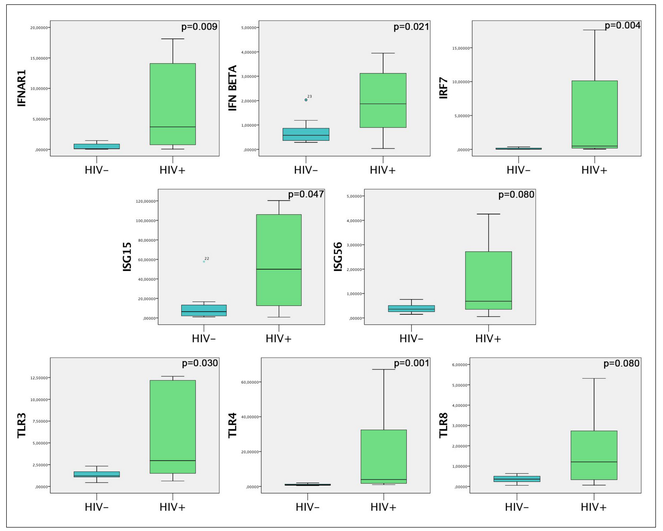
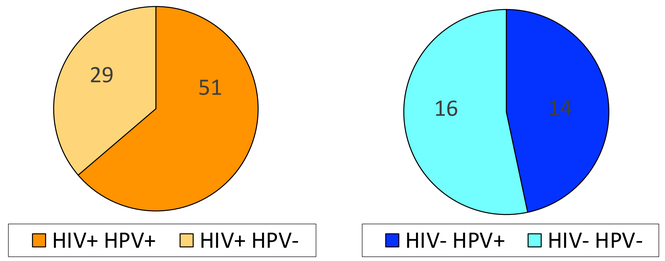


Figure 1.

RESULTS

- HIV+ and HIV- participants showed similar age (49.2 ± 5 and 48 ± 7; p=0.724).
- Anal HPV DNA tested positive in 72.8% of HIV+ and 46.6% of HIV- participants (p=0.008).



- Comparison of local IFN response between HIV+/HPV- and HIV-/HPV- participants showed higher expression of IFNAR1 (p=0.009), IFNβ (p=0.021), ISG15 (p=0.047), ISG56 (p=0.08), IRF7 (p=0.004), TLR3 (p=0.03), TLR4 (p=0.001) and TLR8 (p=0.08) in HIV+/HPV- subjects **(Figure 1)**
- Among HIV+ participants, HPV+ individuals showed a reduced expression of IFNAR1 (p=0.07), IFNβ (p=0.019), ISG15 (p=0.036), ISG56 (p=0.039), TLR3 (p=0.011), TLR4 (p=0.002), TLR8 (p=0.006), TLR9 (p=0.012), IFLλ2 (p=0.009) and IFNλ3 (p=0.038) in respect to HPV- subjects. **(Figure2)**
- Among HIV- participants, expression of IFN related genes was similar between HPV+ and HPV- individuals, with the only exception of IFNβ (p=0.053).
- The presence of a high-risk genotype or low-risk HPV genotype did not show influence on the expression of IFN inducible genes in HIV+ MSM nor in HIV- MSM.
- In both groups, HIV+/HPV+ and HIV-/HPV+, expression of IFN related genes was similar in the presence or absence of SIL.

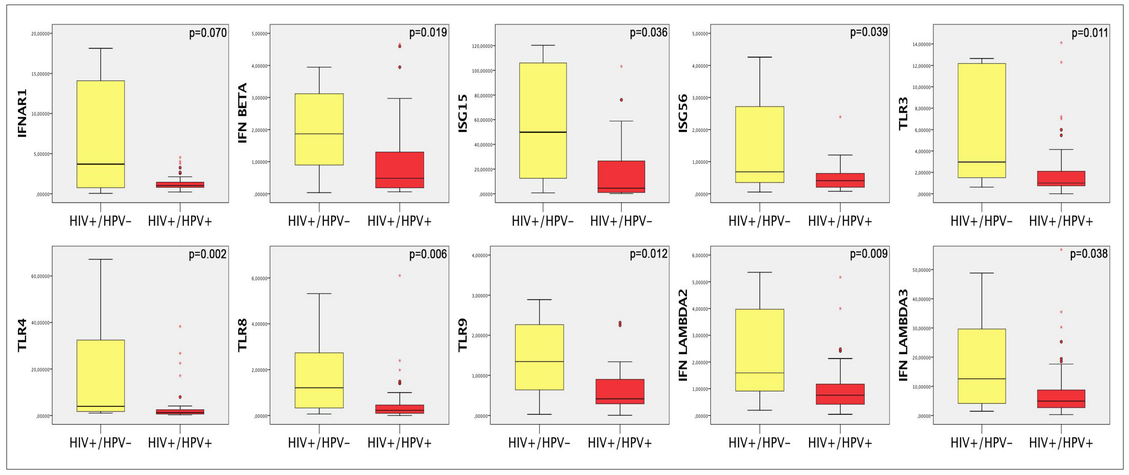


Figure 2.

Anal expression of **IFN** inducible genes is **reduced in HIV+ MSM** with **anal HPV** infection

CONCLUSIONS

- In the absence of HPV infection, HIV+ MSM show higher anal IFN related genes expression in respect to HIV- MSM.
- HPV effectively hijacks anal IFN antiviral response in HIV+ MSM but not in HIV- MSM.
- Anal expression of IFN inducible genes is not influenced by the presence of high-risk HPV or anal SIL.
- HPV hijacking of anal IFN response might play a role in favoring HPV persistence and therefore the subsequent onset of HPV associated clinical manifestations.

ADDITIONAL INFORMATION

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