**Polycystic ovary syndrome (PCOS)** is a disorder caused by a defect of the ovarian cells. This defect results in synthesis of excess androgen and related clinical and biochemical symptoms such as infertility, obesity, and hirsutism.1 The Steroidogenic acute regulatory protein (StAR) has been implicated as a cause of PCOS because it is necessary for cellular synthesis of steroids.2,3 StAR initiates the steroidogenesis process by transporting cholesterol - the precursor for steroids - within the mitochondrial membrane of cells.2 Studies have shown that StAR is overexpressed in the ovarian cells of women with PCOS and rodent models of PCOS3,4, yet *what specific factors regulate this expression are still unknown.*

The **objective** of this study is to determine how other factors regulate StAR and proper androgen levels. Rats will be used for this study because several previous prenatally androgenized models have displayed phenotypes very similar to humans while remaining relatively inexpensive.5,6 I **hypothesize** that GATA-4 will directly interact with transcription factors for StAR resulting in activation of the gene. This hypothesis is based on research that suggested that overexpression of GATA-4 can regulate the StAR gene in ovarian cells.5 The **long-term goal** of this research is to determine how GATA-4 interaction regulates StAR expression.

Aim 1: **Determine the effect of nonsynonymous variation at the GATA sequence within the StAR promoter on rat androgen levels and StAR expression within ovarian cells**

**Approach**: Next-generation sequencing of rat lines will be performed to find StAR promoter sequence variants that affect the GATA sequence. The androgen levels of rats with variant sequences will be evaluated, then CRISPR/Cas9 will be used to introduce sequence variants into rat ovarian cell lines to observe effects of sequence variants on StAR expression.

**Hypothesis**: I hypothesize that the sequence variants of the StAR promoter that change the GATA sequence will result in decreased StAR expression within the rat ovarian cells and decreased androgen levels within the rats.

**Rationale**: Evaluating phenotypes associated with variation at the GATA sequence within the StAR promoter allows for the confirmation of the role of GATA-4 in regulating androgen levels and StAR expression.

Works Cited

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