HPV-mediated cytological abnormalities and high-risk HPV genotypes associate with altered gut microbiota composition and function in cART-treated HIV+ males

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Background
HIV infected individuals feature higher incidence of HPV persistence at both vaginal and anal level. Recently, the gut microbiota has been demonstrated to predict precancerous anal lesions, suggesting that some taxa featuring HIV-associated dysbiosis might fuel HPV persistence and pathogenesis.

Aim
To explore whether the presence of HPV-related cytological abnormalities might be associated with bacterial functional modifications and with HIV-mediated gut mucosal dysfunction (i.e. increased gut permeability, microbial translocation MT and consequent immune activation IA) within the anal district of cART-treated HIV+ males.

Methods

Patients
✓ HIV+ males on suppressive cART (HIV-RNA<40cp/ml) and asymptomatic for STD were enrolled at the Clinic of Infectious Diseases, Dept of Health Sciences, ASST Santi Paolo e Carlo, University of Milan.

Specimen collection
✓ Anal swab, blood, stool

Lab analyses
✓ Anal HPV genotyping by qPCR and sequencing analysis
✓ Plasma microbial translocation (MT) markers: sCD14 (ELISA), LPS (LAL), 16S rDNA (qPCR)
✓ Intestinal permeability (calprotectin, I-FABP)
✓ Fecal microbiota composition: relative abundance, α- and β-diversity (MiSeq Illumina®)
✓ Predicted metabolic function (PICRUSt)
✓ T-cell activation: CD38+CD8+ and CD45R0+CD38+CD8+

Statistical analyses
✓ Mann-Whitney, Kruskall-Wallis. Chi-squared tests

Results III:

a. aHPV patients showed a marked dysbiosis, with higher proportion of Prevotellaceae and lower Leuconostocaceae

b. the presence of high-risk HPV genotypes, irrespective of cytological abnormalities, seemed to have a greater impact on gut dysbiosis, with hrHPV displaying higher proportion of Prevotellaceae and Veillonellaceae, but lower Bacteroidaceae, Lachnospiraceae and Rikenellaceae as compared to lrHPV

Results IV: predicted metabolic function
HIV+ patients with HPV-mediated cytological abnormalities and/or high-risk HPV genotypes showed increased abundance of genes related to immune system activation and to metabolic syndrome

Discussion
• The presence of HPV-related cytological abnormalities within the anal district is characterized by unique bacteria composition and functional metagenomic capacity, supporting a pathogenic link between gut microbiota and HPV.
• From a clinical standpoint, the observations of a Prevotellaceae-rich/Bacteroidaceae-poor profile, coupled with changes in metabolites involved in sustaining immune activation and co-morbidities seem to support the establishment of a pro-inflammatory environment that favors high-risk HPV genotype persistence and HPV-mediated cytological abnormalities.