MON-204: Gut Bacterial Composition Correlates with an Improved PCOS Phenotype after Co-Housing

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Approximately 10% of reproductive-aged women worldwide are affected by polycystic ovary syndrome (PCOS). In addition to infertility, many women with PCOS have an increased risk of developing type 2 diabetes, cardiovascular disease, and non-alcoholic fatty liver disease. Studies have shown that the human gut microbiome is altered in humans with metabolic disorders such as obesity and type 2 diabetes and these changes may contribute to metabolic dysfunction. Additionally, studies have reported that changes in the gut microbiome are associated with PCOS in women and in rodent models. These changes include lower alpha diversity (species richness) and changes in specific Bacteroidetes and Firmicutes many of which are also altered in other metabolic diseases. In previous work, we investigated whether the gut microbiome was altered in a PCOS mouse model using letrozole, a nonsteroidal aromatase inhibitor, to increase endogenous testosterone levels and decrease estrogen levels. Letrozole treatment of pubertal female mice results in hallmarks of PCOS including elevated testosterone and LH, acyclicity, polycystic ovaries, and a metabolic phenotype. In the current study, we tested whether manipulation of the gut microbiome in the PCOS mouse model via co-housing improved reproductive and metabolic phenotypes and whether these changes correlated with gut microbial composition. Pubertal female mice were implanted with a placebo or letrozole pellet and divided into 3 groups with two mice per cage: co-housed placebo mice, letrozole mice or placebo and letrozole mice. Our results demonstrated that co-housing letrozole-treated mice with placebo mice resulted in substantial improvement of PCOS reproductive and metabolic phenotypes. Testosterone and LH levels, estrous cycling and ovulation were normalized in letrozole-treated mice co-housed with placebo mice compared to letrozole-treated mice housed together. In addition, weight, fasting blood glucose and insulin levels, and insulin resistance were decreased in letrozole-treated mice co-housed with placebo mice compared to letrozole-treated mice housed together. Using 16S rRNA sequencing, we observed that co-housing letrozole-treated mice with placebo mice did not result in substantial changes in alpha diversity but were associated with changes in specific bacterial genera that may be candidates for pre- or probiotic therapies. Our results suggest that manipulation of the gut microbiome may be a potential treatment option for PCOS.

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