

Role of the reproductive tract microbiota in fertility

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The human reproductive tract microbiota is unique: no other species has a commensal Lactobacillus- dominant microbiota. Microbes in the vagina, cervix and uterus are associated with pregnancy and fertility outcomes, but the exact mechanism and optimal composition are not well described. We hypothesize that a particular Lactobacillus species, *L. crispatus*, is associated with optimal reproductive outcomes, compared to the other most common Lactobacillus species (*L. iners*) or non-Lactobacillus microbes. We propose a pilot study of 60 women presenting for in vitro fertilization treatment: 30 with male factor infertility (normal uterus, tubes and ovarian function) and 30 with idiopathic infertility (normal evaluation of uterus and tubes, normal ovarian function but no conception after 1 year of trying). We will collect vaginal swabs, the embryo transfer catheter (to sample intrauterine microbiota influencing pregnancy implantation) and a stool sample. We will perform 16S rRNA sequencing of the microbial community in each sample, and will measure pro-inflammatory cytokines in the vaginal swab eluate. We will compare the microbial community between 1) women with idiopathic infertility vs. male factor controls and 2) women who achieve pregnancy and those who do not. We will compare vaginal markers of inflammation between women who do and do not achieve pregnancy, and will assess whether the impact of the reproductive tract microbiota is dependent on the host mucosal immune response. Finally, the gut microbiota will be compared between women with idiopathic vs. male factor infertility to identify broader differences in microbial colonization outside the reproductive tract.