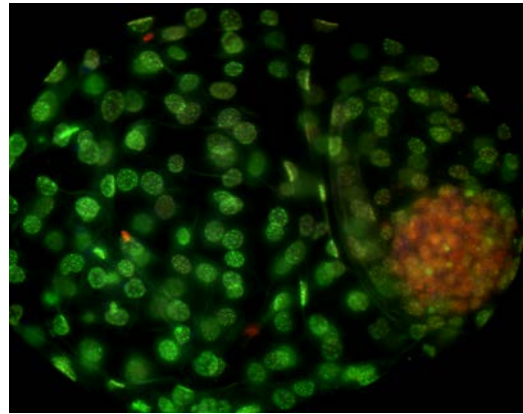


Methyl donors and epigenetic regulation of the early embryo

P.J. Hansen
 Dept. of Animal Sciences
 University of Florida



Feedstuffs

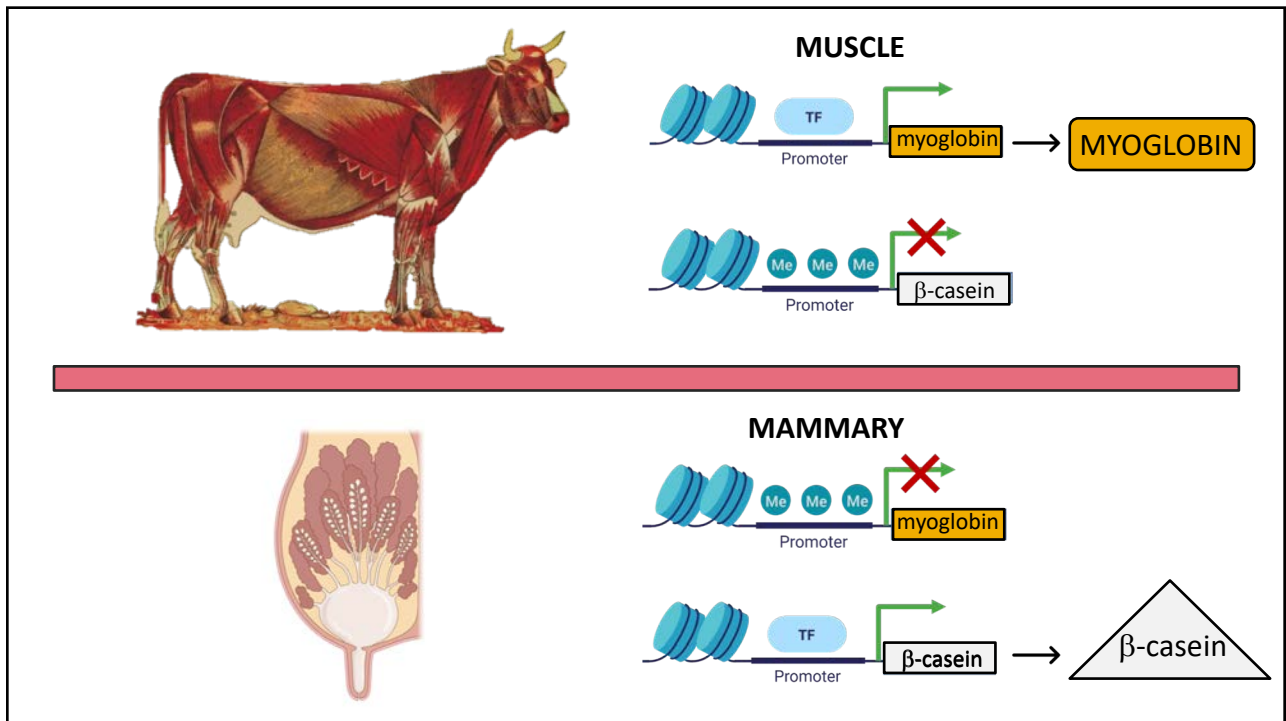
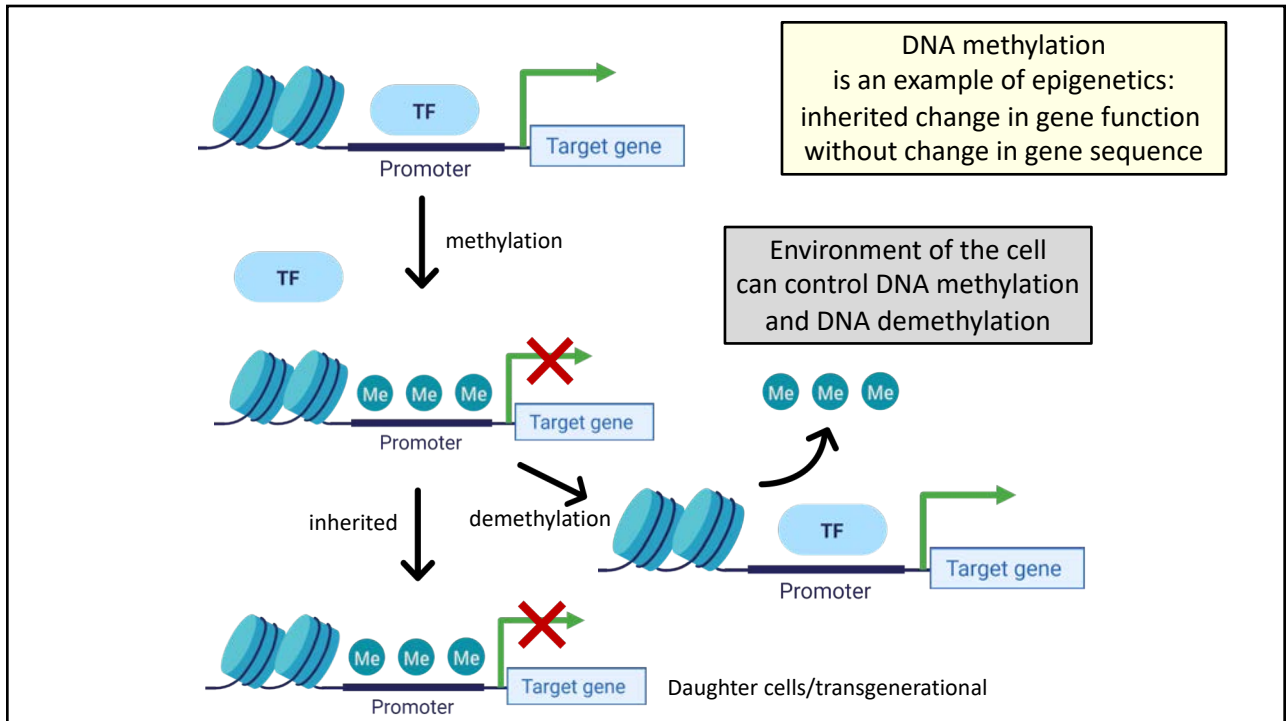


Take-home messages

- Changing DNA methylation during the earliest stages of life, when the embryo is developing from the one-cell stage to the blastocyst stage (day 7 in the cow), can change the program of development to affect postnatal phenotype
- Providing methyl donors is one way to change DNA methylation
- There is the opportunity to improve growth, reproduction or lactation by altering DNA methylation at critical times in development

Example of this idea

- Effects of choline treatment of embryos produced in vitro on birthweight and growth of the resultant calf

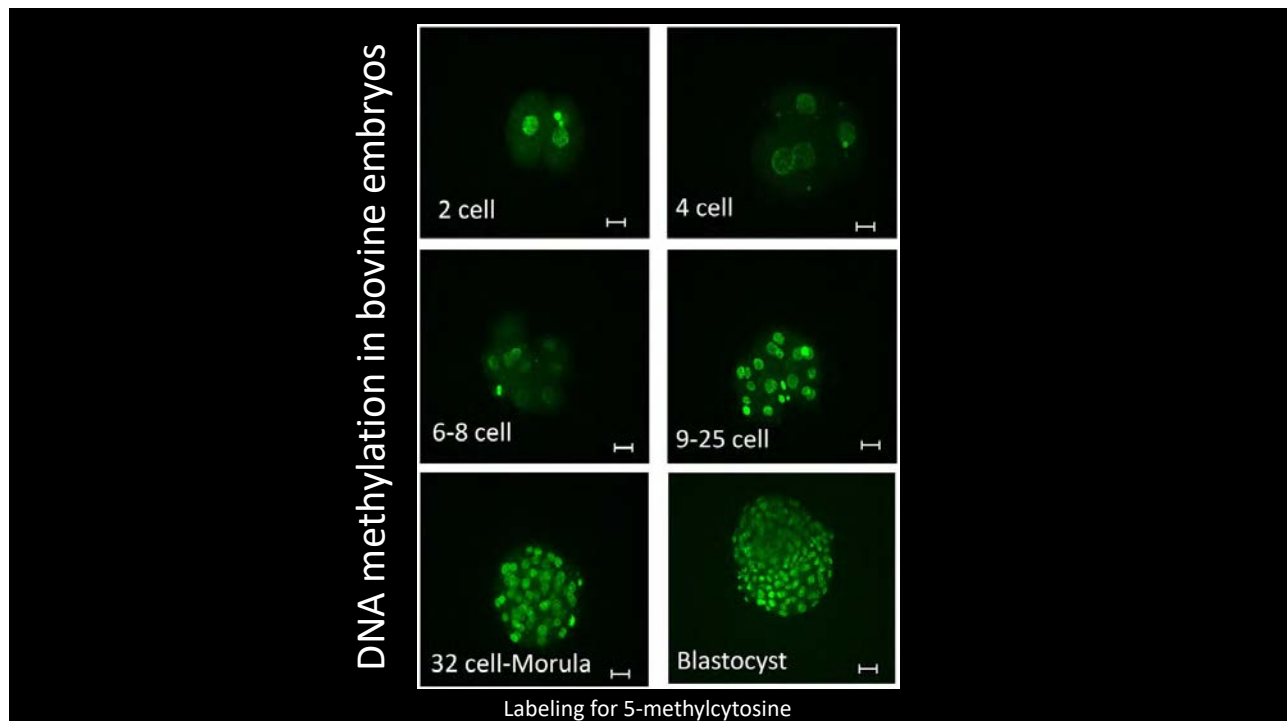


Take-home messages

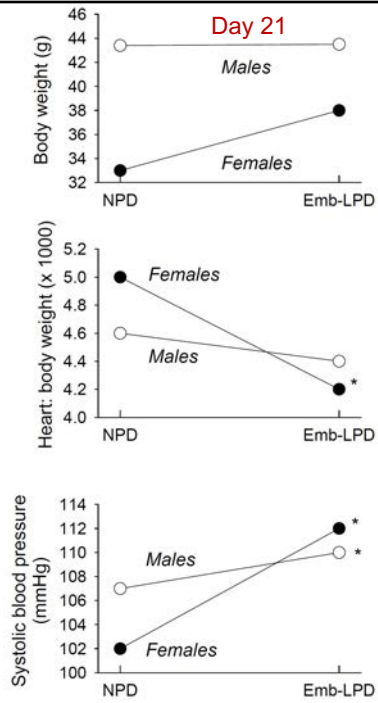
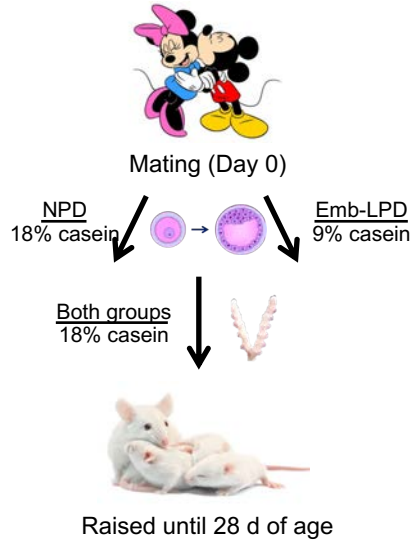
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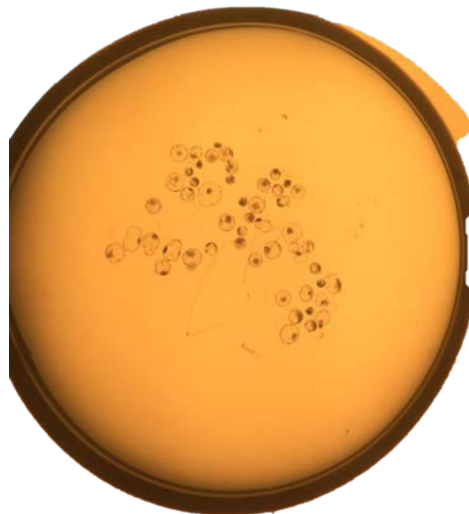


Consequences of Being Born From a Mother Fed a Low Protein Diet During the Preimplantation Period
(Watkins et al., Biol. Reprod. 78:299 (2008))



EXAMPLE OF ABERRANT PROGRAMMING
LARGE OFFSPRING SYNDROME
FOLLOWING EMBRYO PRODUCTION IN VITRO

- Salts
- Sugars
- Amino acids
- Fatty acids
- Proteins
- miRNA
- Exosomes
- Surface tension
- Motion
- Cell-cell interactions





98 kg at birth
picture at 2 days of age



8722 – IVF

Dried placenta weight – 9.1 g
Cotyledon diameter – 3.5 cm
Fetal weight – 152 g
Liver weight – 6.6 g
Heart weight - 1.4 g



7348 – IVF + CSF2

Dried placenta weight – 34.1 g
Cotyledon diameter – 5.6 cm
Fetal weight – 354.3 g
Liver weight – 18.6 g
Heart weight - 4.5 g

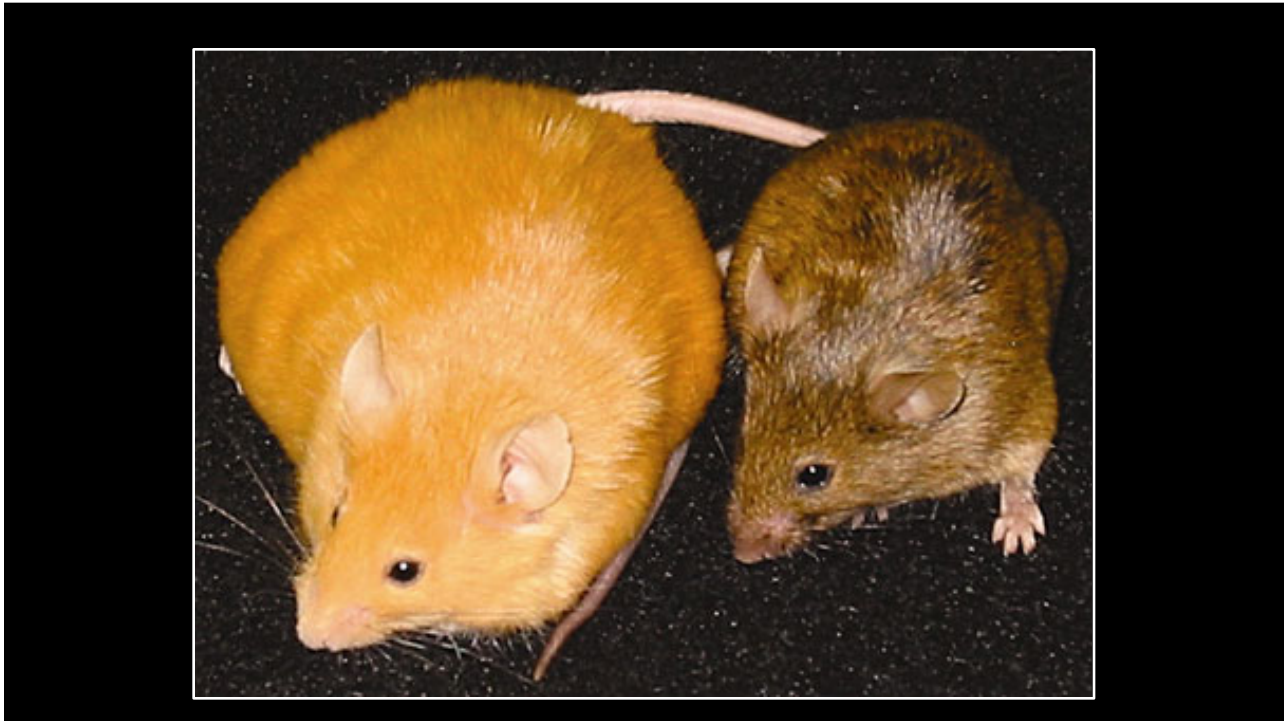
Take-home messages

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Example of this idea

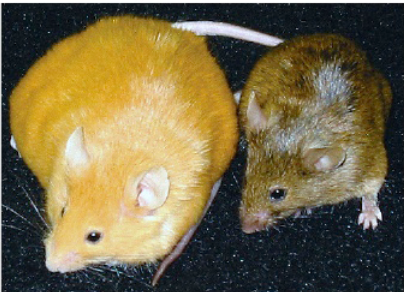
- Effects of choline treatment of embryos produced in vitro on birthweight and growth of the resultant calf





active inactive
 Agouti


These Two Mice are Genetically Identical and the Same Age



The mother of this mouse received a **normal mouse diet**

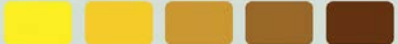

The mother of this mouse received a diet **supplemented** with choline, folic acid, betaine and vitamin B12

<http://learn.genetics.utah.edu/content/epigenetics/nutrition/>

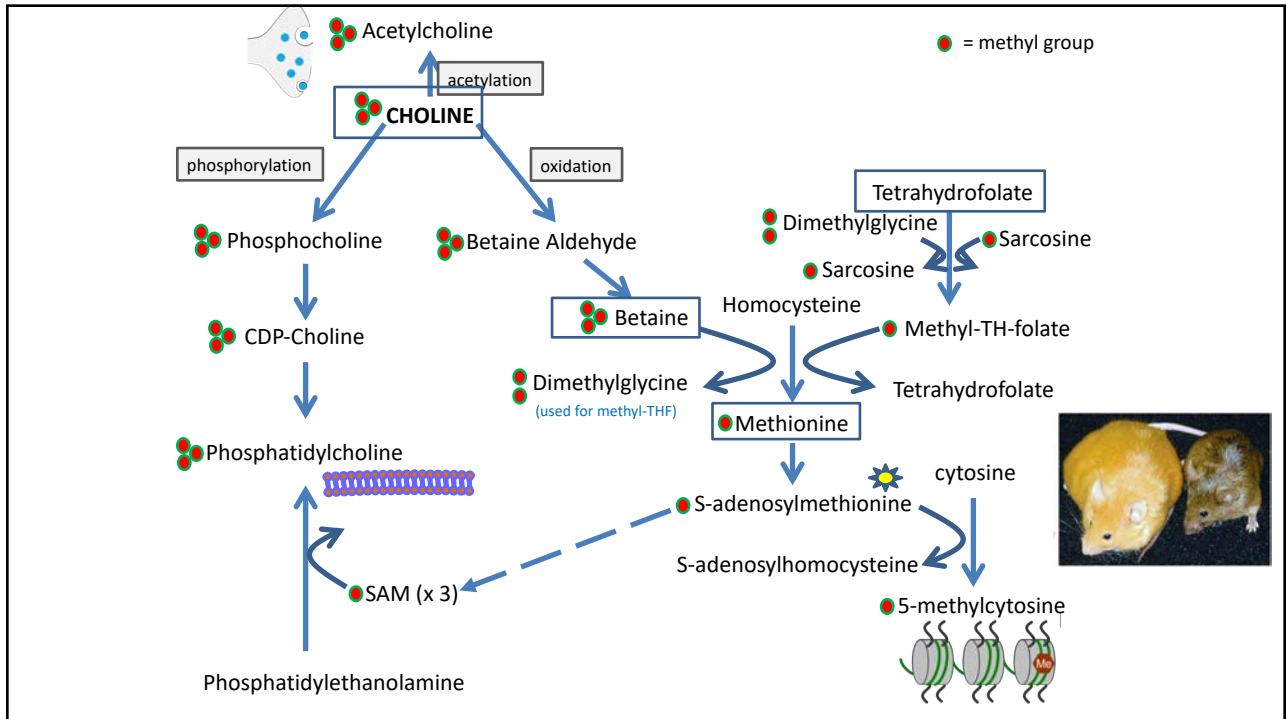
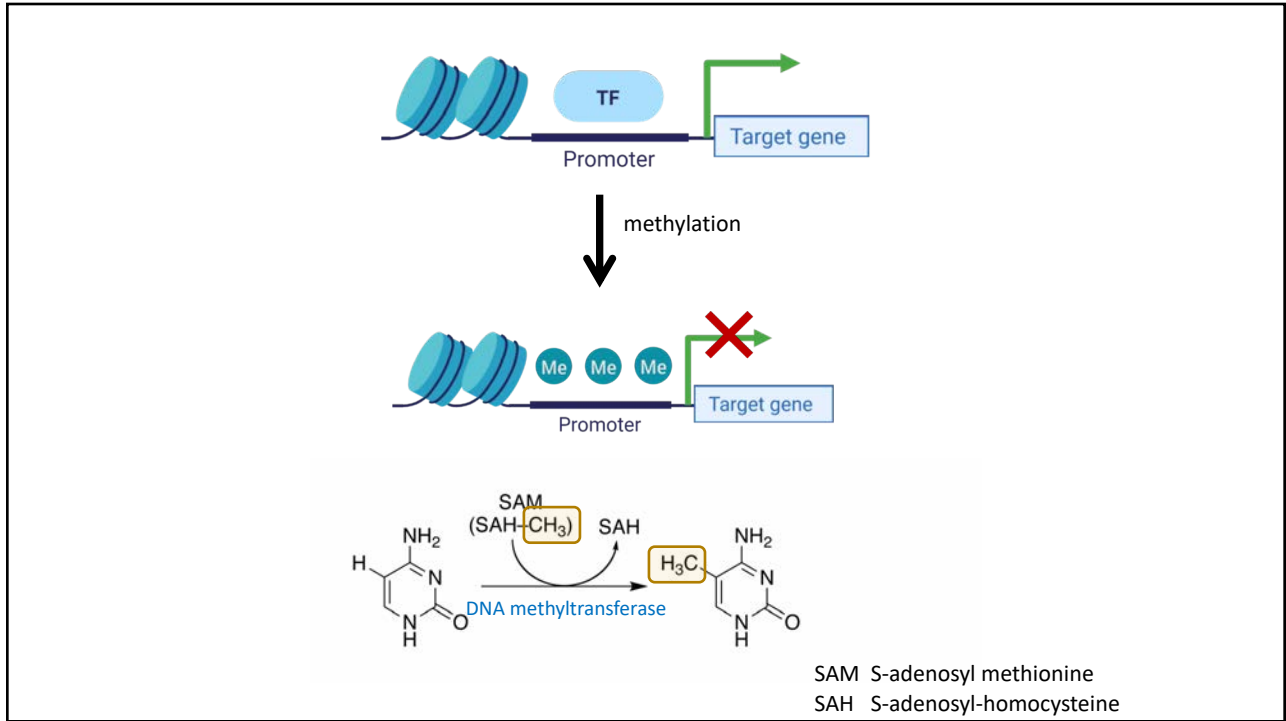


Randy L. Jirtle

Methylation of agouti locus

Methyl donors	→	Hypermethylated
Genistein	→	Hypermethylated
Ethanol	→	Hypermethylated
Radiation	→	Hypermethylated
		
Bisphenol A	→	Hypomethylated
<i>In vitro</i> culture	→	Hypomethylated
		

Epigenomics 6:447 (2014)



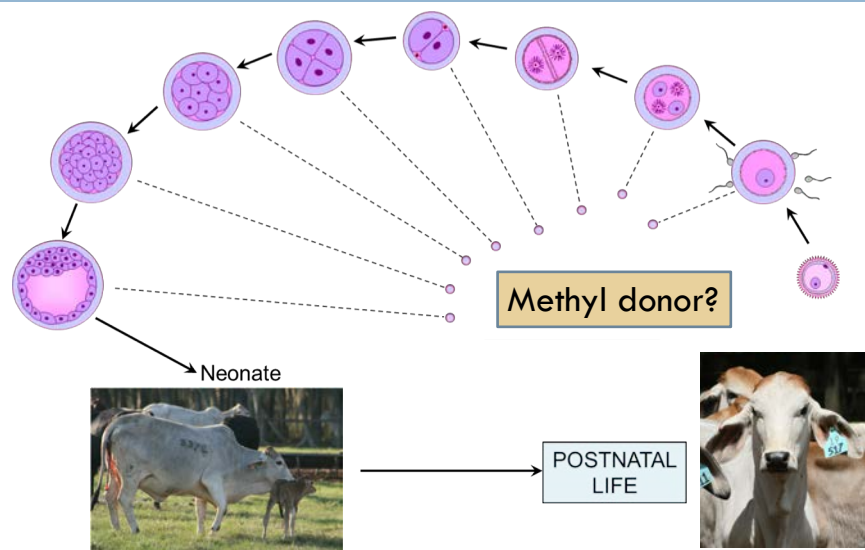
Take-home messages

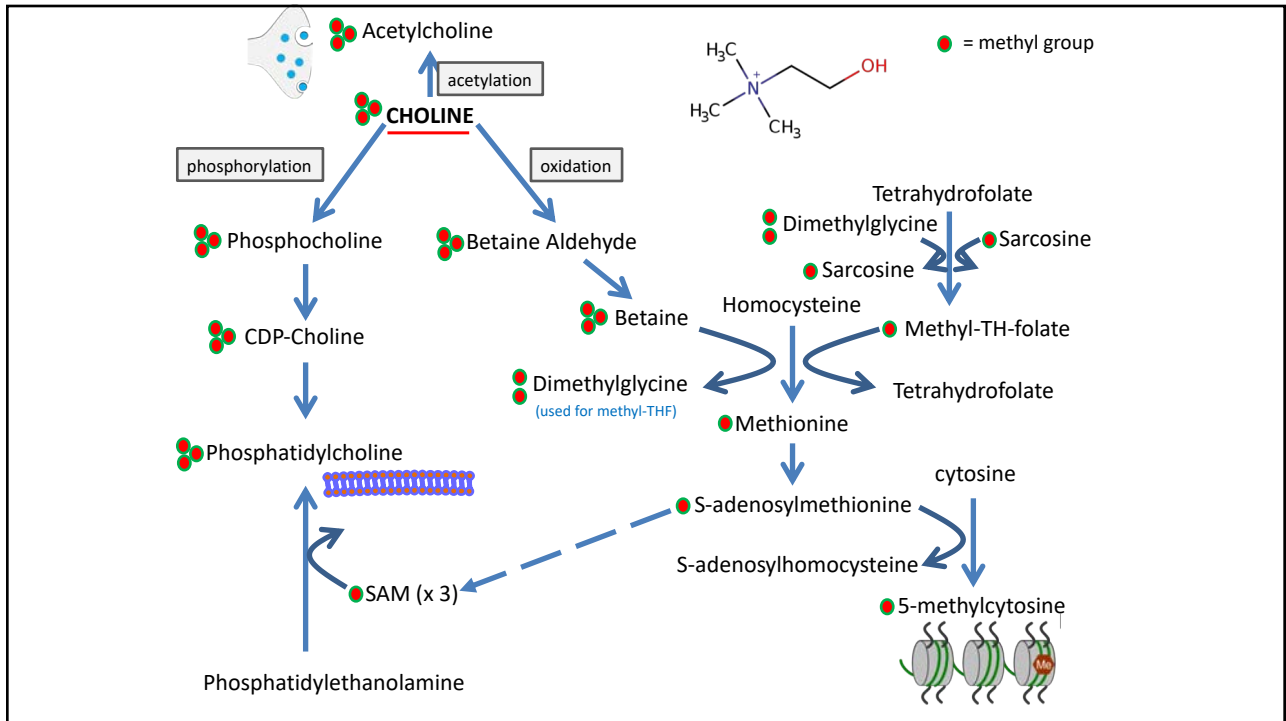
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Example of this idea

- Effects of choline treatment of embryos produced in vitro on 🌻 birthweight and growth of the resultant calf

Does feeding of choline program the embryo to affect the calf?

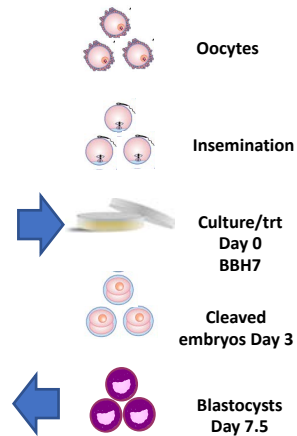




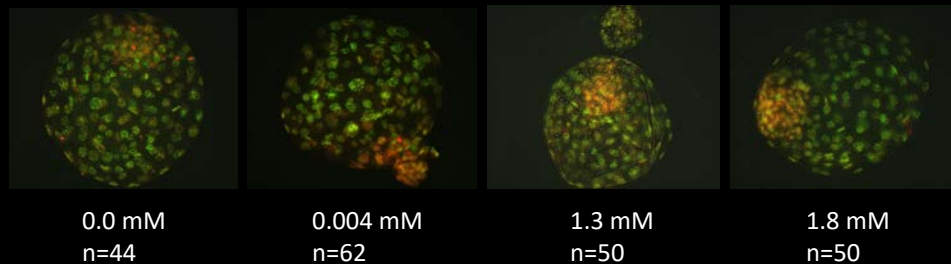
Choline effects on embryo development

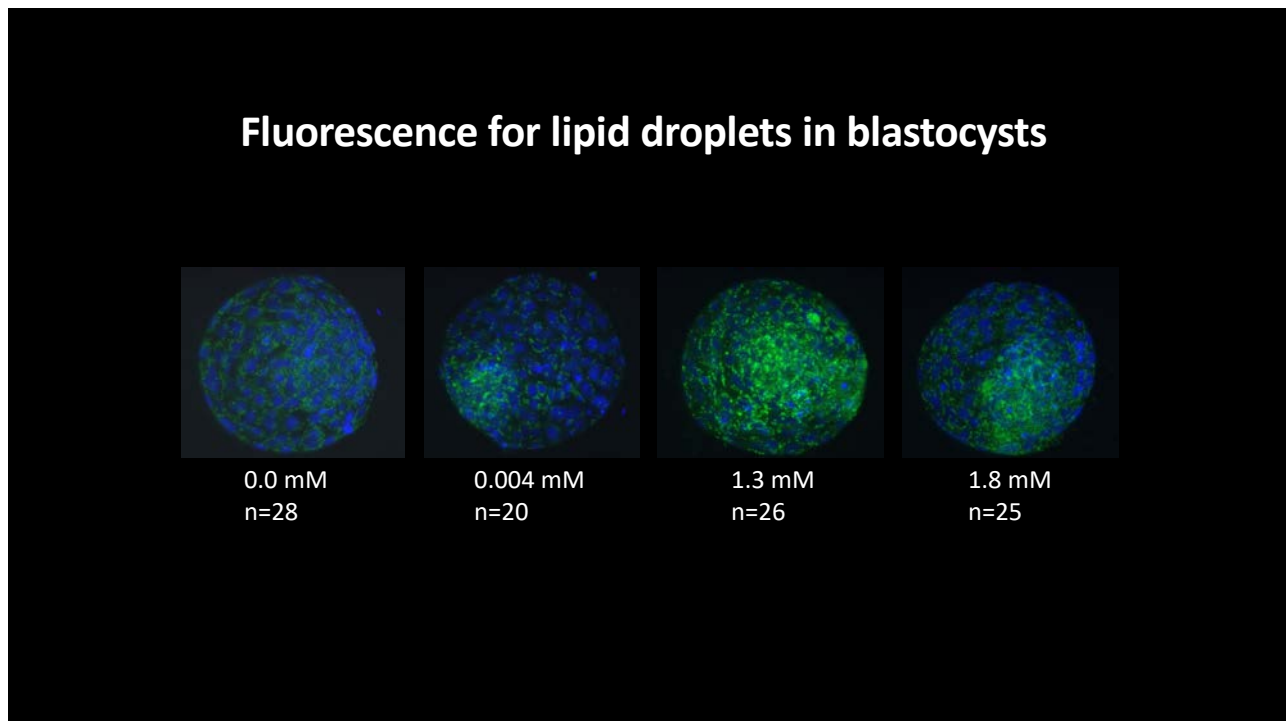
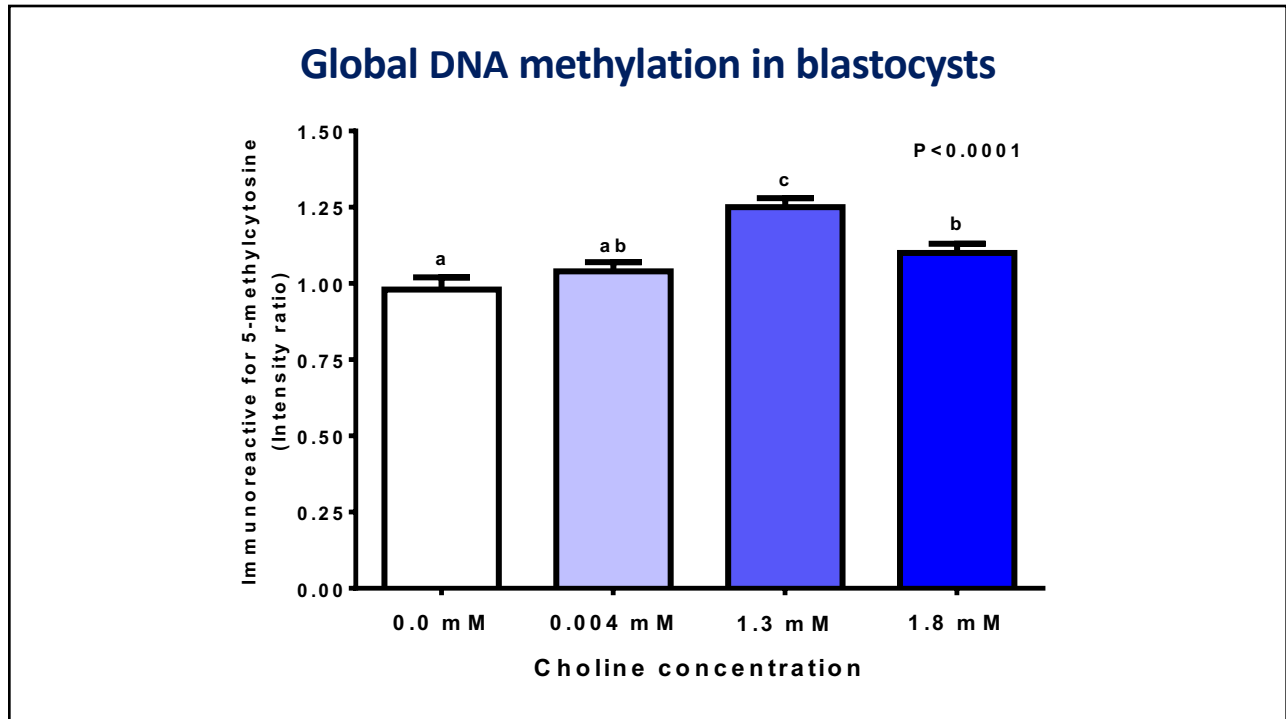
Criteria for concentration selection	[Choline chloride]	Sodium Chloride
Control	0.00 mM	6.37 mM
Total concentration of free choline in plasma of lactating dairy cows at week 1 postpartum	0.004 mM	6.37 mM
Total concentrations of choline in plasma of lactating dairy cows at week 1 postpartum	1.30 mM	5.07 mM
Total concentrations of choline in plasma of lactating dairy cows at week 1 postpartum assuming feeding RPC increased [choline] by 0.5 mM	1.80 mM	4.57 mM

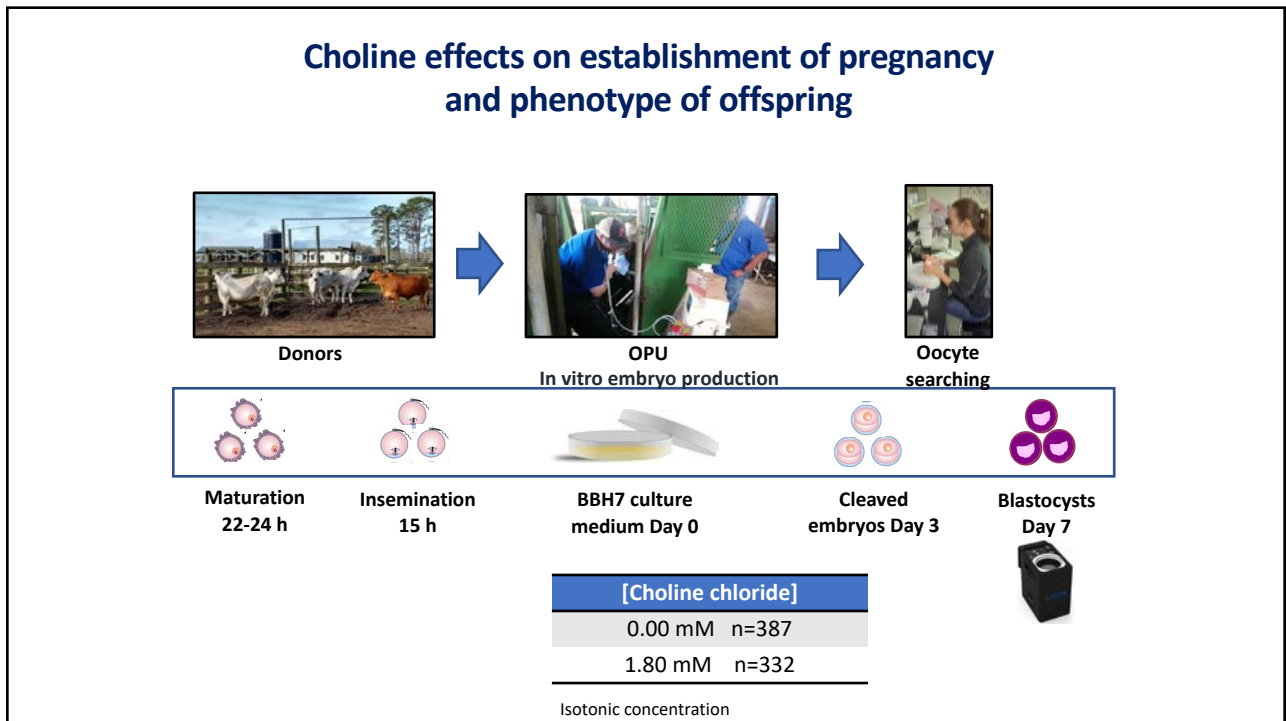
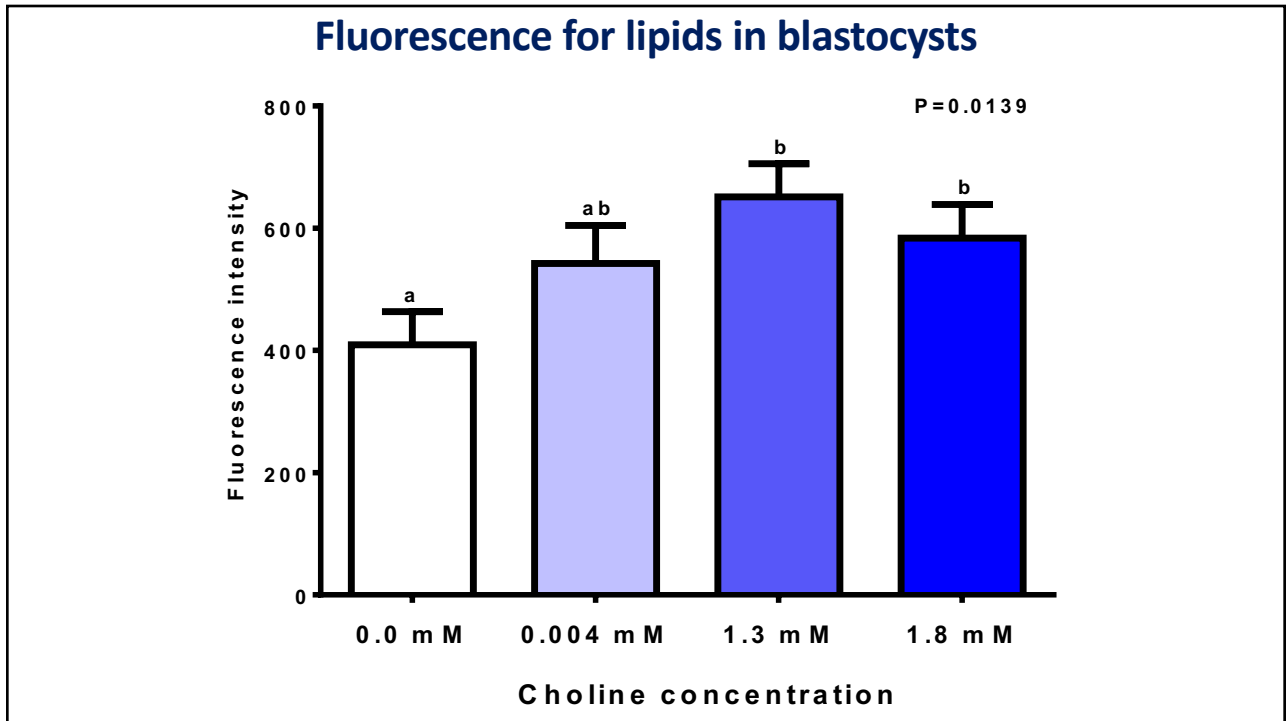
Artegoitia *et al.*, 2014; Zenobi and Staples, unpublished



Immunofluorescence intensity for 5-methyl cytosine in blastocysts







Choline effects on establishment of pregnancy and phenotype of offspring



Embryo transfer
Vehicle n=57 ET
Choline n=43 ET



Pregnancy diagnosis
28 d after ET



Birth weight



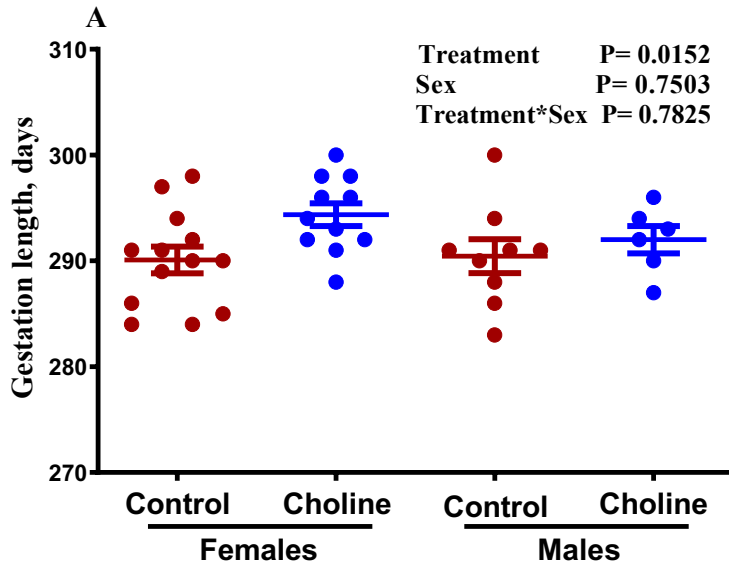
Weaning weight

Statistical analysis

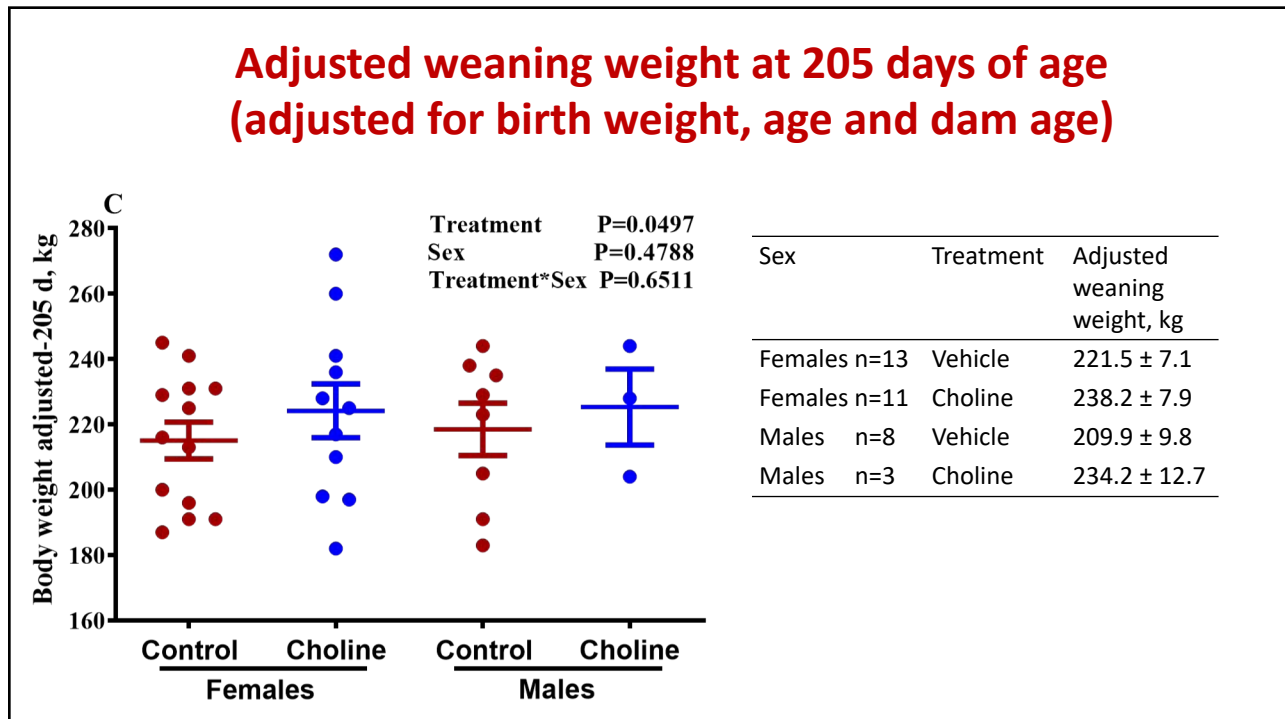
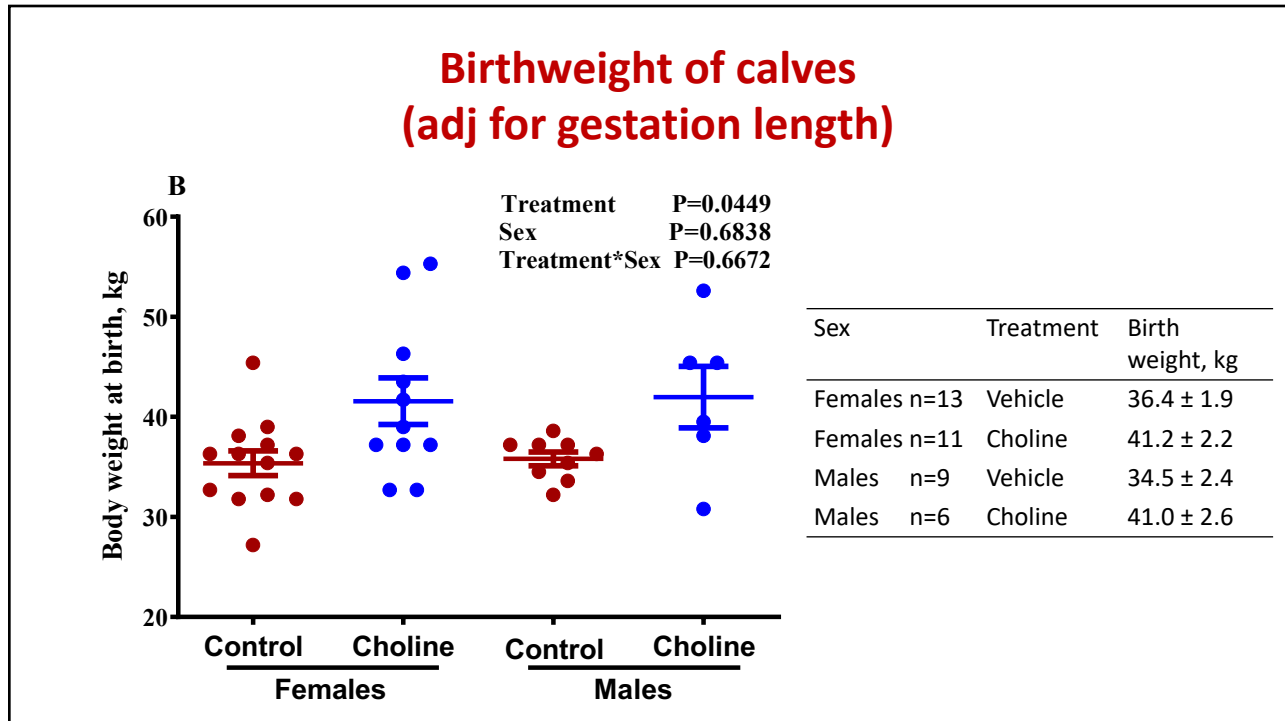
- For embryo development and pregnancy rate, proc Glimmix binary distribution, treatment and sire effects were included in the model

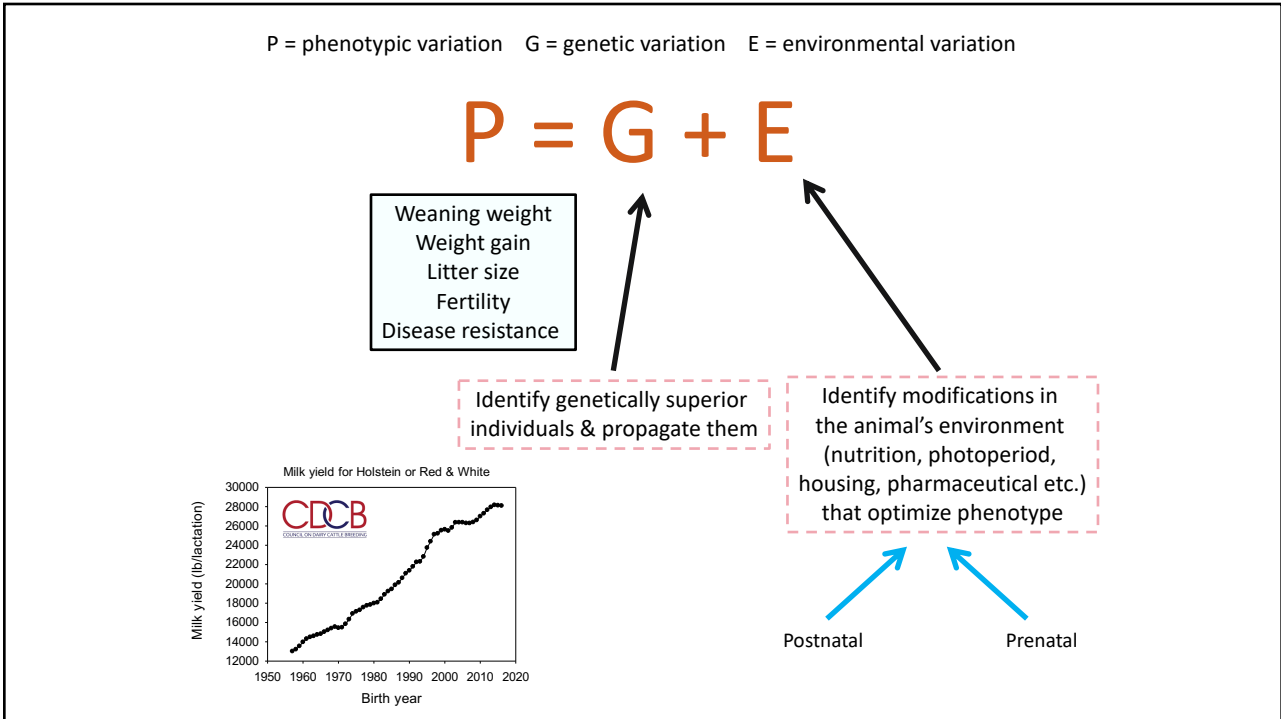
- For birth weight and weaning characteristics of calves, proc GLM, treatment, donor and sire effects were included in the model

Gestation length



Sex	Treatment	Gestation length, days
Females n=13	Vehicle	289.8 ± 1.4
Females n=11	Choline	294.6 ± 1.5
Males n=9	Vehicle	289.6 ± 1.7
Males n=6	Choline	293.6 ± 1.38





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R01 HD088352

Danny Driver
Audy Spell

Bert Faircloth
Michelle Driver



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