EXCESSIVE MATERNAL WEIGHT GAIN DURING GESTATION LEADS TO OFFSPRING WITH INCREASED ADIPOGENIC POTENTIAL IN THE IMMEDIATE PERINATAL PERIOD IN PIGS

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Gestational weight gain in the U.S.

- Institute of Medicine recommendations

Prepregnancy BMI	Total Weight Gain	
	Range in kg	Range in lbs
Underweight (< 18.5 kg/m^2)	12.5-18	28-40
Normal weight (18.5-24.9 kg/m^2)	11.5-16	25-35
Overweight (25.0-29.9 kg/m^2)	7-11.5	15-25
Obese (≥ 30.0 kg/m^2)	5-9	11-20

Recommended GWG decreases with increasing prepregnancy BMI

- Approximately 20% of all pregnancies in the US gain more than the recommended amount of weight. Overweight and obese women are at particular risk.
- Excess weight gain presents health risks for both mother and offspring

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Pig Model

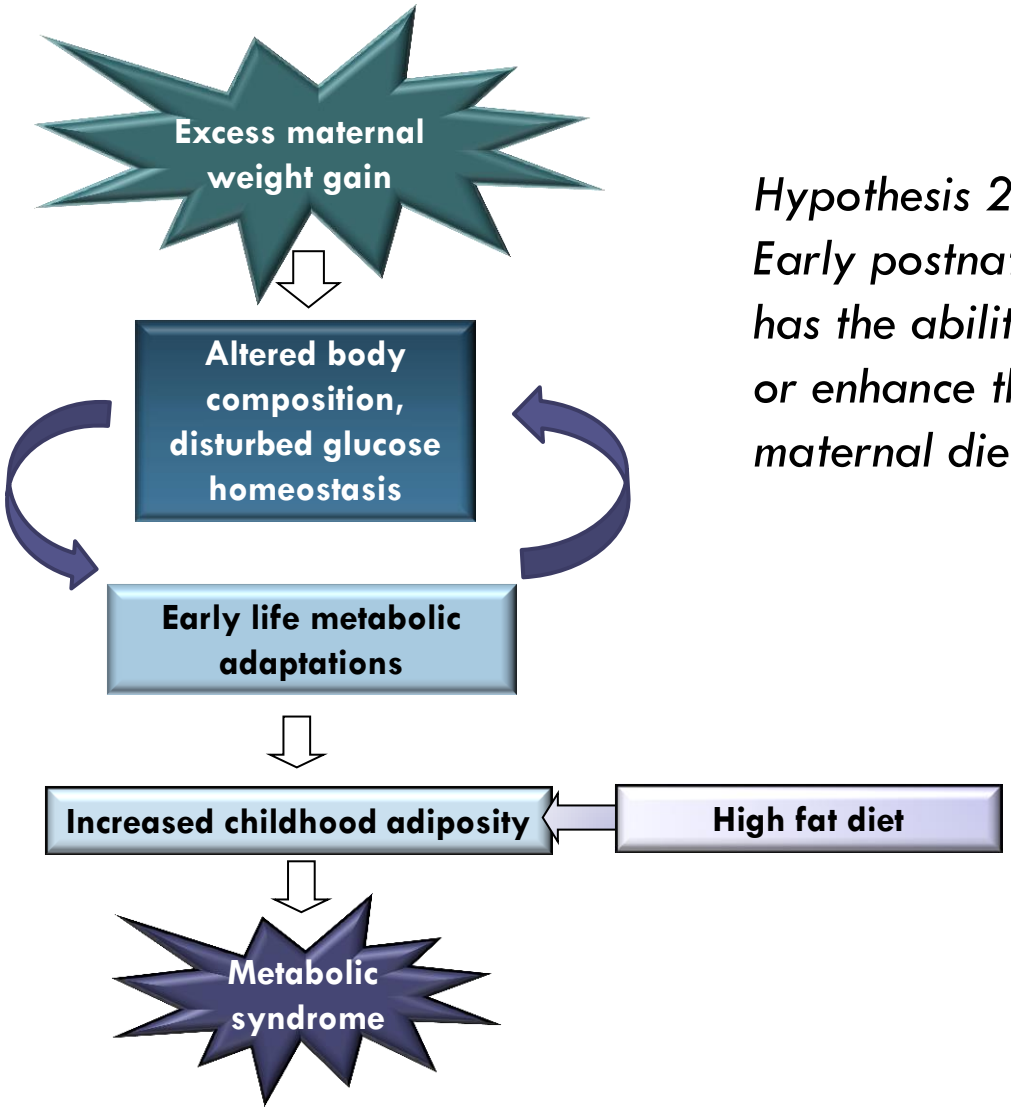
- Pig model serves as a good bridge between mouse and humans
- Studies in mice can be replicated in pigs

Perinatal Nutrition in Pigs

Piglet diet before weaning can be manipulated to cause maximum epigenetic effects during the perinatal period

Study hypotheses

Hypothesis 1:
Excessive weight gain during pregnancy due to increased energy intake will result in programming modifications that predispose offspring to obesity and aspects of the metabolic syndrome.



Hypothesis 2:
Early postnatal nutrition has the ability reverse or enhance the effect of maternal diet.

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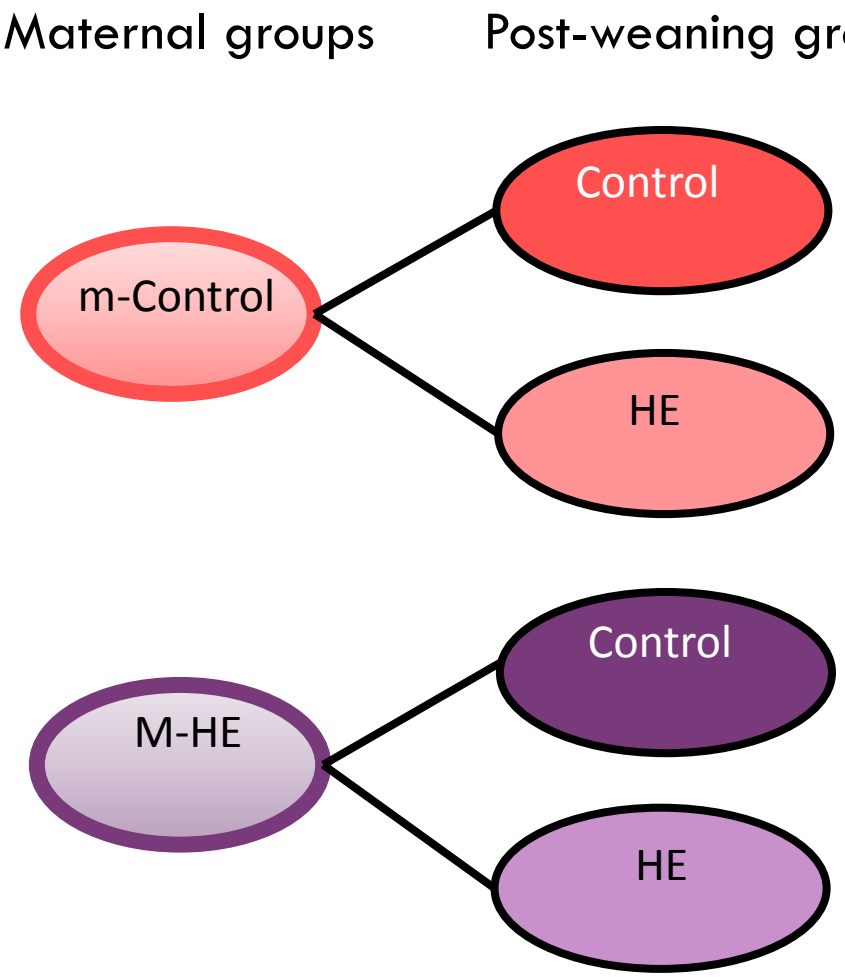
Study Design

Maternal Diets:
m-Control: chow gestation diet
M-HE: high energy gestation diet
- Increased energy intake (kcal) by ~50%
- Matched for protein intake (g/day)



Post-weaning Diets:
Control: chow piglet diets
HE: high fat piglet diets
- Increased fat content of diet by 10-15%

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Experimental methods for determining programming of offspring

•Adipose, Liver & intestine mRNA for transcript analysis

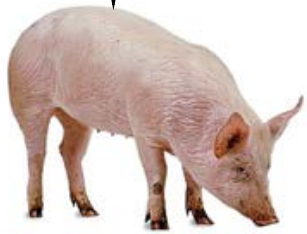
•Serum for glucose, insulin and NEFA analysis

Weaning: assigned to post-weaning (Pwn) diet

Suckling period

Growth phase (9 weeks)

•Weights measured every 1-2 weeks



Birth

3 weeks

12 weeks

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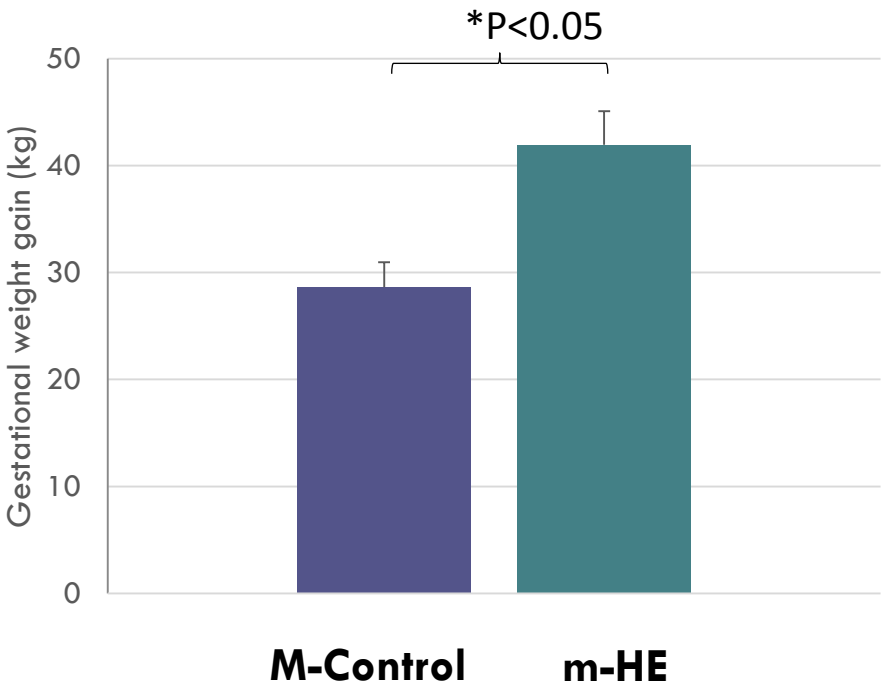
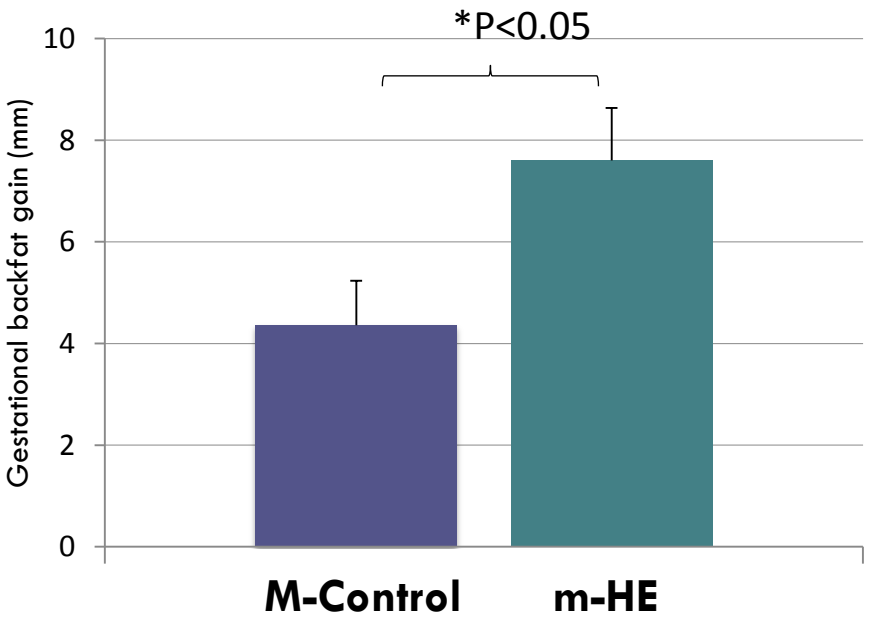
High energy diet increased maternal weight gain and adiposity during gestation





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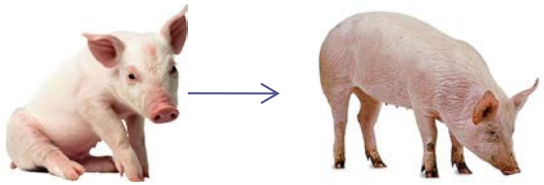
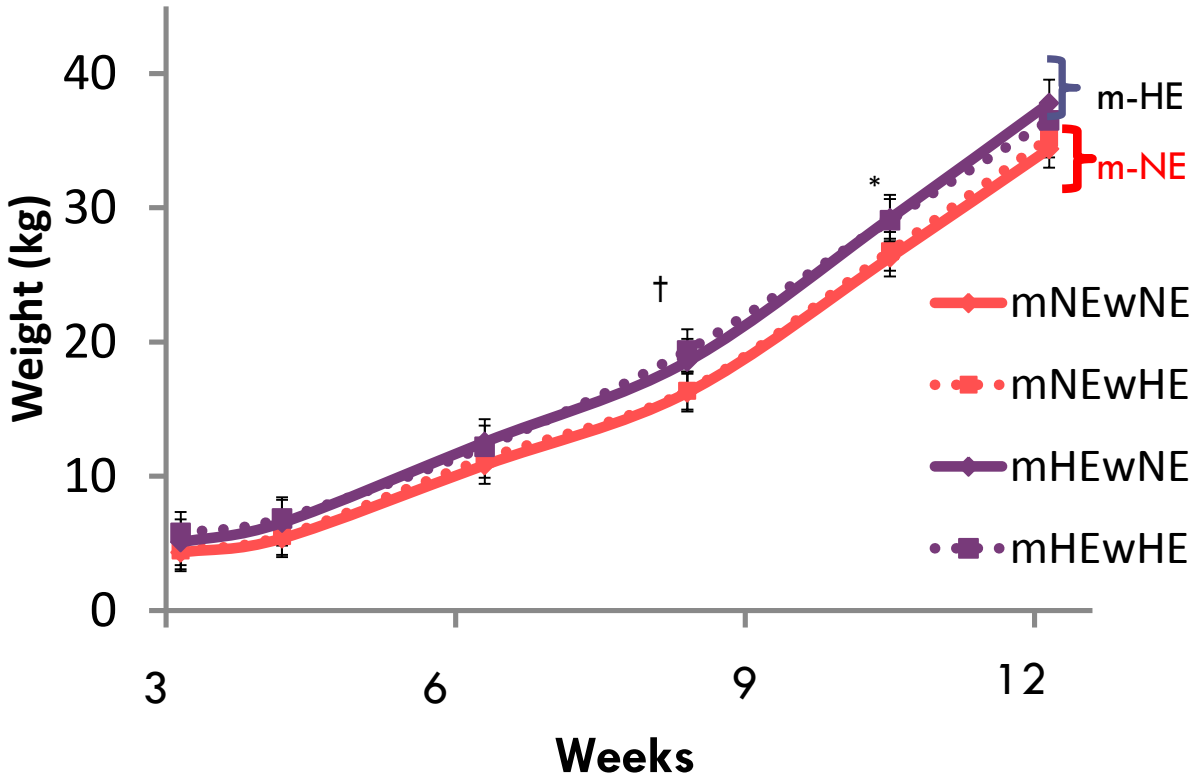
Offspring from sows fed a HE diet weighed more at 8 and 10 weeks of age.



Increased childhood adiposity

Main effect	P-value
Mat	0.12
Pwn	0.93
Mat*Pwn	0.85
Day	**<0.05**
Mat*Pwn*Day	0.95



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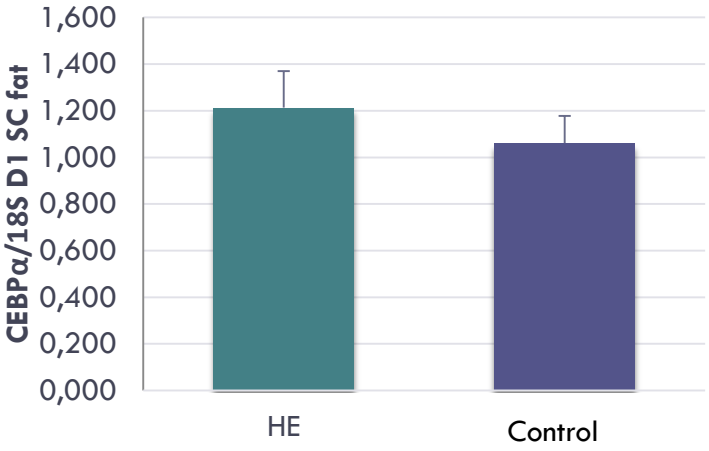
Feeding a HF diet to offspring from HF diet fed sows induced disturbed offspring glucose homeostasis

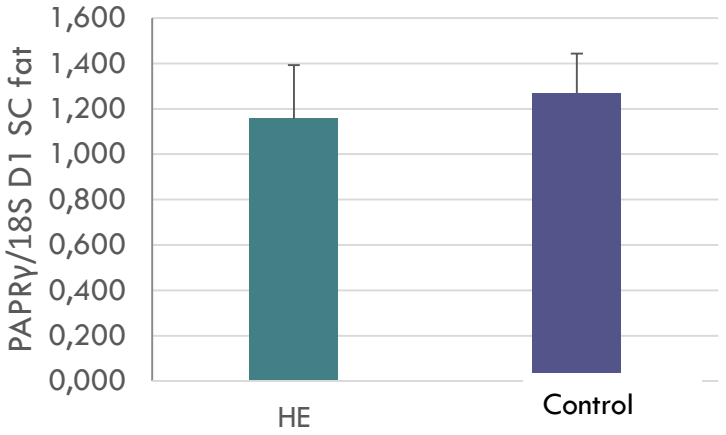
	Maternal Diet					P-Values		
	M-Control		M-HE					
	p-Control	p-HE	p-Control	P-HE	CI	Mat	Pst.natal	M x P
Glucose (mg/dl)	70	80	64	102*†	(67.3, 90.9)	0.47	**<0.05**	0.21
Insulin (ng/ml)	0.016	0.013	0.010	0.021†	(0.011, 0.019)	0.92	0.24	0.08
NEFA (mmol/L)	0.43	0.43	0.62	0.31*	(0.34,0.56)	0.87	0.12	0.11

† Significantly different (P<0.05) from control group of the maternal group (mHE→wNE)

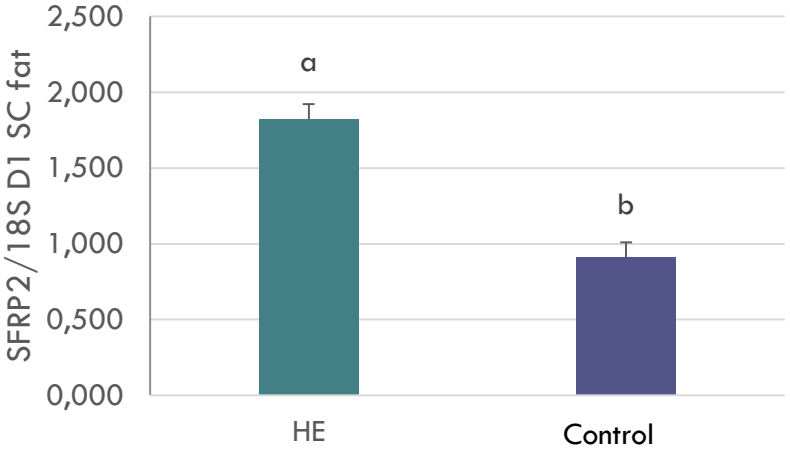
* Significantly different (P<0.05) from offspring of control dams fed the same post-weaning diet (mNE→wHE)

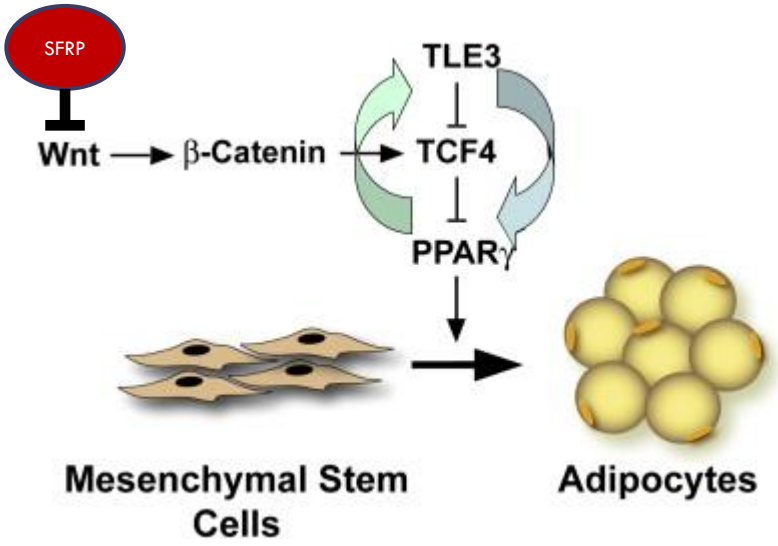
Adipose CEBPα and PPARγ at 48 hr



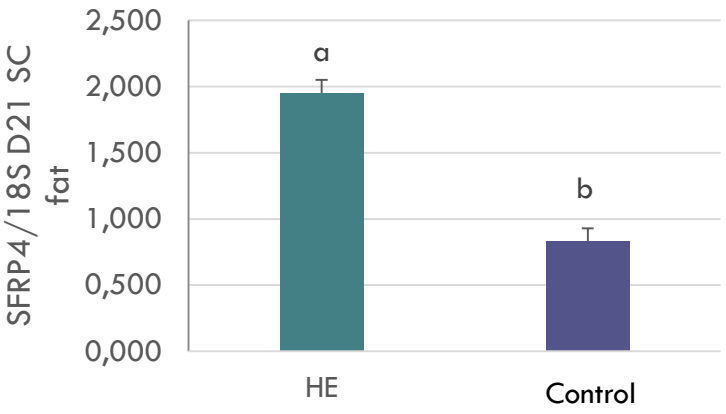


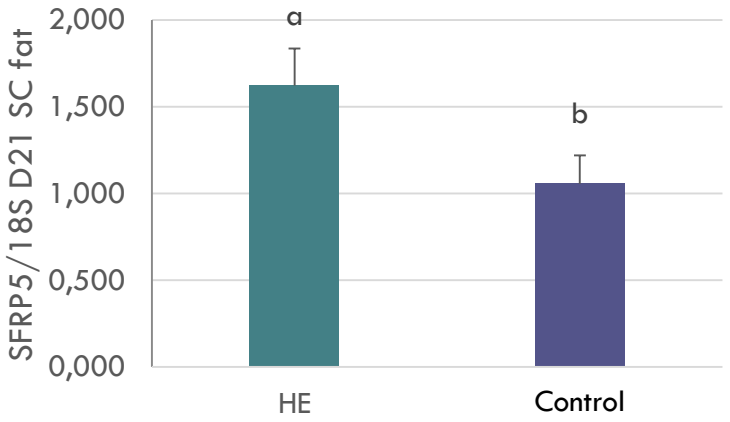
Adipose SFRP2 at 48hr



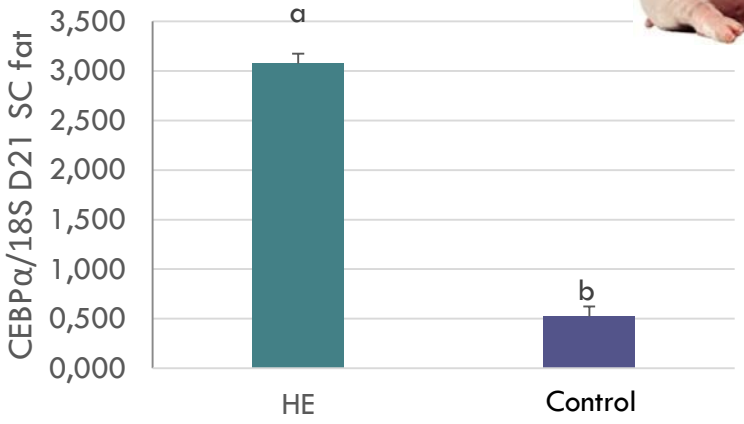


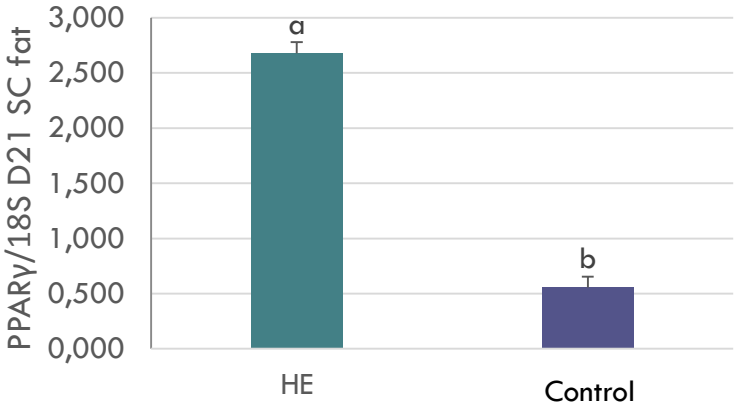
Adipose SFRP4 and SFRP5 at 3 wks



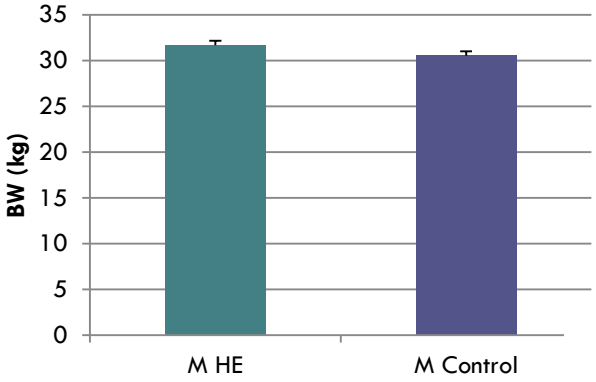


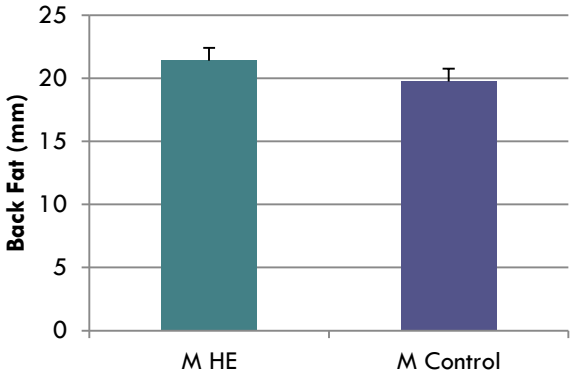
Adipose CEBPα and PPARγ at 3 wks

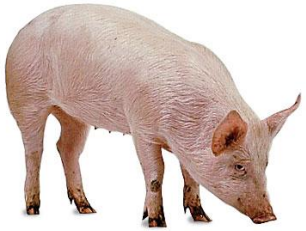


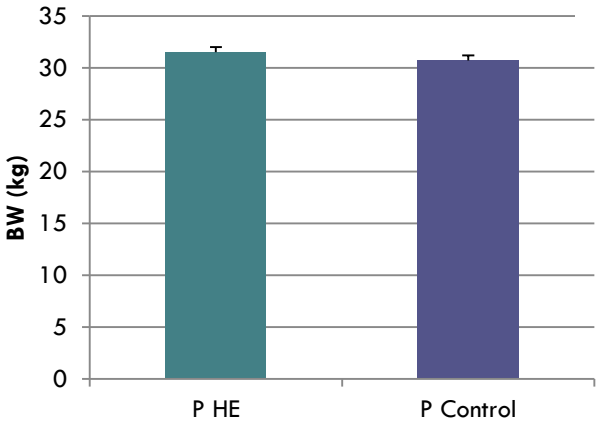


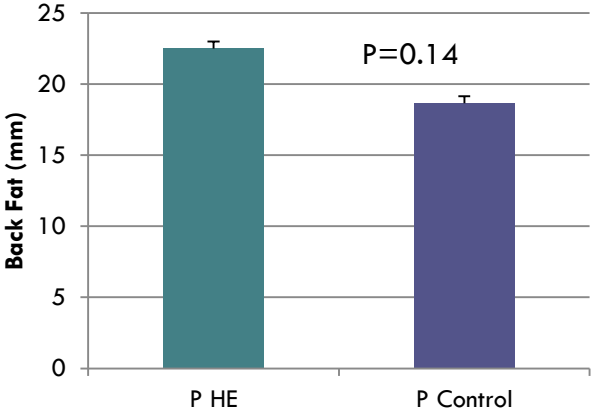
At 3 Months


35
30
25
20
15
10
5
0
BW (kg)
M HE
M Control

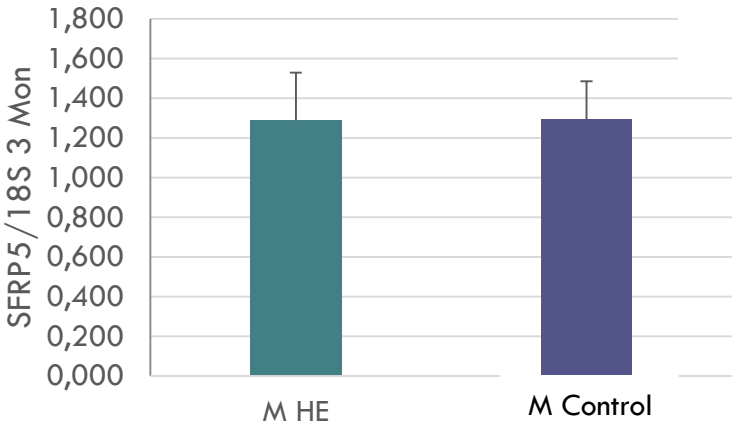

25
20
15
10
5
0
Back Fat (mm)
M HE
M Control

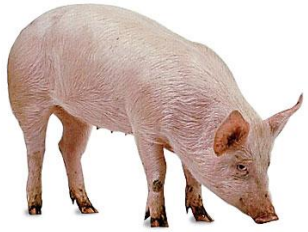


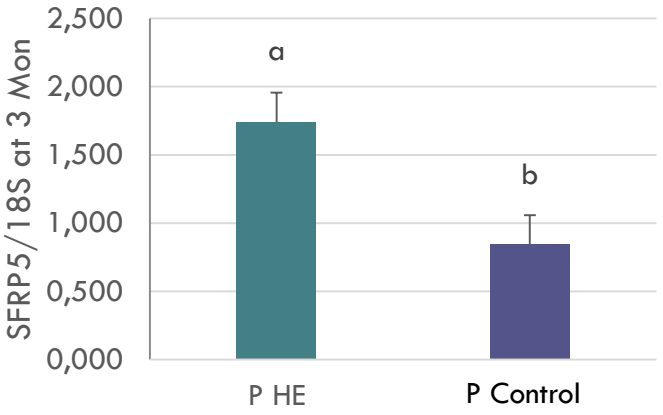

35
30
25
20
15
10
5
0
BW (kg)
P HE
P Control


25
20
15
10
5
0
Back Fat (mm)
P=0.14
P HE
P Control

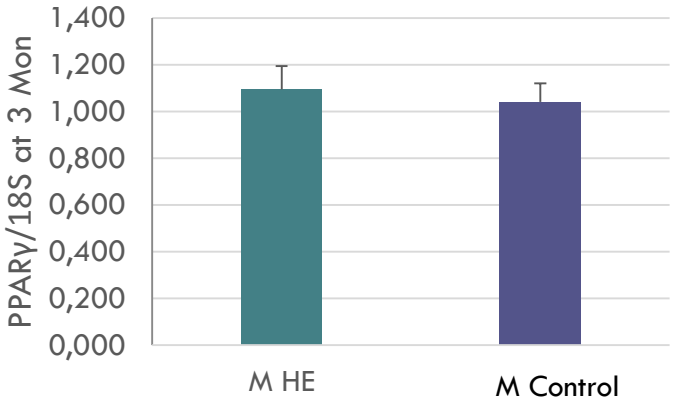
Adipose SFRP5 at 3 Mon

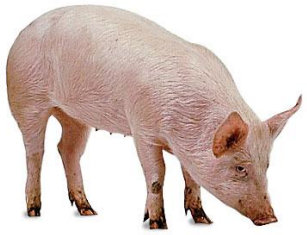


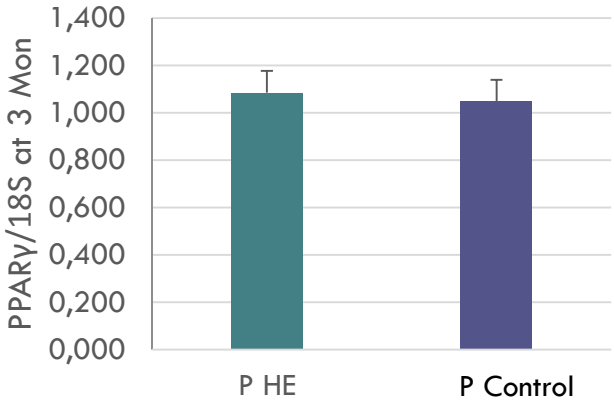


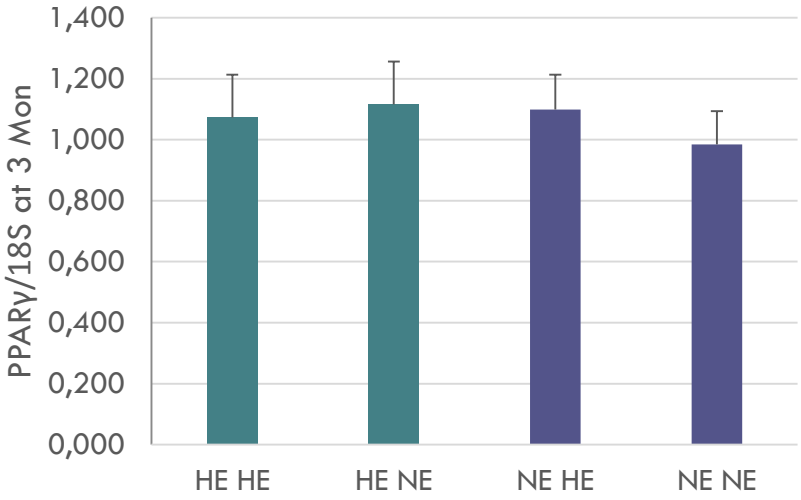


Adipose PPARγ at 3 Mon

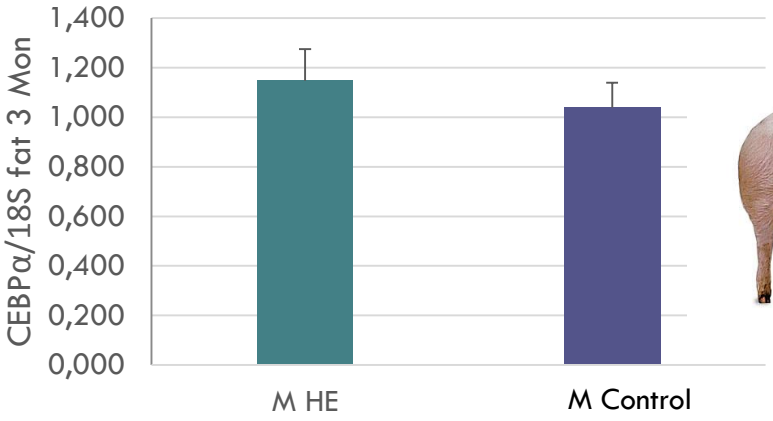


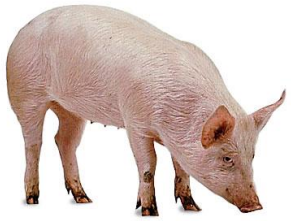


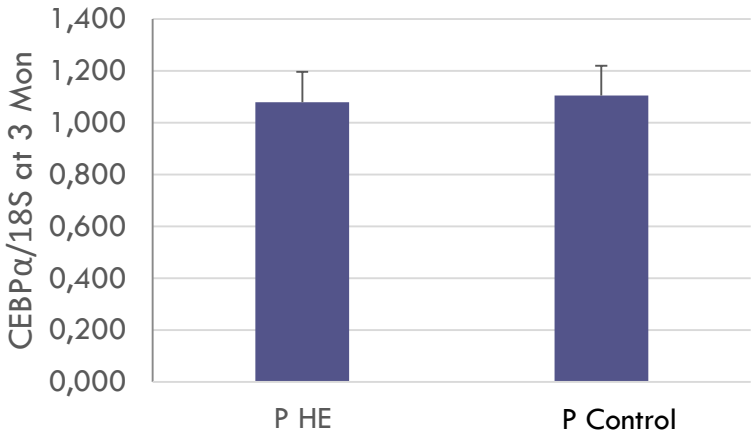


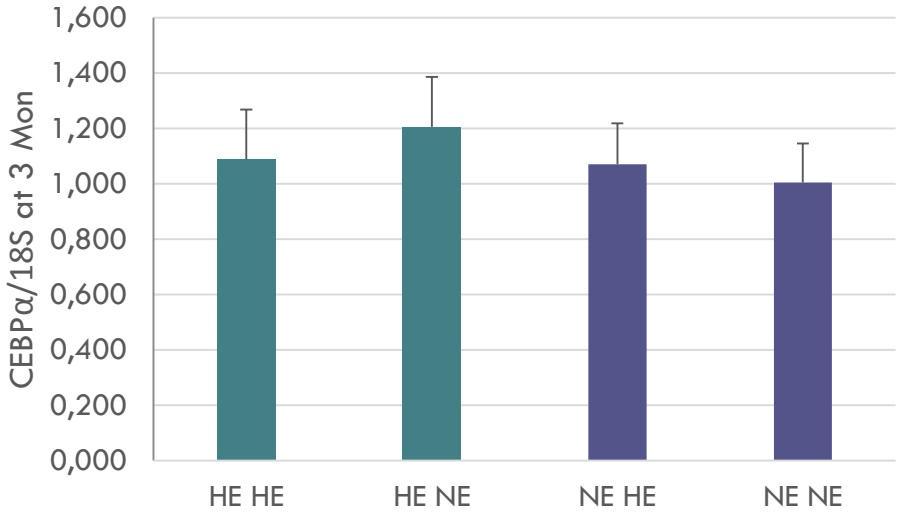


Adipose CEBPα at 3 Mon









Summary

- Offspring of mothers that gained excess weight during pregnancy:
  - Weighed more at 8 weeks and 10 weeks of age, although were not significantly different at the end of the study
  - Had higher expression of increased adipogenesis at 48 hr (SFRP2) and 3 wks (CEBPα, PPARγ, SFRP4, and SFRP5).
  - These indicators were lost at 12 wks

- Pigs were still relatively young at sacrifice, so this might not be a good time to see the final effect of fetal programming in pigs
- Postnatal diet might play a more dominant role in the determination of offspring adiposity in pigs.

Questions?

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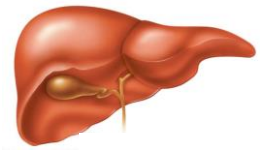
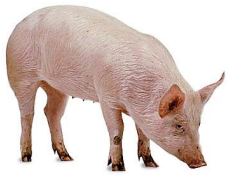
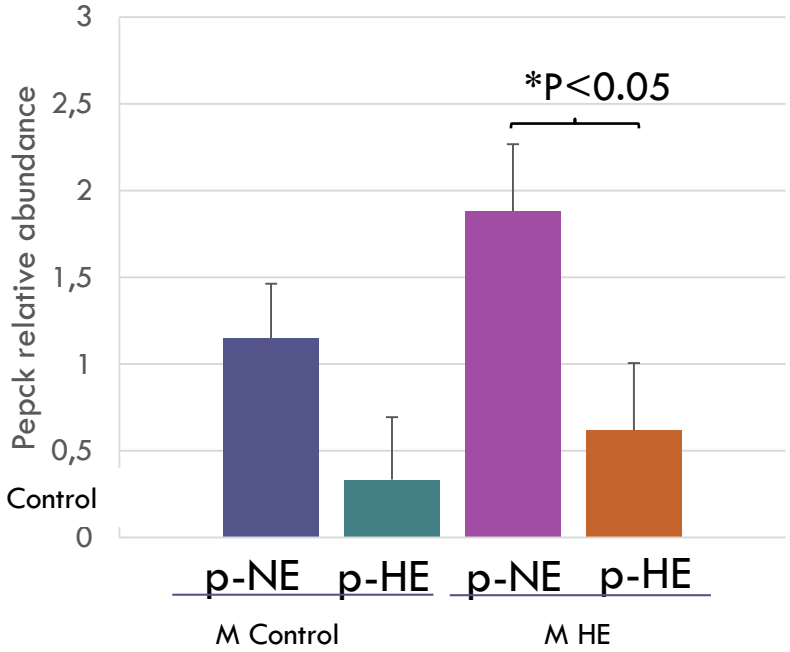


Relative abundance of liver transcripts at 12 wks



Early life metabolic & growth adaptations



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Arentsen et al., 2014 Nutrition Research (In Press)

Maternal Gestation Nutrient Intake

	Control	High Energy
Total intake, kg/day	2.05	3.0
Total Protein, g/day	370	395
Total Lysine, g/day	16.03	15.8
Total Fat, g/day	119	178
Metabolizable Energy, kcal/day	6761	10144