The Gut Microbiome and its Influence on Hormones and Fertility

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Development of Question

- A woman's fertility is majorly affected by her level of the hormone estrogen (Goldstein et al. 1982)
- The main cause of infertility in women is a hormonal imbalance (Unuane et. al 2011).
- Estrogen levels are affected by body mass index, thyroid function, and genetics
- Bacteria in the digestive tract may also affect a woman's estrogen levels (Adlercruetz et. al 1976)
- Gut microbiome- a mini ecosystem of fungi, viruses, and bacteria inside a person that regulate host health (Shreiner et. al 2015)
- Intestinal bacteria thought to regulate estrogen levels are referred to as the "estrobolome."
- Dysregulation of the estrobolome is associated with disorders such as polycystic ovary syndrome or endometriosis (Baker et. al 2017)

Figure 1: Zebrafish *(Danio rerio)* are suitable model organisms for human reproduction and fertility (Hoo et. al 2016) due to presence of Kisspeptin, a hormone utilized in beginning of the signaling cascade, and extremely similar structures of signaling pathways in sex hormone production.

Research Question

If populations of intestinal bacteria are modulated, will levels of circulating sex hormones change and affect fertility?

Significance of Question

1 in 8 couples of reproductive age will experience difficulties conceiving and having children (CDC 2019). Today, more than 60% of married couples with children have two parents in the workforce (Bureau of Labor Statistics 2017). Additionally, society continues to promote advancement of career before children. However, our biological clocks have not changed. As a result, couples are being forced to consider their reproductive health as part of family planning.

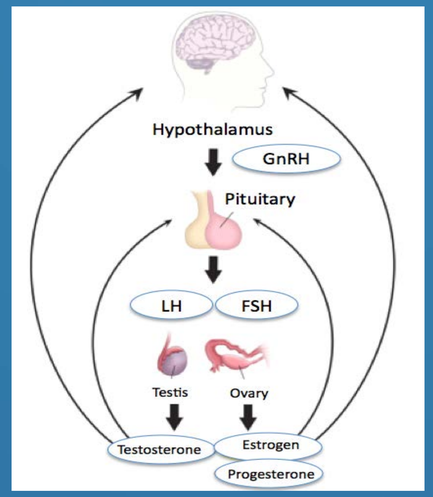

Figure 2: A generalized example of structure of the signaling cascade taking place during sex hormone production. The hypothalamus, anterior pituitary gland, and gonads work in tandem to regulate the reproductive system. Therefore, the system is referred to as the HPG axis.

Aims and Hypotheses of the Study

- Use a broad-spectrum antibiotic to decrease overall diversity of the gut microbiome
- Examine effects of treatment by mating behavior, number of fertilized eggs, and hormone production
- Hypothesis: a decrease in bacterial diversity will decrease the overall fertility

- Target specific phyla known for affecting the production of estrogen, such as *Bacteroides* using appropriate antibiotics
- Conversely, I can increase the population by targeting other phyla, allowing *Bacteroides* to flourish
- Hypothesis: This treatment directly impacts signal pathways in the hypothalamus and pituitary gland necessary to the process of egg maturation

- Males and females have similar signaling pathways to produce testosterone and estrogen (Silverthorn 2016)
- Examine the impact the microbiome has on the reproductive physiology of females versus males
- However, a specific phylum of bacteria has not been identified as affecting the production of testosterone

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