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Title

The Role of Gut Microbial Bile Acid Deconjugation on PCOS

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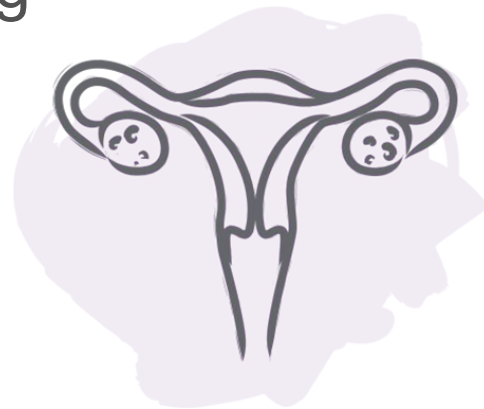
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The Role of Gut Microbial Bile Acid Deconjugation on PCOS

Shiantel Chiang
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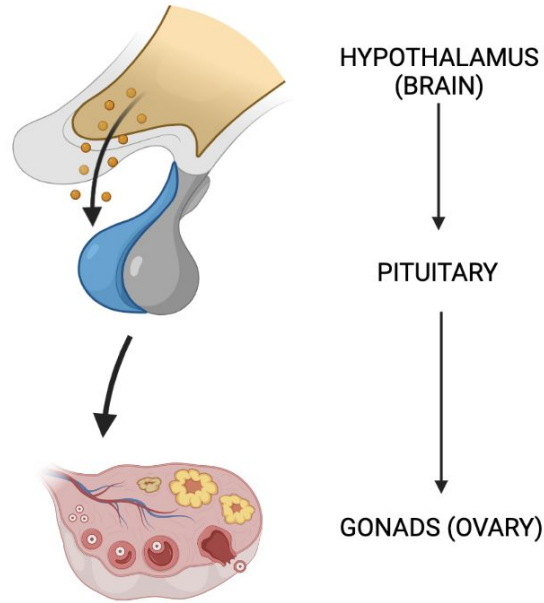


Polycystic ovary syndrome is the leading cause of infertility.

- Women with PCOS who do get pregnant have higher risk of complications

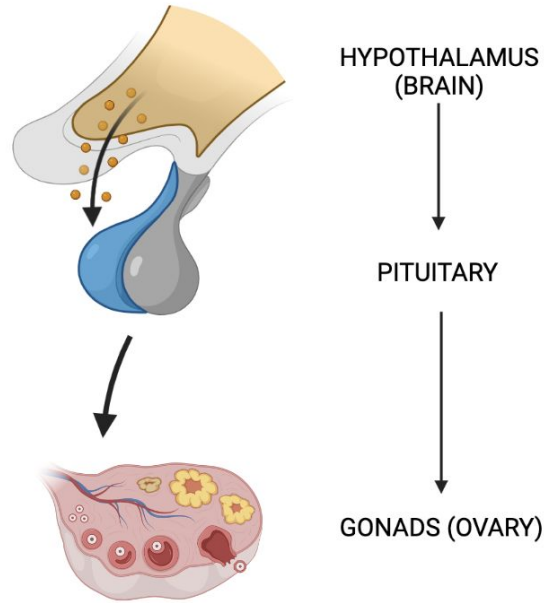
Polycystic ovary syndrome is the leading cause of infertility.

Reproductive Symptoms (HPG axis)



Polycystic ovary syndrome is often ineffectively treated.

Reproductive Symptoms (HPG axis)



Metabolic Symptoms

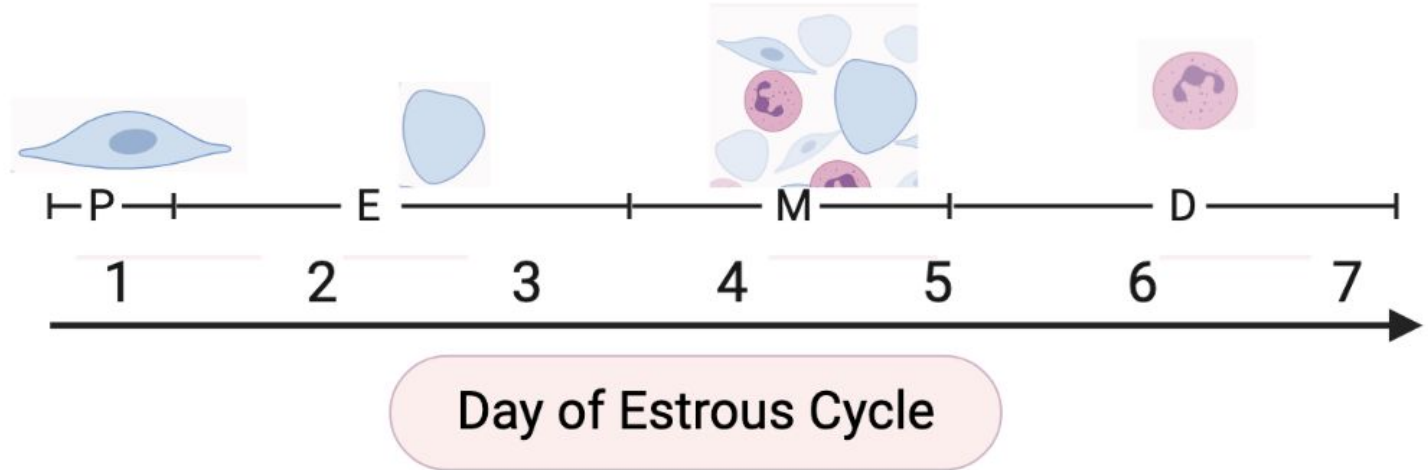


Weight loss often ineffective

The LET mouse model replicates PCOS phenotype.



LET model (PCOS)

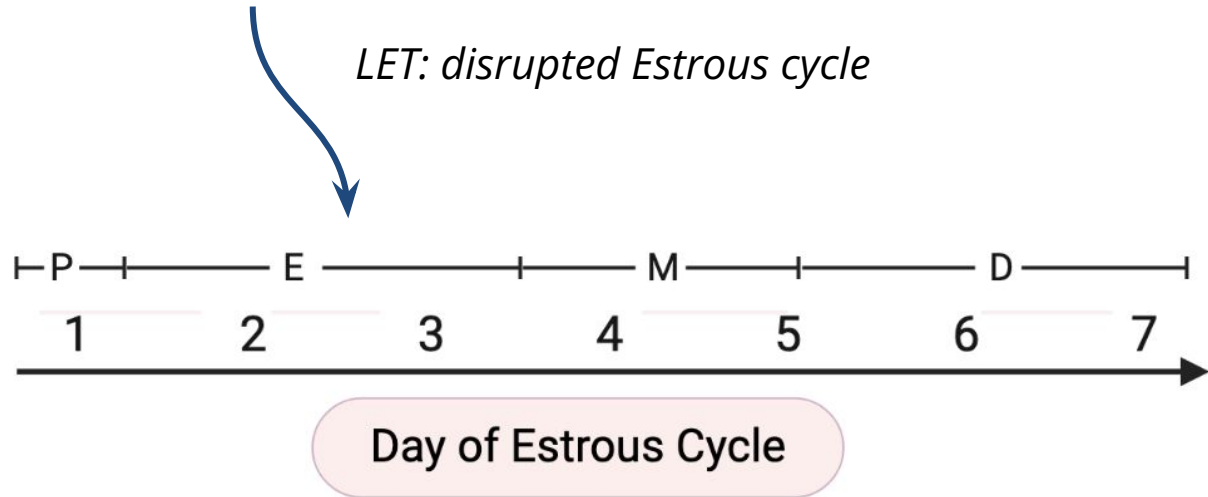


The LET mouse model replicates PCOS phenotype.



LET model (PCOS)

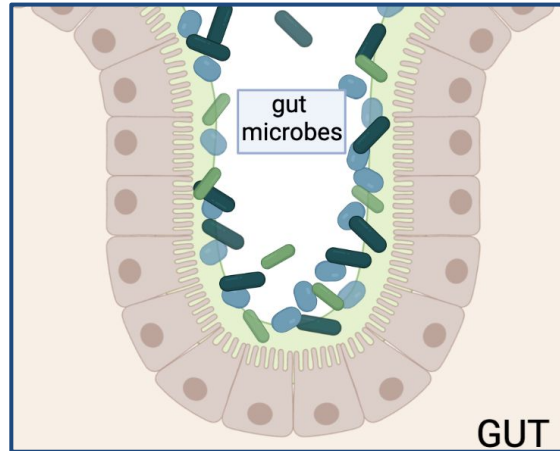
LET: disrupted Estrous cycle



Gut microbiome differences observed in PCOS women.

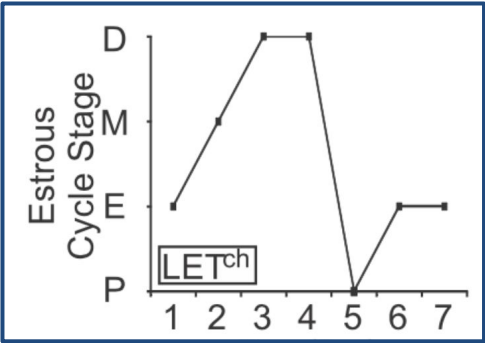
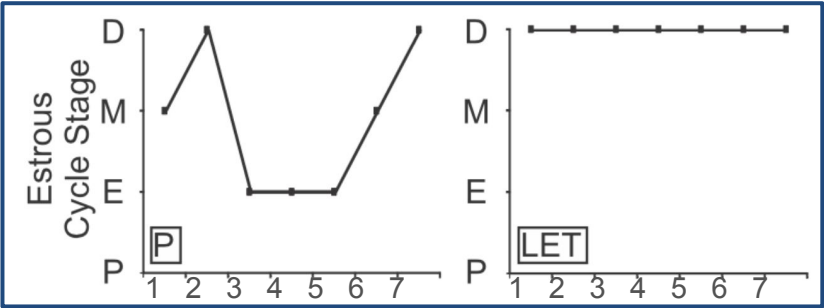


- Affects host metabolism
- What about host reproductive health?



Exposure to healthy gut microbiome ameliorates PCOS in mice.

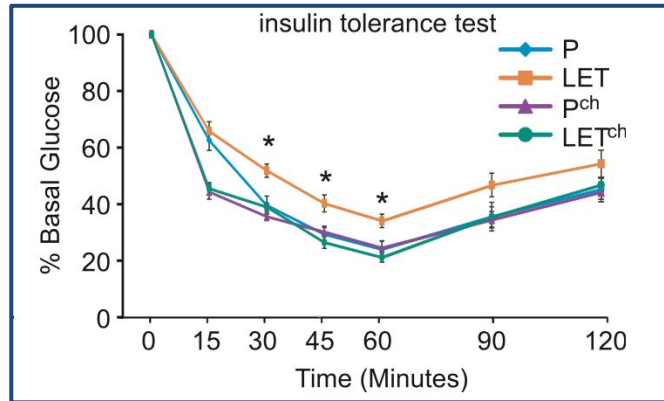
REPRODUCTIVE PHENOTYPE



P: placebo (normal)
LET: letrozole (PCOS)
LET^{ch}: LET+P cohoused

Exposure to healthy gut microbiome ameliorates PCOS in mice.

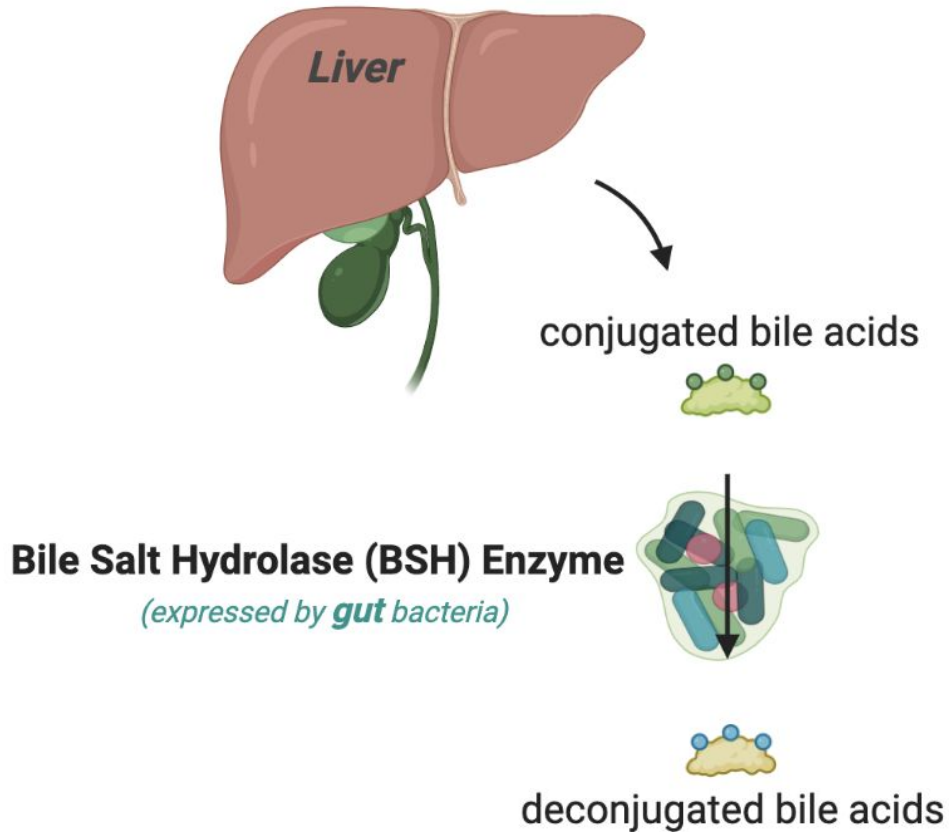
METABOLIC PHENOTYPE



- Differences in bile acid composition between LET vs P mouse

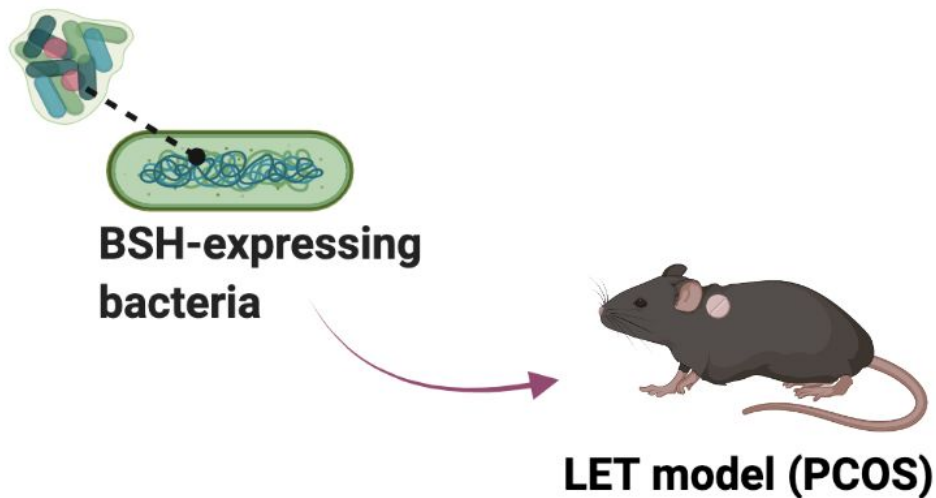
P: placebo (normal)
LET: letrozole (PCOS)
LET^{ch}: LET+P cohoused

Gut microbes that express BSH can modify bile acids.



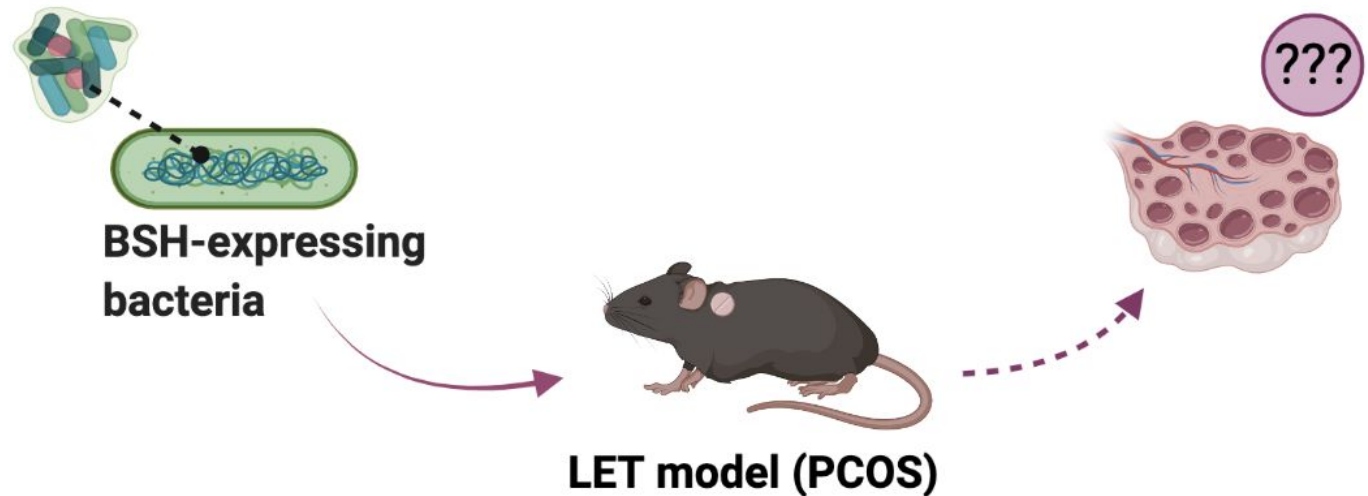
BSH-expressing ENB facilitate bile acid deconjugation in mice.

- Bacteria will colonize the mouse gut stably and perpetually



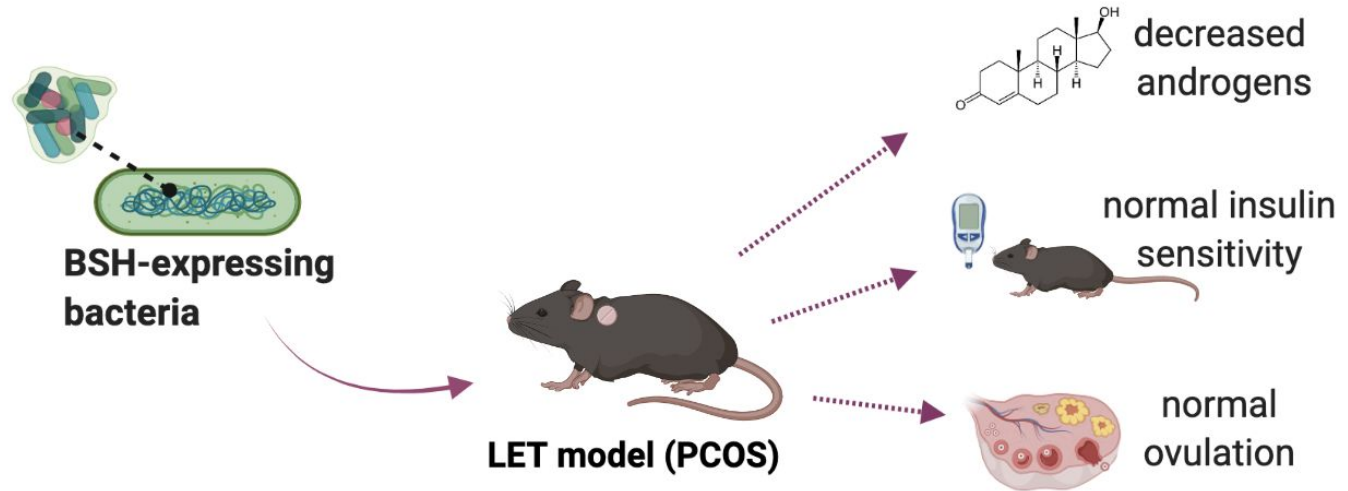
RESEARCH QUESTION

Does bacterial bile acid deconjugation affect metabolic and reproductive dysfunction in a PCOS mouse model?

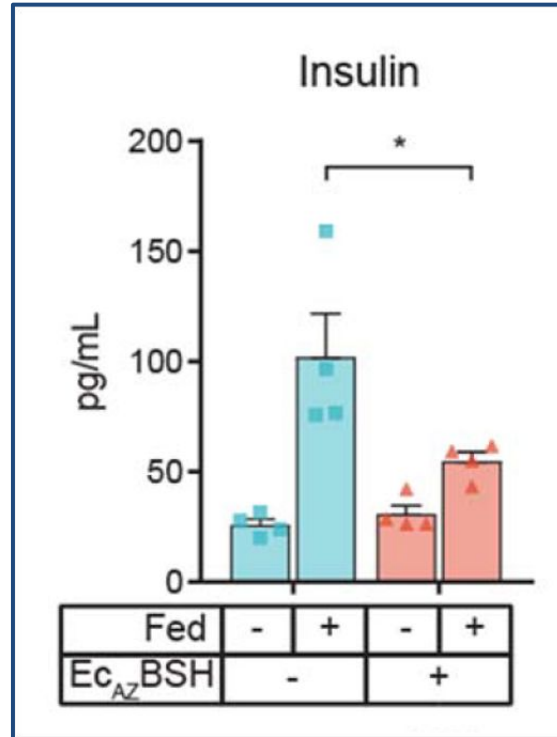


HYPOTHESIS

Introducing our BSH-expressing ENB to a PCOS mouse model will protect against metabolic and reproductive dysfunction of PCOS.

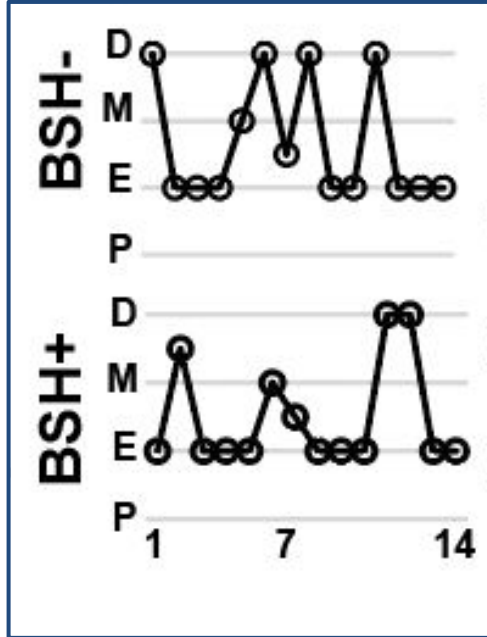


Mice with BSH-expressing ENB have improved insulin response.



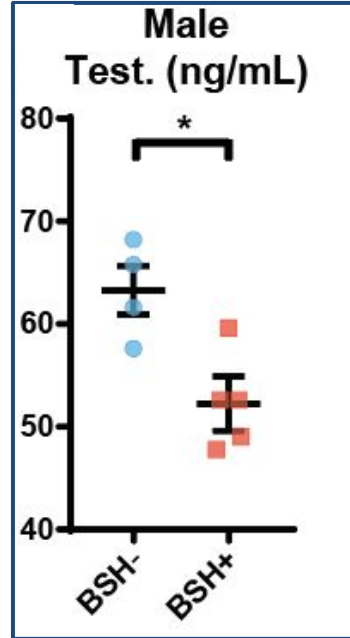
- Insulin resistance
 - Cells not responding to insulin → high levels of circulating insulin
- BSH- vs BSH+ mice
 - BSH improves insulin response

BSH does not affect normal mouse estrous cyclicity.



- BSH- and BSH+ ENB given to normal female mice
- BSH by itself does not affect estrous cyclicity

Mice with BSH-expressing ENB have decreased androgen levels.

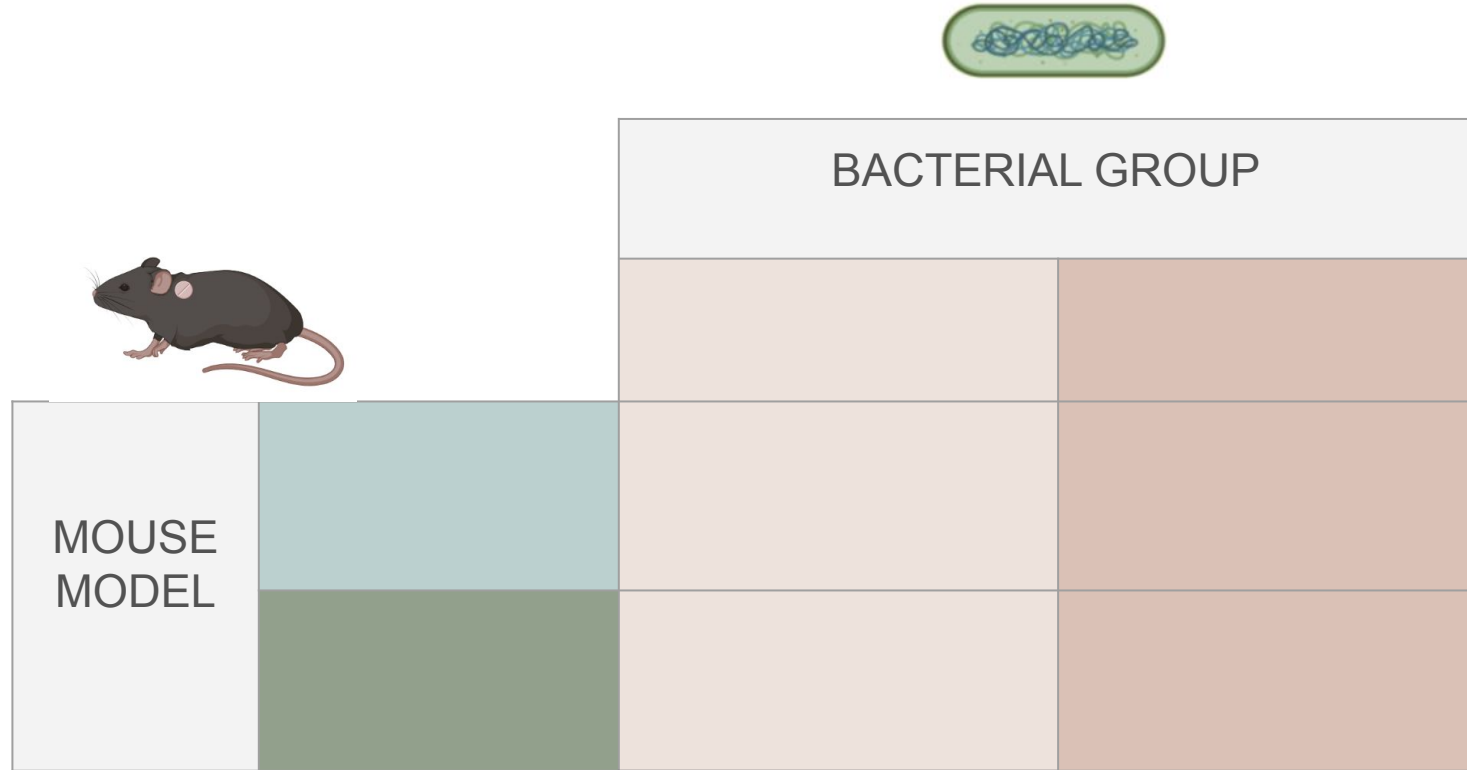


- Recall: PCOS women have elevated androgen levels
- Measure testosterone (androgen) hormone levels
- BSH+ mice have reduced testosterone levels

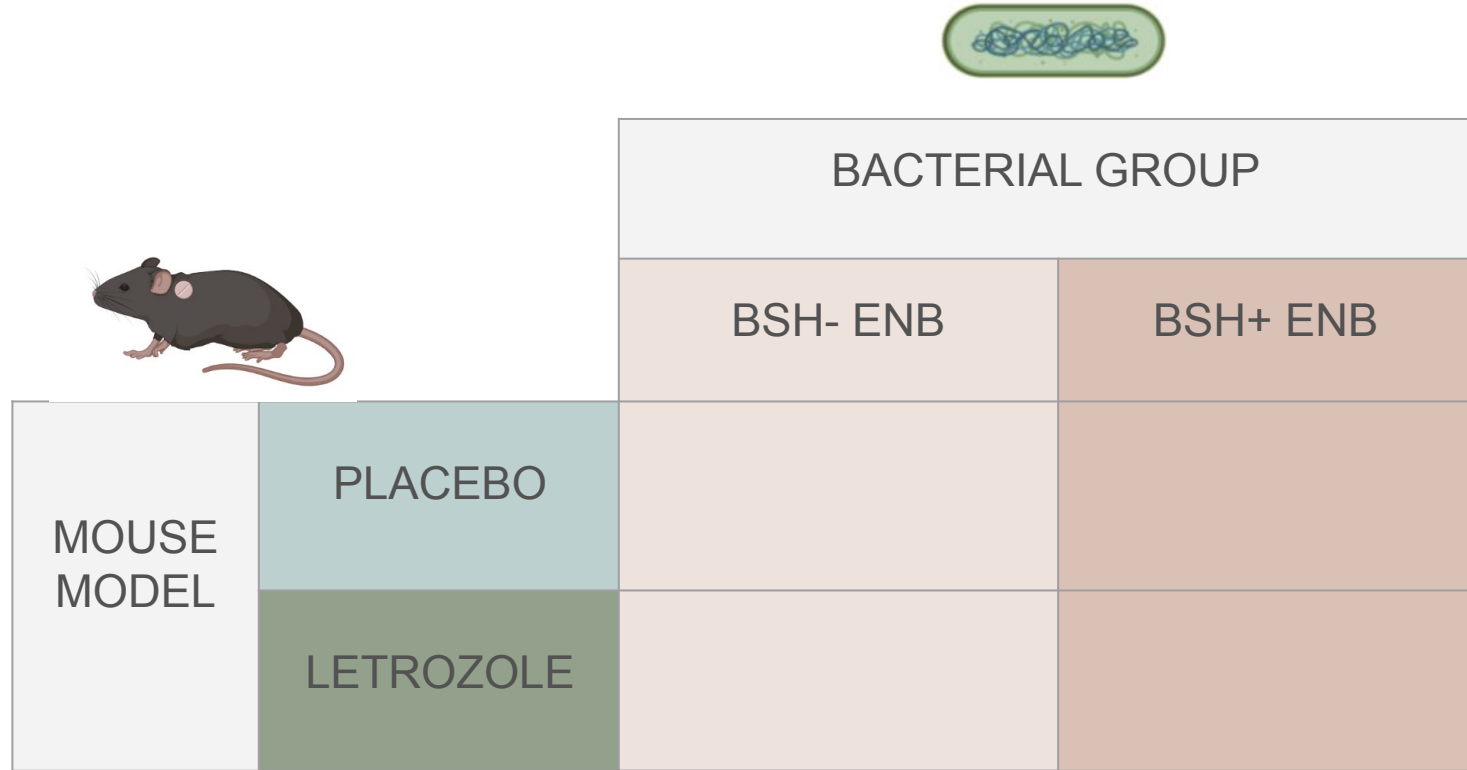
METHOD: 2X2 Experimental Design



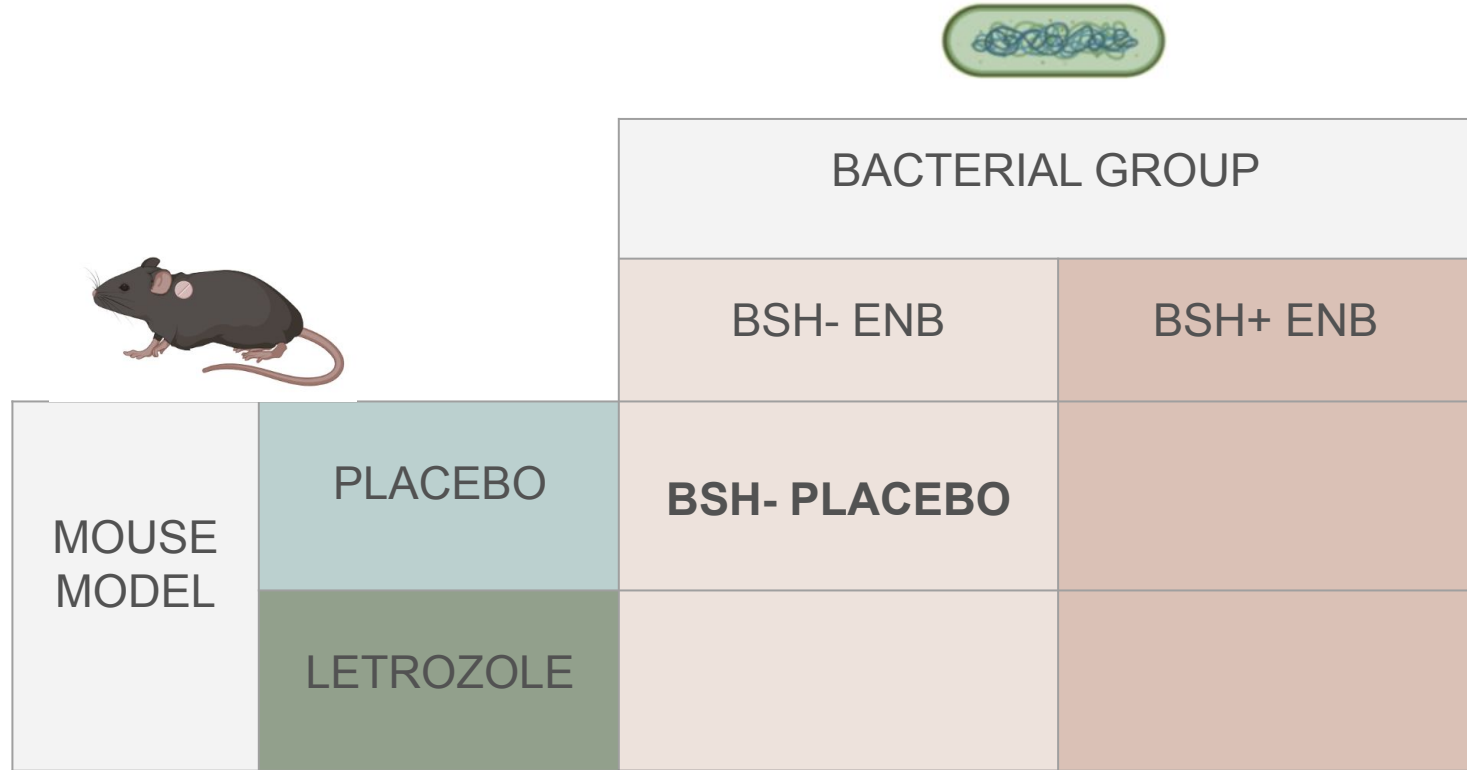
METHOD: 2X2 Experimental Design



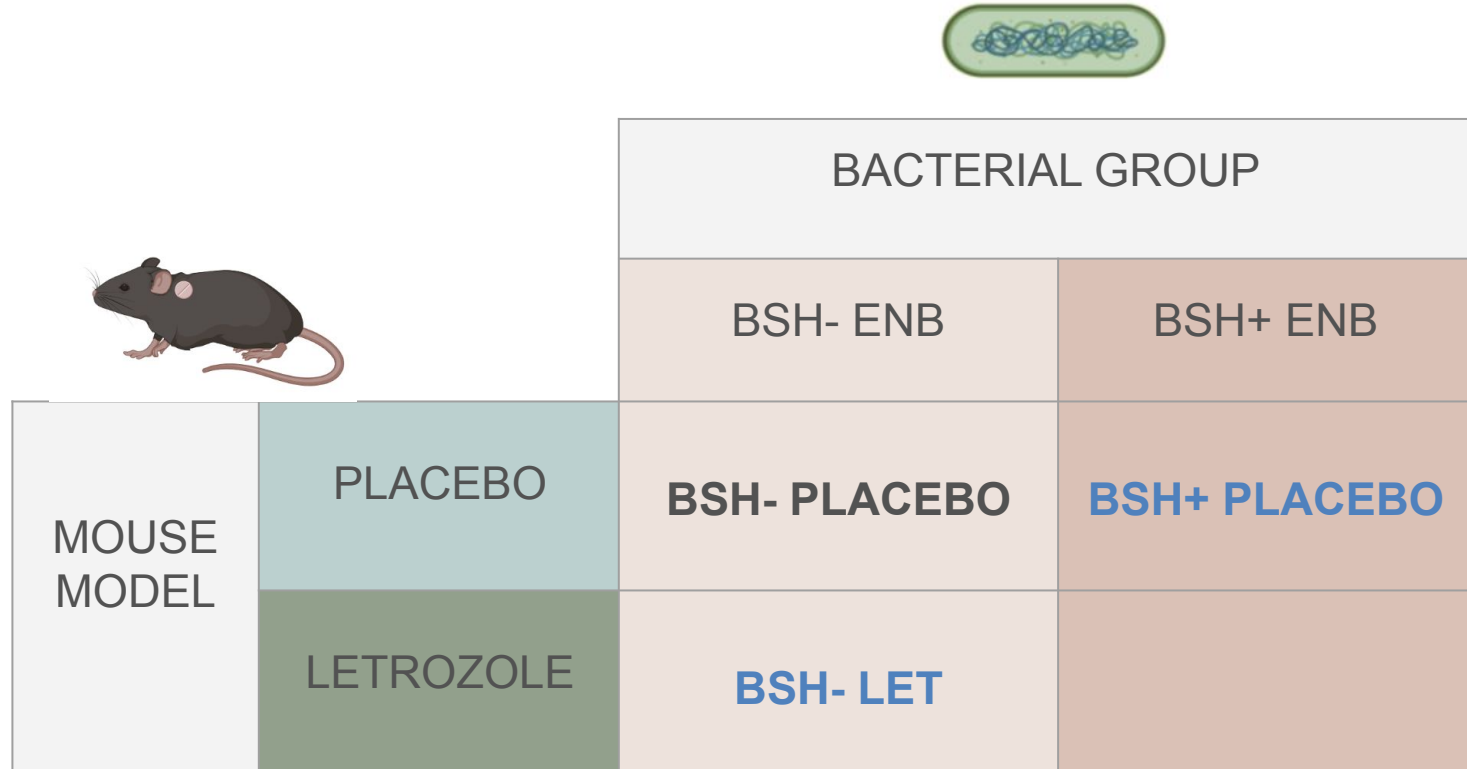
METHOD: 2X2 Experimental Design



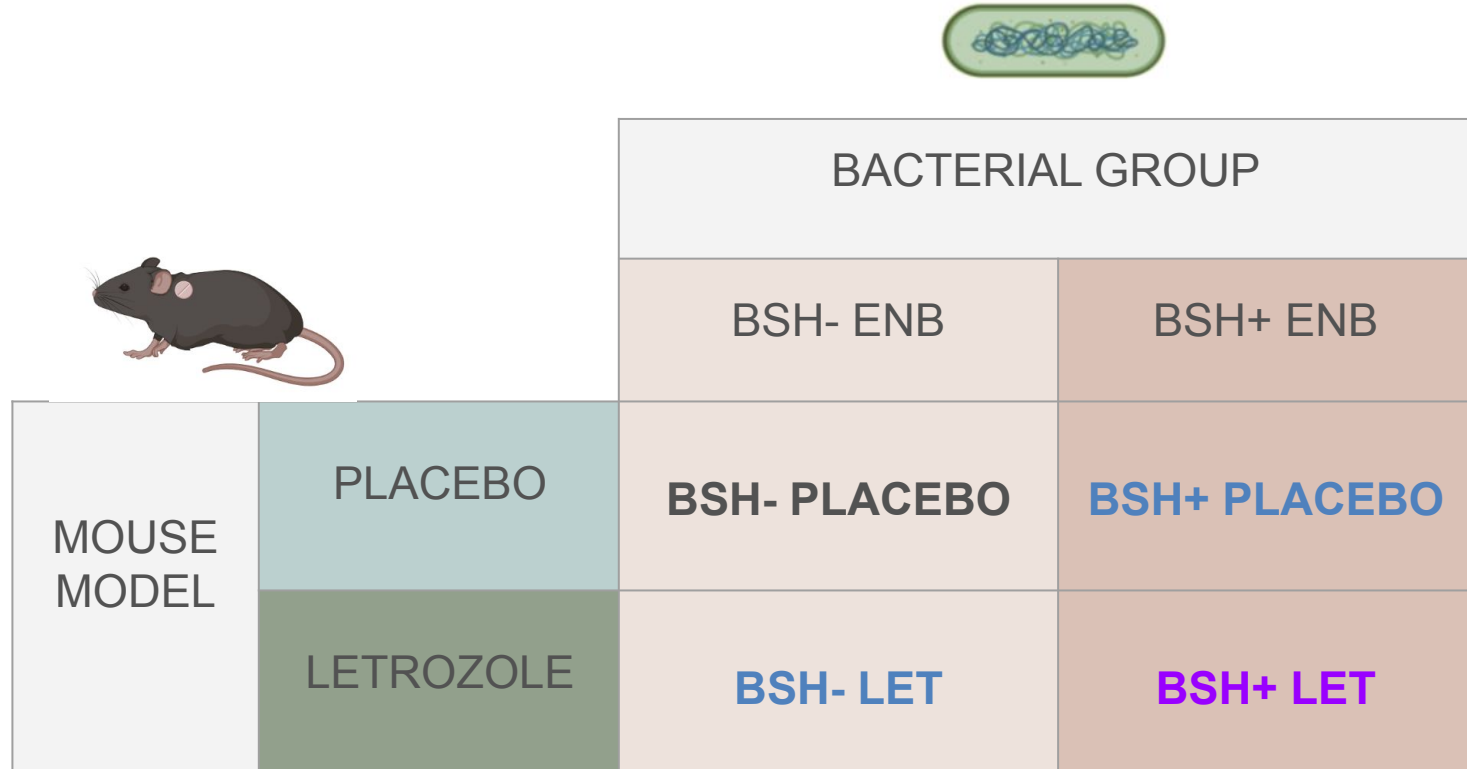
METHOD: 2X2 Experimental Design



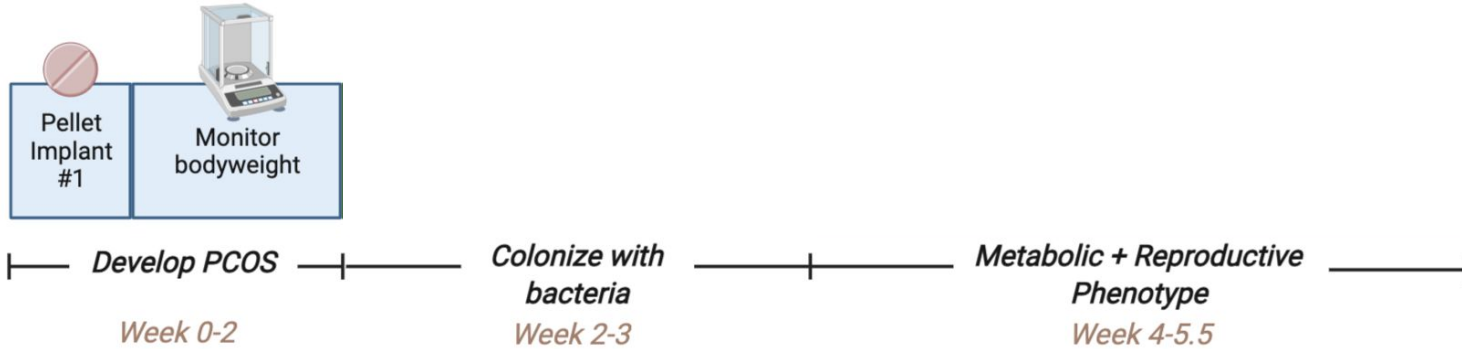
METHOD: 2X2 Experimental Design



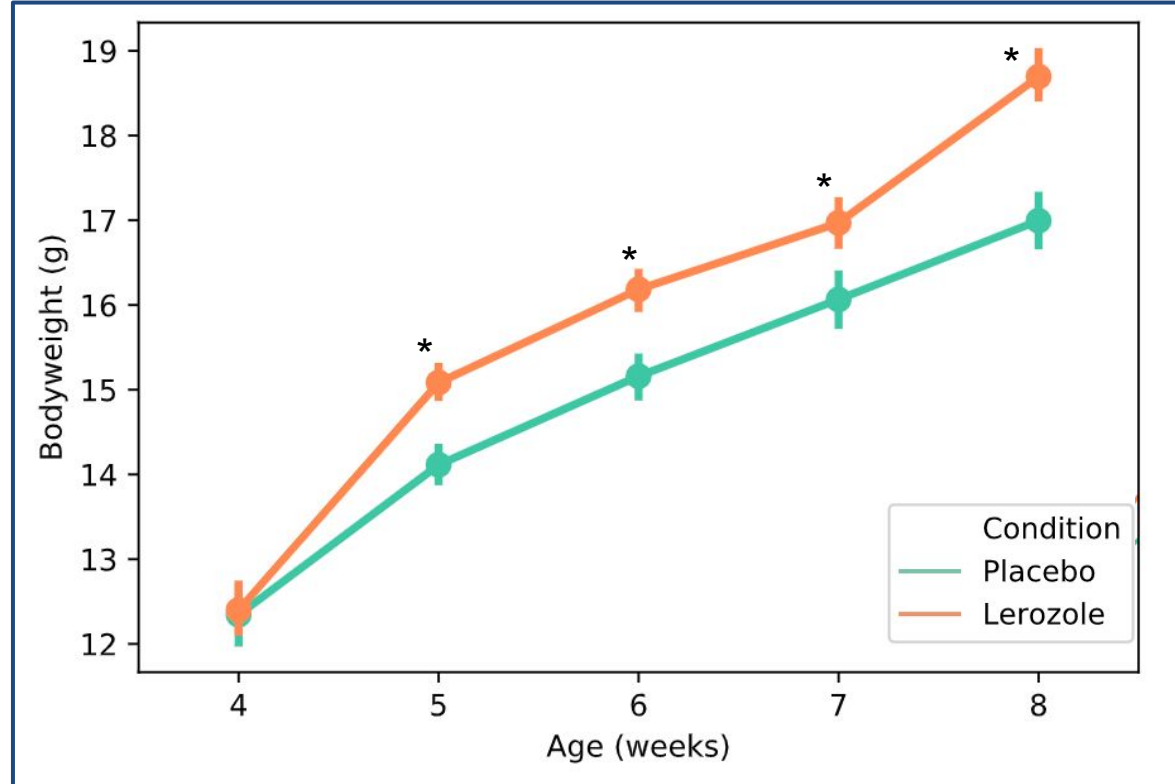
METHOD: 2X2 Experimental Design



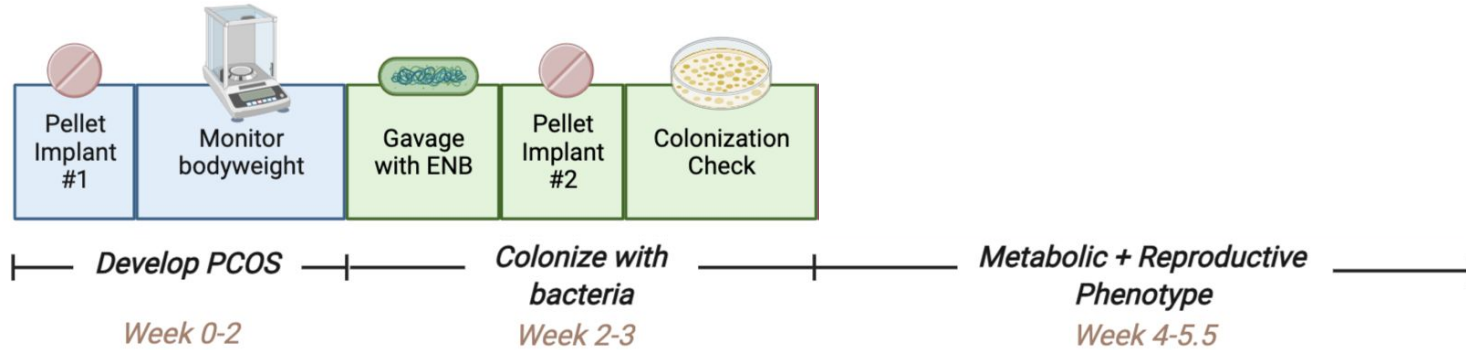
Experimental Timeline



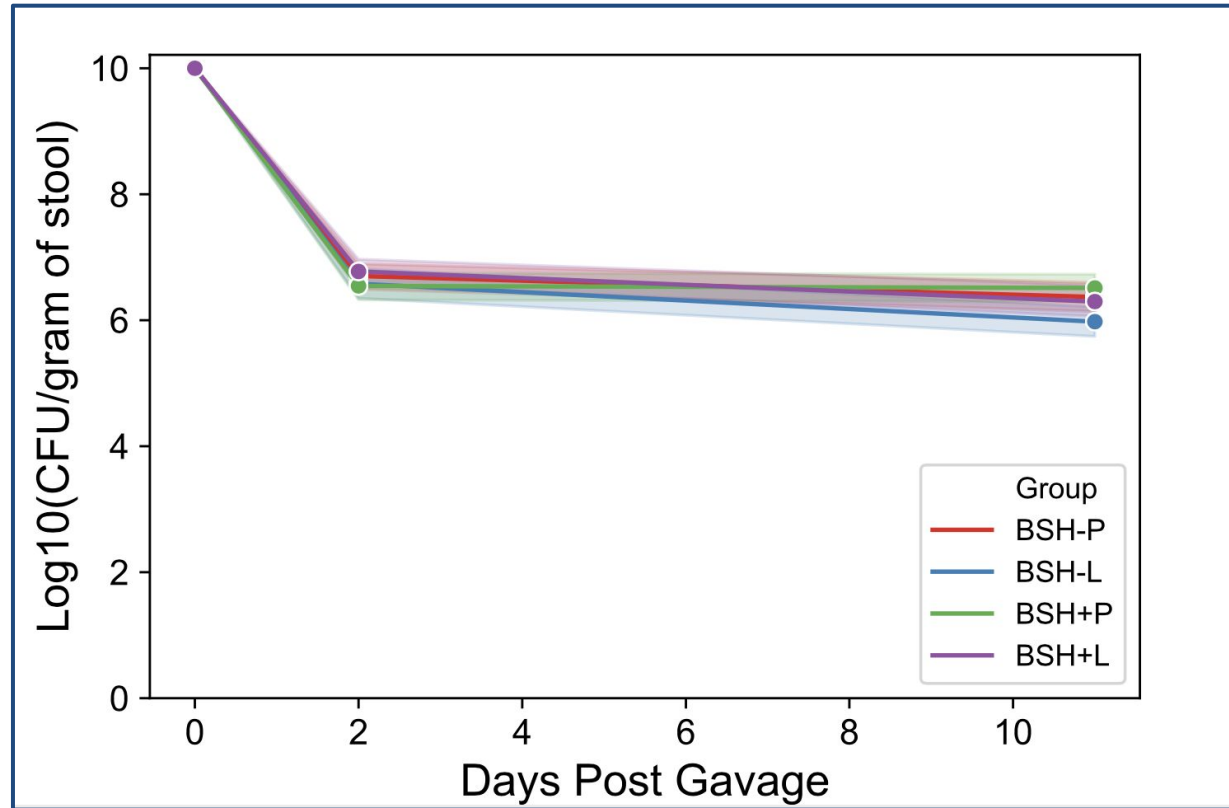
P vs. LET Bodyweights



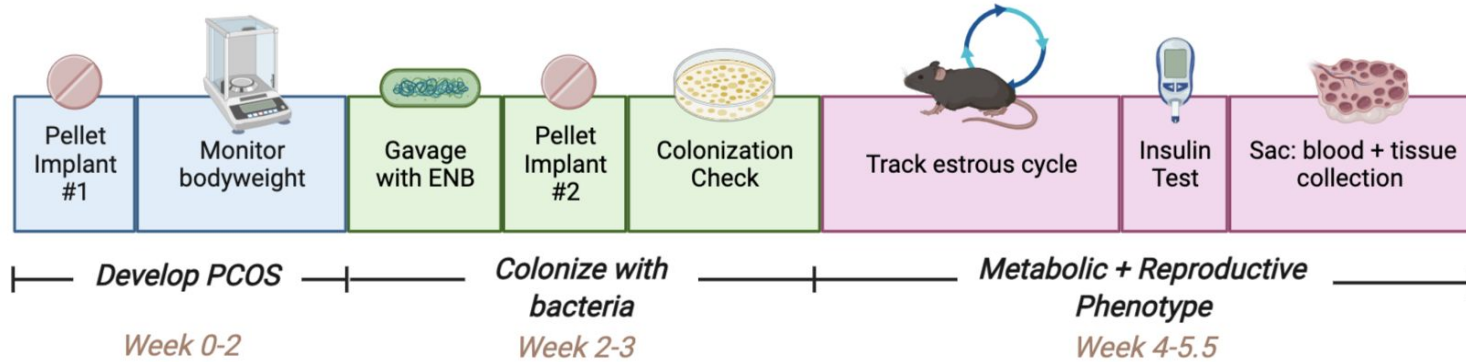
Experimental Timeline



ENB Colonization Levels



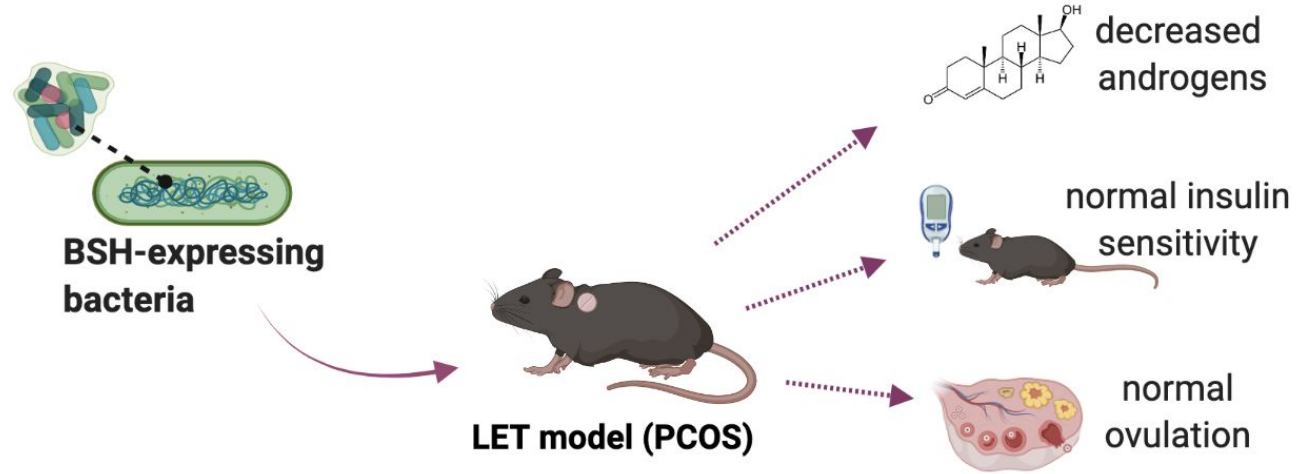
Experimental Timeline



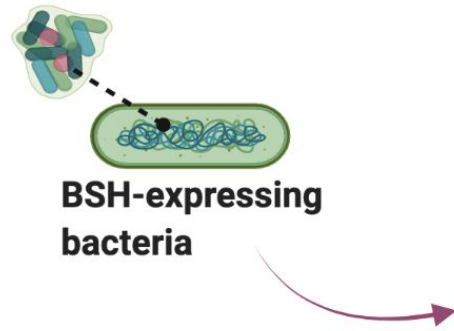
Future Directions

- ▶ Bile acid receptor KO study (FXR, TGR5)
- ▶ Using BSH as a prevention for PCOS (as opposed to treatment intervention)

Summary



Summary



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HYPOTHALAMUS
(BRAIN)

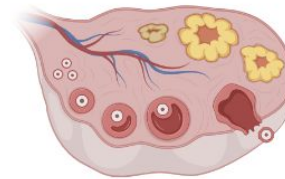


PITUITARY



GONADS (OVARY)

?



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