

Common Pathogen Found in Fallopian Tube

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ABOUT THE STUDY

Several sexually transmitted microorganisms, including *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Mycoplasma* species have been shown to cause anatomical damage to the human fallopian tube mucosa. Microbiological analyses of upper genital tract infections using cultivation have largely focused on these sexually transmitted pathogens, or on organisms known to be associated with bacterial vaginosis. Microbial communities in healthy human fallopian tubes have yet to be well described, as in the absence of disease, they are considered to be sterile. We hypothesized that the healthy fallopian tube harbours a diverse resident microbiota at all stages of the reproductive cycle, even in the absence of infection or inflammation. Here, we use culture-independent microbial community profiling in conjunction with cultivation to characterize this healthy fallopian tube microbiota, explore community-level shifts in microbiota related to hormonal changes and anatomical differences, and determine the pathogenic potential of resident microbial populations. We report striking differences in the microbial diversity of the fallopian tube identified only by the cultivation-independent technique.

Microbial community composition differed significantly between pre-menopausal and post-menopausal women, as well as those receiving exogenous progesterone treatments. Community composition was compared pairwise between cohorts using Metastats (see Methods) to identify significant differences and the specific taxa driving those differences. Comparative rarefaction analysis was used to explore differences in overall community diversity between pairs of cohorts. *Staphylococcus* sp. was the most abundant bacterial genus recovered from the fallopian tubes throughout all stages of reproductive life in the absence of exogenous hormone treatment. The administration of exogenous progesterone treatment via the use of Mirena intra-uterine devices during the proliferative and secretory phases of the cycle resulted in an increase of staphylococcal dominance.

Mirena intra-uterine devices also resulted in a significant overabundance of *Pseudomonas* sp., *Brevundimonas* sp. and *Atopobium vaginae* as compared to normal cycling women not exposed to an exogenous hormone supplementation during the

secretory phase of the menstrual cycle. These women demonstrated an overabundance of *Lactobacillus* sp. and *Enterococcus faecalis*. Significant differences in microbial community composition and diversity were also found between pre-menopausal and post-menopausal women. Fallopian tubes from post-menopausal women demonstrated lower taxonomic richness than those collected from pre-menopausal women. In contrast to pre-menopause, in post-menopause there was an absence of lactobacilli and an over-abundance of *Staphylococcus* sp., *Prevotella* sp. and *Propionibacterium* sp.

Biogeography of microbial communities

Microbial communities were compared between the left and right fallopian tubes as well as the ampulla and isthmus to determine if bacterial populations demonstrated site-specific differences. The microbial community within the ampulla demonstrated a significantly greater abundance of *Enterococcus* sp. Community profiles also differed significantly between the left and the right fallopian tubes. *Lactobacillus* sp., *Enterococcus* sp. and *Prevotella* sp. and were more abundant within the left tube versus the right tube, whilst *Staphylococcus* sp. were more abundant in fallopian tubes collected from the right side.

Antibiotics and the fallopian tube microbiota

Antibiotic treatment had a significant effect on microbial diversity and community composition. The antibiotic treated cohort demonstrated lower overall taxonomic richness than the non-treated group. Antibiotic-treatment was associated with the absence of key targeted anaerobes including *Atopobium* sp., *Porphyromonas* sp., *Prevotella* sp. and *Clostridium* sp., which were identified in the corresponding non-treated group. *Staphylococci* were present in both groups, but were less abundant in the antibiotic-treated group, despite not being a target of the antimicrobial prophylaxis.

Due to the use of pooled samples to form cohorts, we examined potential confounding factors which might lead to observed differences between the antibiotic-treated and untreated groups. For example, the pre-menopause group was over-represented in the antibiotic treatment group and the post-menopause group was over-represented in the non-treatment group; however, some

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key distinguishing community members were not detected in the pre-menopausal and post-menopausal cohorts (*Serratia* sp., members of the genera *Flavobacterium*, *Paenibacillus* and *Paucibacter*

and the Comomonadaceae family). It should be noted that these species may be present in the community in quantities below the detection level.