



Metabolic fingerprints of different clinical conditions affecting female genital tract

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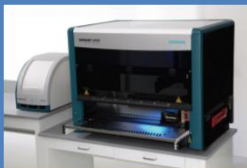
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INTRODUCTION AND PURPOSE

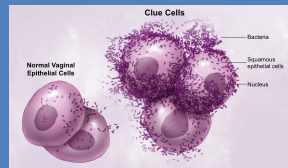
The vaginal microbiota of reproductive age women is often dominated by different species of *Lactobacillus*. They play a crucial role in maintaining the health and functioning of the female genital tract, preventing the overgrowth of endogenous pathogens and impeding the colonization of exogenous microorganisms. The depletion of lactic acid-producing lactobacilli, together with the increase of different species of facultative or strictly anaerobes, can result in the switch from a normal vaginal microbiota to a clinical condition known as bacterial vaginosis (BV). The vaginal environment of healthy and BV-positive women have been extensively studied, as well as the composition of vaginal metabolites produced by microbes and host cells. Besides that, less is known about the vaginal microbiome in case of STIs, as *Chlamydia trachomatis* (CT) infections. The aim of this study was to analyze the metabolic signatures of the vaginal niche in 3 different conditions: healthy, BV and CT infections.

METHODS

Since July 2016, all the pre-menopausal women attending the STI Outpatients Clinic of Sant'Orsola-Malpighi Hospital in Bologna (Italy) and meeting one of the following criteria were enrolled: presence of vulvo-vaginal symptoms or presence of risk factors for CT infection. Patients with vulvo-vaginal candidiasis were excluded from this study. For all the patients, after a clinical visit, a vaginal swab was collected for molecular CT detection (Versant CT/GC DNA 1.0 Assay; Siemens), whereas Amsel criteria were used for BV assessment. Moreover, for each woman, an additional vaginal swab stored in saline was collected for metabolomic analysis: after centrifugation, 1 ml of cells-free supernatant was added to 160 µL of a D₂O solution of 3-(trimethylsilyl)-propionic-2,2,3,3-d₄ acid sodium salt 6.25 mM. ¹H-NMR spectra were recorded with an AVANCE spectrometer (Bruker). Similarities among the metabolic profiles of samples were investigated by means of a principal component analysis (PCA). Differences in metabolites concentrations were analysed using ANOVA test based on Tukey contrast. The study was approved by the Hospital Ethical Committee.



Versant system for CT diagnosis



Clue cells



¹H-NMR analysis of metabolic profiles

RESULTS

Among all the women enrolled, 25 were considered healthy, 18 received a diagnosis of BV and 22 were positive for CT. Comparing the profile of metabolites characterizing the three groups, the striking peculiarities of women with BV, flattened down any difference between healthy women and women harboring *Chlamydia* (Fig NMR1). Indeed, the concentration of 45 over the 67 molecules quantified were statistically different between women harboring BV and healthy women. In the second scoreplot (Fig NMR2), asymptomatic (AC) and symptomatic (SC) women harboring *Chlamydia* are also represented. In the loadingplots, the molecules mostly responsible for the grouping of samples are depicted, according to sparsity principle.

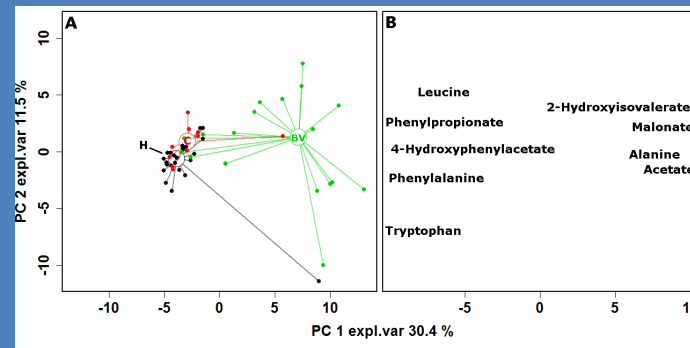


Fig NMR1: Scoreplot (A) and loadingplot (B) of a PCA calculated on the concentration of the molecules showing a statistical difference between women with BV (BV) and healthy women (H). In the loadingplot, the molecules mostly responsible for the grouping of samples are depicted, according to sparsity principle.

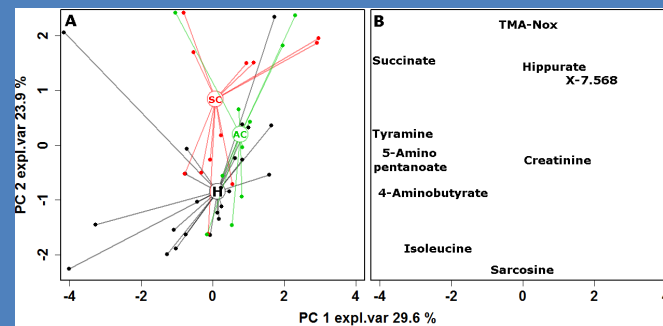


Fig NMR2: Scoreplot (A) and loadingplot (B) of a PCA calculated on the concentration of the molecules showing a statistical difference between healthy women (H) and women with *Chlamydia* in its asymptomatic (AC) and symptomatic (SC) forms.

CONCLUSIONS

Specific metabolic signatures characterize different clinical conditions of the vaginal tract. At a metabolic level, CT-positive women are more similar to healthy than BV-subjects.