

# Endometriosis and the human microbiome

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## Introduction:

The pathogenesis of endometriosis remains uncertain. However, there is evidence that genetic, immune, and environmental factors contribute to the development of the disease. Several studies have shown a relationship between endometriosis and autoimmune diseases. There is also mounting evidence that human associated microbiota, specially the gut microbiota, influence the pathogenesis of some autoimmune diseases. In this study we sought to evaluate the vaginal and intestinal microbiomes in women with and without endometriosis. As far as we know, we are the first to assess the role of human microbiota in endometriosis.

## Patients and Methods:

Rectal and vaginal samples were collected during the menses and follicular phases of the menstrual cycle from 40 endometriosis and 24 control patients. All samples were collected using Sterile Catch-All sample collection swabs and extracted using the MoBio Powersoil extraction kit. 16S rRNA gene amplicon libraries were prepared from the extracted samples (Preheim et. al., 2013) and were sequenced using the Illumina MiSeq platform.

Correlations of 16S rRNA data with clinical metadata (disease state, disease severity, self reported pain) were conducted using a random forest based machine-learning approach (Papa et al, 2012). Community state types of the vaginal samples were assigned using the MCclassifier tool.

## Results:

Of the samples that we collected, the vaginal samples were the most informative. The distribution of vaginal community state types (CSTs) observed in endometriosis and control subjects in this study reflects the distributions observed previously in women of European descent. In the menses time point we observe a loss of two Lactobacillus dominated CSTs, CST II and V, compared to follicular phase. We also observe a larger amount of flux into CST IV-A during menses in endometriosis patients than in control patients. CST IV-A consists of a heterogeneous mix of anaerobic bacteria that is not dominated by Lactobacillus species. Within the vaginal menses samples, we built a classification model capable of predicting the stage of disease (early verses late) with accuracy and precision. No significant differences were observed between the rectal samples of endometriosis and control patients.

## Conclusions:

Although no significant statistically differences were found between women with and without endometriosis, here we describe the human microbiome and the distribution of vaginal CSTs observed in women with endometriosis for the first time. Furthermore, we built a machine-learning model capable of predicting the stage of disease from vaginal samples during menses. In the future, larger studies should consider evaluating the human microbiome, specifically during the menses stage of the menstrual cycle, and its role in the pathogenesis of endometriosis.

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Keywords : endometriosis; pathogenesis; human microbiome

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