Session #25

"Epigenetic origins of litter phenotype and implications for post-natal performance"

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PIC

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Outline

1. Evidence for induced “litter phenotypes” in commercial sow populations.

2. In utero crowding effects on prenatal development

3. Metabolic (epigenetic) effects on prenatal development

4. Implications for management.

1. Evidence for induced “litter phenotypes” in commercial sow populations

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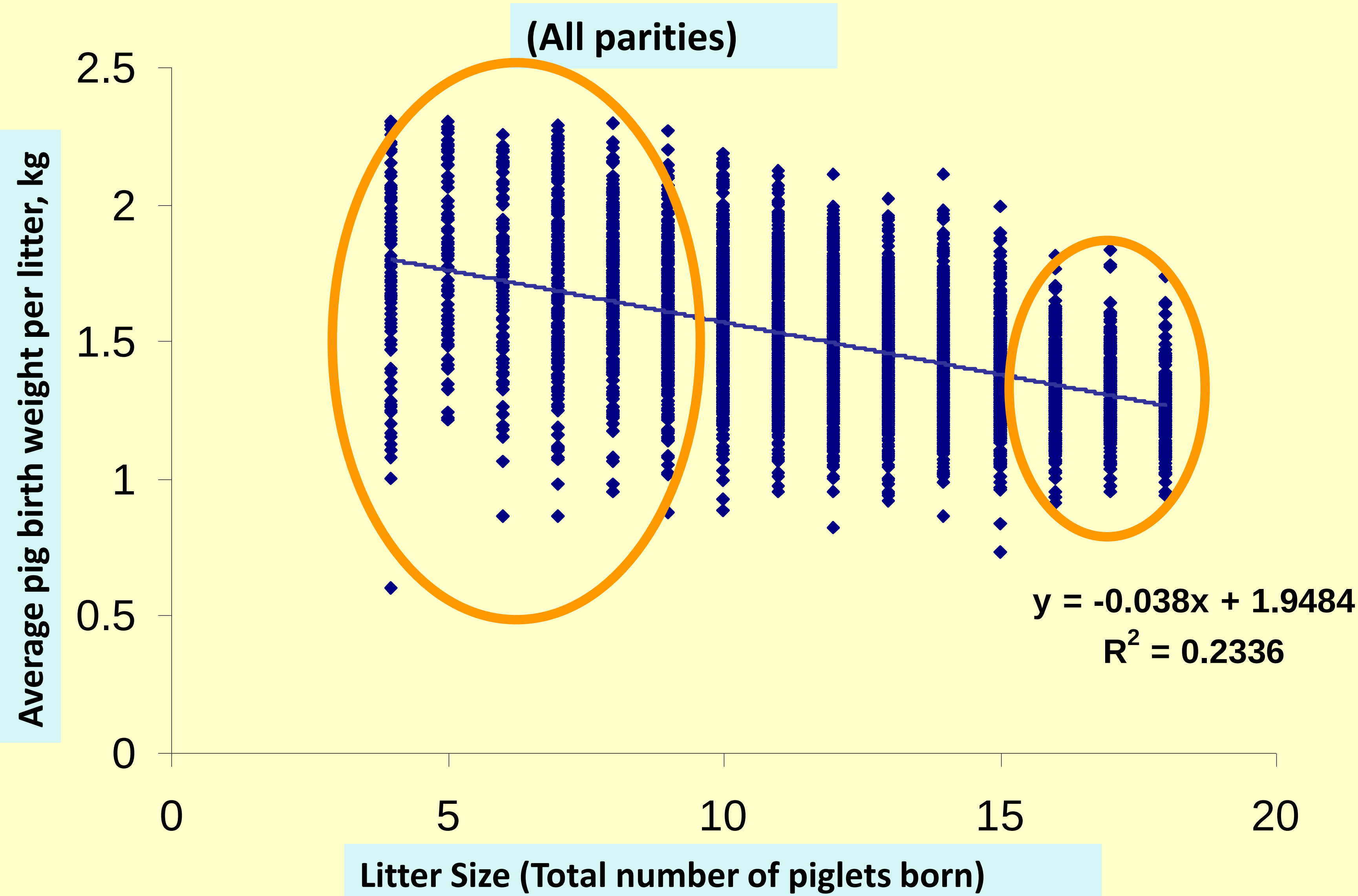
Correlation between birth weight and litter size



(M. Smit, 2007. MSc project – Univ. Alberta/Univ. Wageningen)

Characteristics of ““hyper-prolific”” sows

Production data recorded for individual hyperprolific, white-type, sows from commercial units in Brittany, France.

Sow parity	Total pigs born	Pigs born dead	Pigs born live	Adjusted litter size 48 h after farrowing
7	***20***	***6***	***14***	***12***
2	15	2	13	13
5	***19***	***5***	***14***	***11***
2	15	1	14	11
9	***14***	***1***	***13***	***12***
5	***13***	***0***	***13***	***12***
4	19	1	18	13
2	12	0	12	12
5	***13***	***1***	***12***	***10***
5	***18***	***0***	***18***	***11***
4	16	1	15	12
1	10	2	8	12
4	16	0	16	12
5	***18***	***3***	***15***	***11***
8	***22***	***5***	***17***	***11***
5	***13***	***7***	***6***	***12***

(Data are from personal communication, Leneveau, P.)

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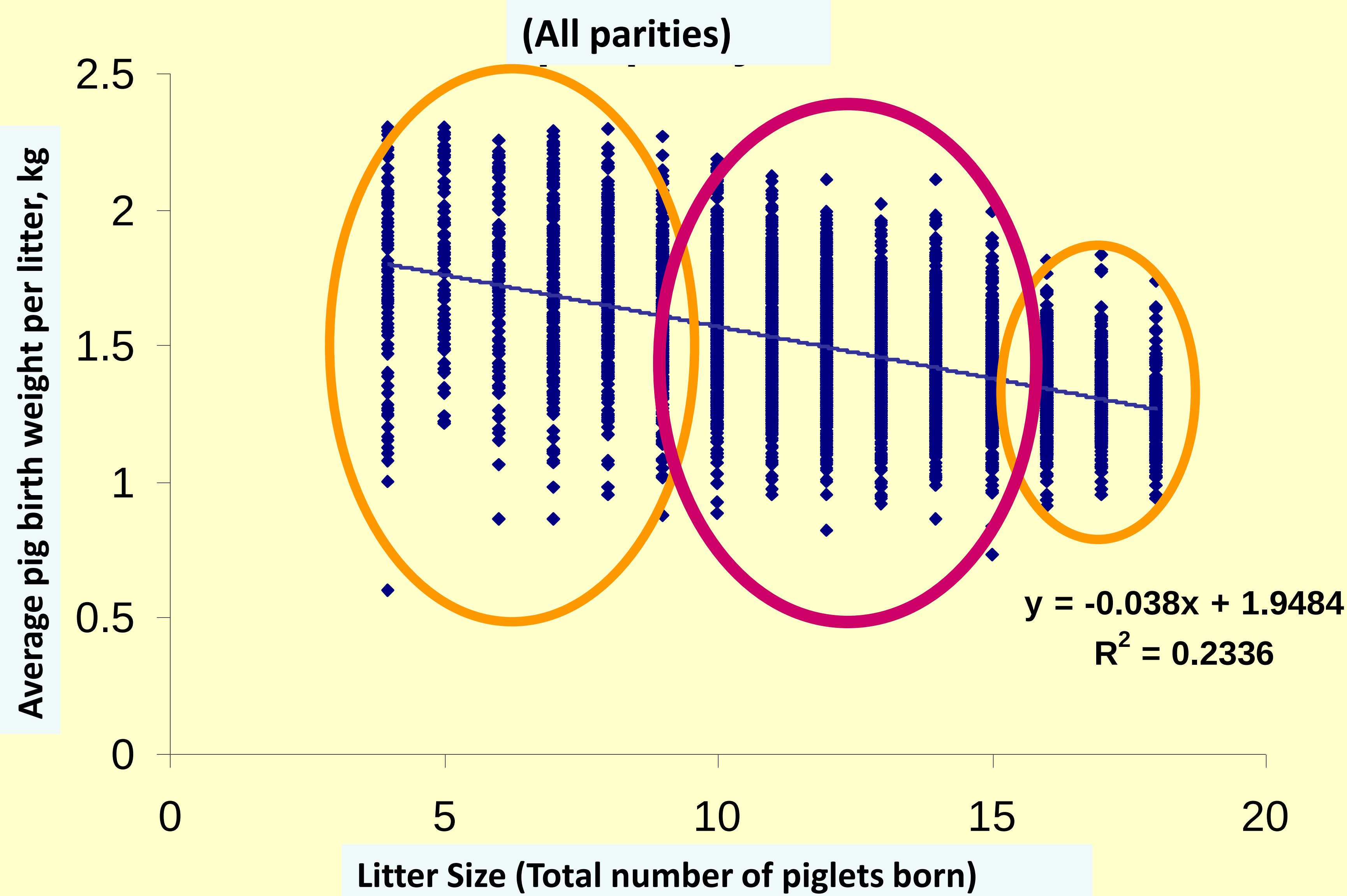
Negative ethical impacts need considering

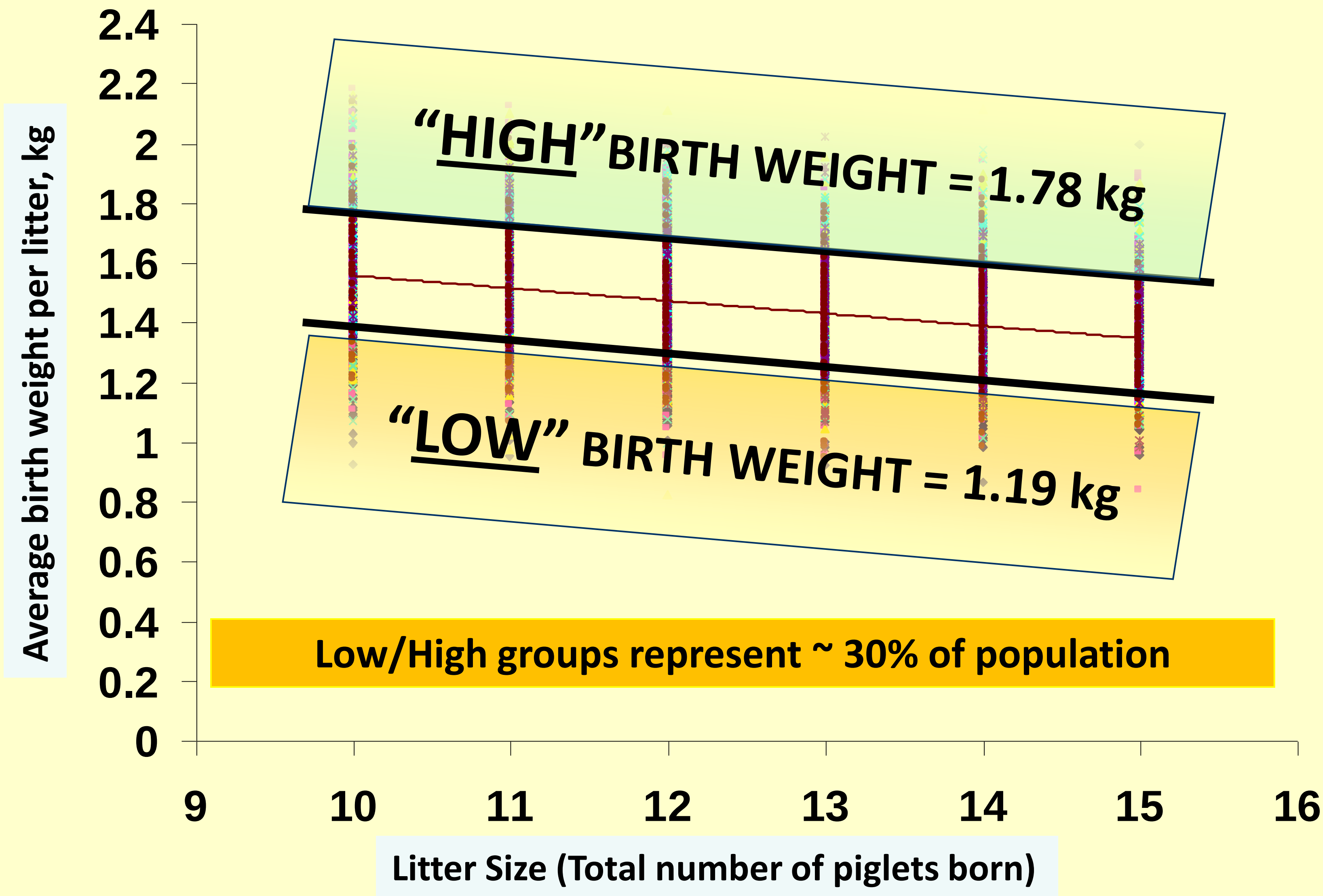
Boulot et al., 2008

Correlation between birth weight and litter size



(M. Smit, 2007. MSc project – Univ. Alberta/Univ. Wageningen)

Correlation between birth weight and litter size
(all parities)



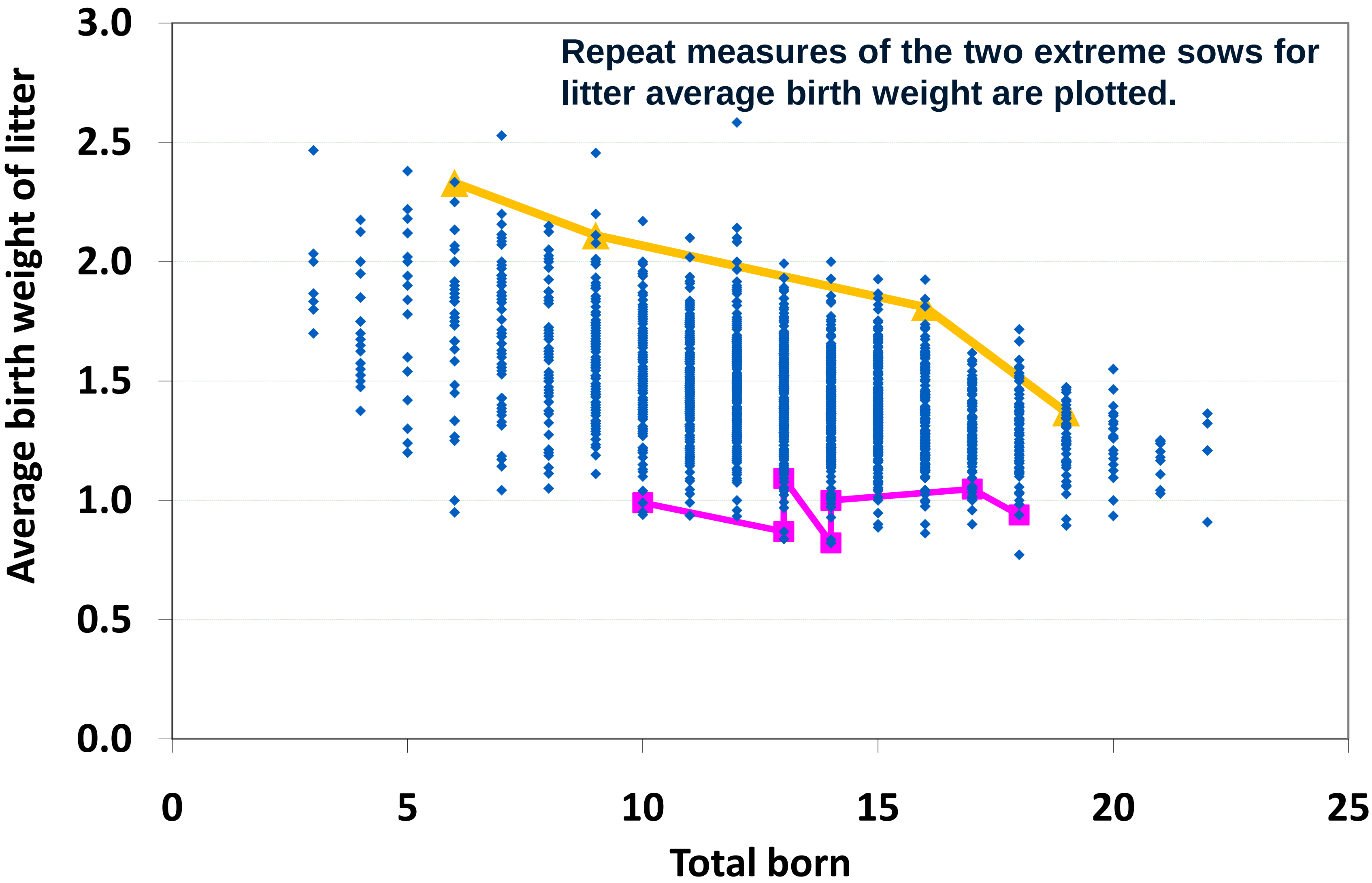
Characteristics of High and Low average birth-weight litters (n = 1,094)

	"High"	"Low"	*P*-Value
Ave Birth Weight	1.8 ± 0.01	1.2 ± 0.01	< 0.001
Total born	12.3 ± 0.08	12.3 ± 0.07	0.91
Born Alive	11.7 ± 0.09	11.0 ± 0.09	< 0.001
Born Dead	0.6 ± 0.07	1.2 ± 0.06	< 0.001
Weaned	10.8 ± 0.10	9.4 ± 0.10	< 0.001

(M. Smit, 2007. MSc thesis – Univ. Alberta / Univ. Wageningen)

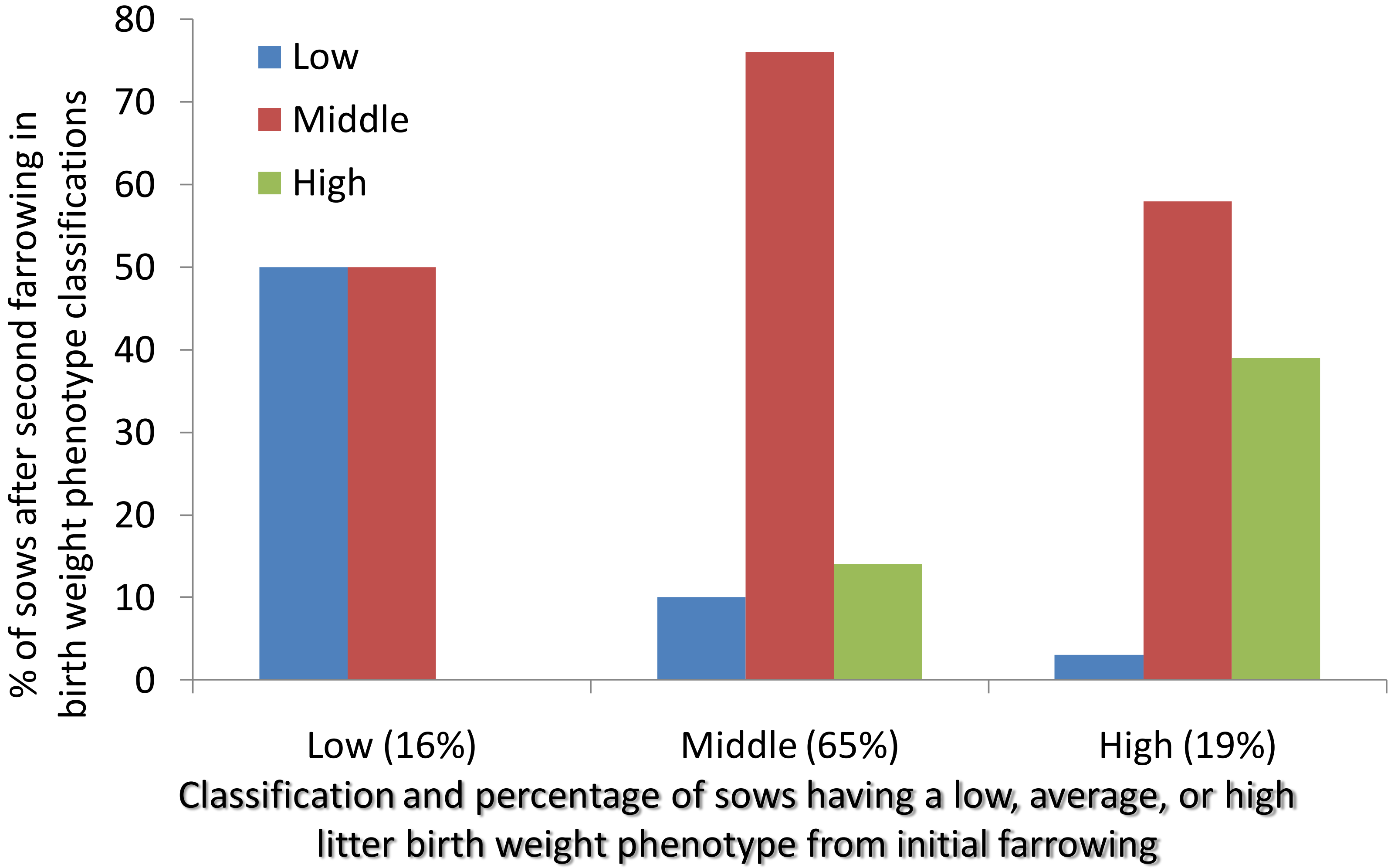
What is the repeatability of litter phenotype in commercial sows?

Relationship between litter average birth weight and litter size in a nucleus sow population.



(Knol et al., 2010)

Repeatability of sow birth weight phenotype (172 litters total)



(Preliminary data of Smit et al., 2010)

2. In utero crowding effects on prenatal development

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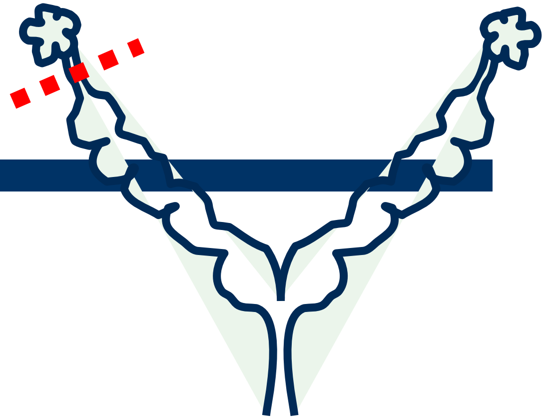
Experimental Studies



60 sows
(Genex – 3rd parity)

30 sows – Control

(Relatively Crowded)

15 sows (d30)

15 sows (d90)

30 sows - Oviduct Ligation

(Non-Crowded)

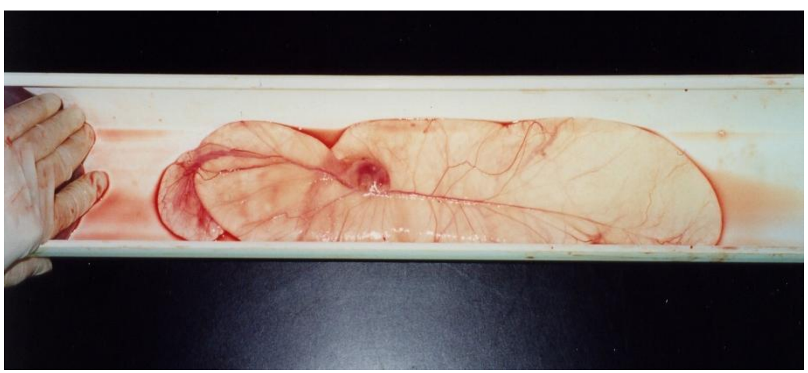
15 sows (d30)

15 sows (d90)

(Town et al., 2004: Reproduction 128, 443-154)

Study Design – Animals

Necropsy at day 30… ….or day 90



- for analysis of fetal and placental development
- organ and muscle development at day 90

Effects at d 30	Control (Relatively Crowded) N = 15	Ligated (Non Crowded) N = 15	P
"Available" ovulation rate	19.2 ± 0.5	10.5 ± 0.6	<0.001
Number of viable embryos (d30)	15.1 ± 0.8	9.3 ± 0.8	<0.001
Embryo survival (%)	79 ± 3	91 ± 2	0.01
Embryo weight (g)	1.15 ± 0.05	1.22 ± 0.05	NS
Placental weight (g)	19.2 ± 1.0	26.2 ± 1.4	<0.001

(Town et al., 2004: Reproduction 128, 443-154)

Myogenesis

Biphasic pattern of prenatal muscle development

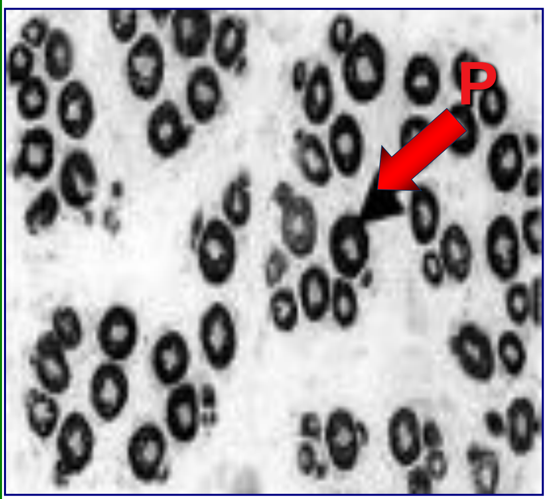
primary myofibres

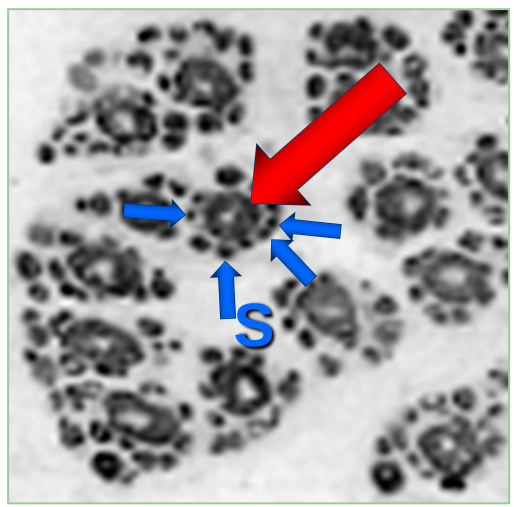
secondary myofibres

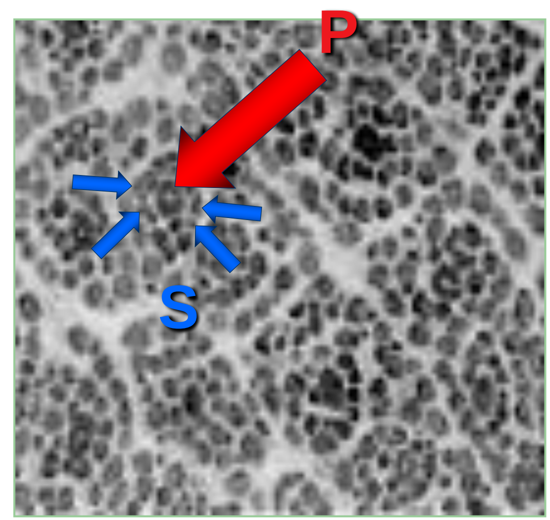
total number of myofibres is fixed

birth

d 35 | **d 55** | **d 90**





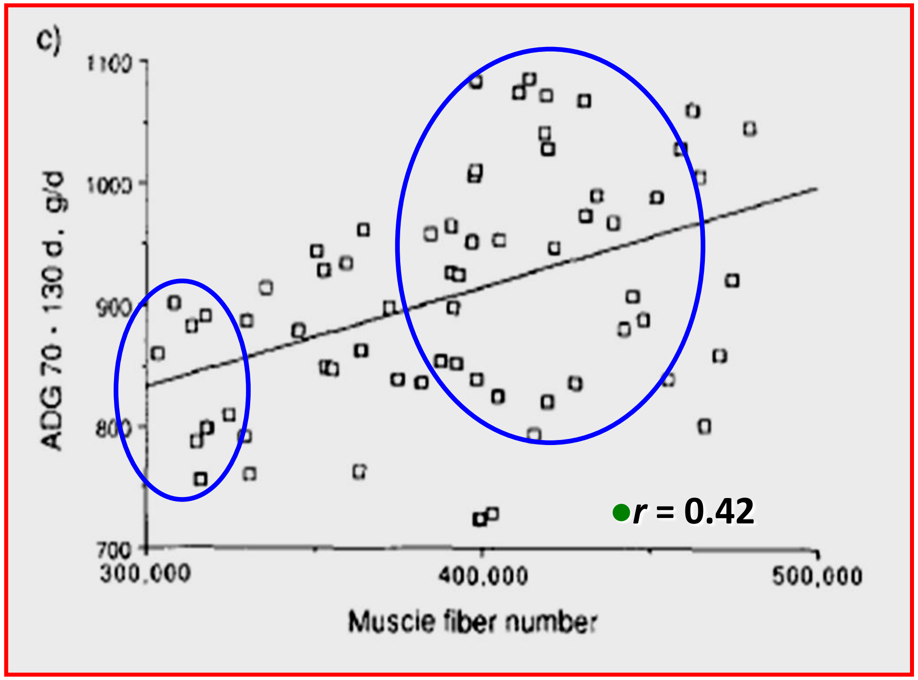


(Guiseppe Bee after Picard et al., 2002 Reprod. Nutr. Dev. (2002) 415-431)

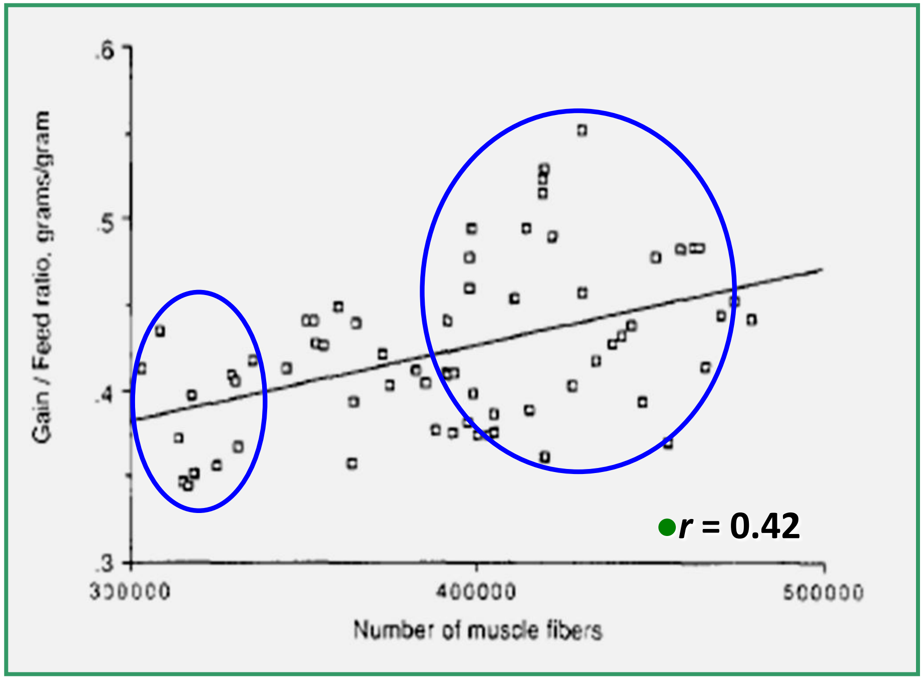
Total myofibre number (TFN)

Importance for postnatal growth

ADG vs. TFN



G/F vs. TFN



(Dwyer et al. 1993 J. Anim. Sci. 1993. 71:3339-3343)

Effects at d 90	Control (Crowded) N = 15	Ligated (Non Crowded) N = 15	P
Number of fetuses	14.4 ± 0.5	9.4 ± 0.7	< 0.001
Survival to d 90 (%)	75.5 ± 2.5	84.4 ± 3.2	< 0.05
Fetal weight (g)	588 ± 18	679 ± 18	< 0.05
Placental weight (g)	219 ± 8	274 ± 14	< 0.05
Brain:Liver wt ratio	1.17 ± 0.04	0.97 ± 0.04	< 0.05
Brain:Muscle wt ratio	10.49 ± 0.43	9.25 ± 0.33	< 0.05

(Town et al., 2004: Reproduction 128, 443-154)

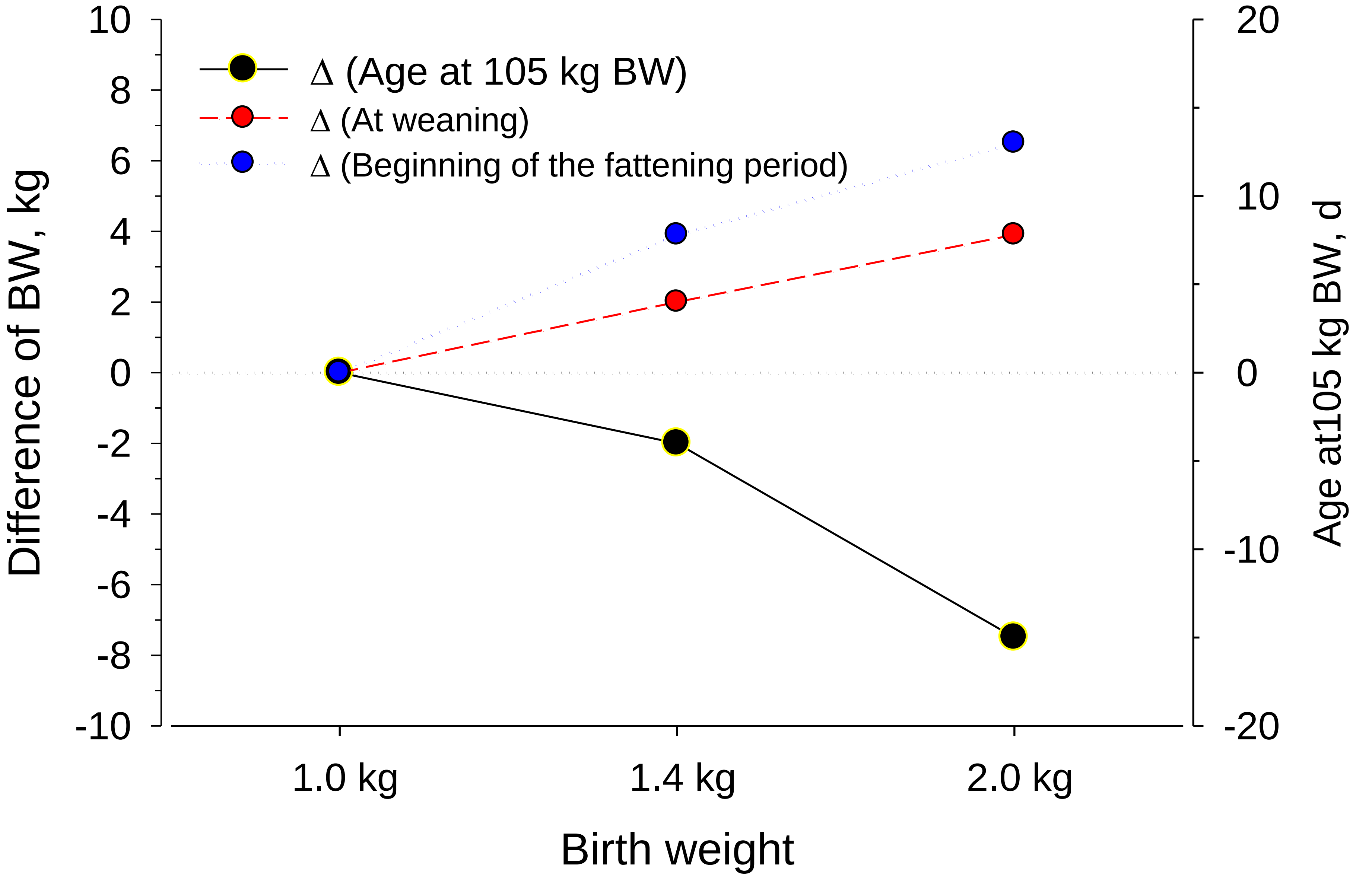
Conclusions

“Brain sparing” effects occur in lower birth-weight piglets, <u>and in low average birth weight litters</u>

Effects on fetal development may not be normalized as part of post-natal compensatory growth (e.g. muscle fibre number initially set by d90-95?)

Difference of BW at **weaning** and at beginning of the **fattening** period

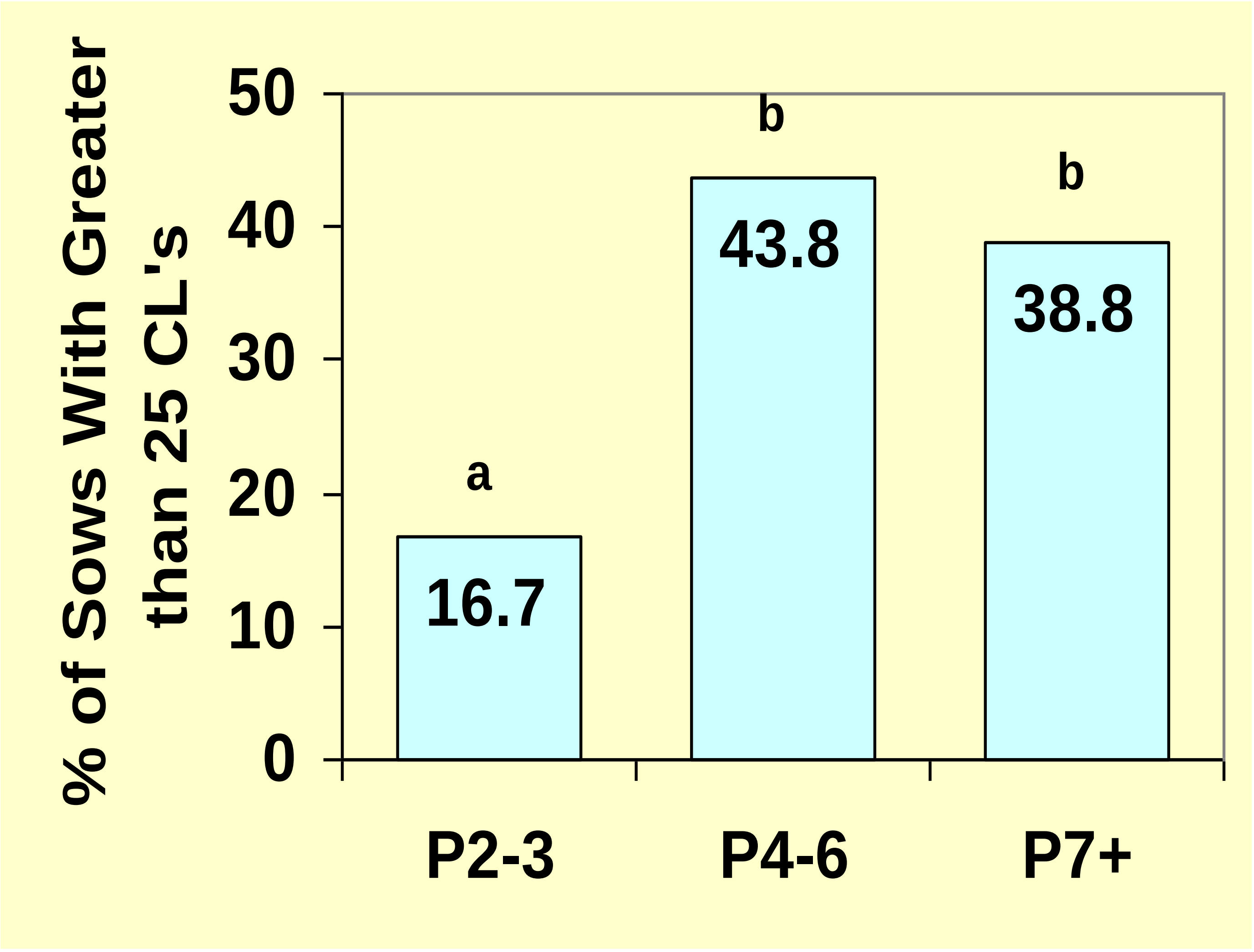
Difference of age at 105 kg BW



(Quiniou, 2002 Livestock Production Science (2002) 78:63-70)

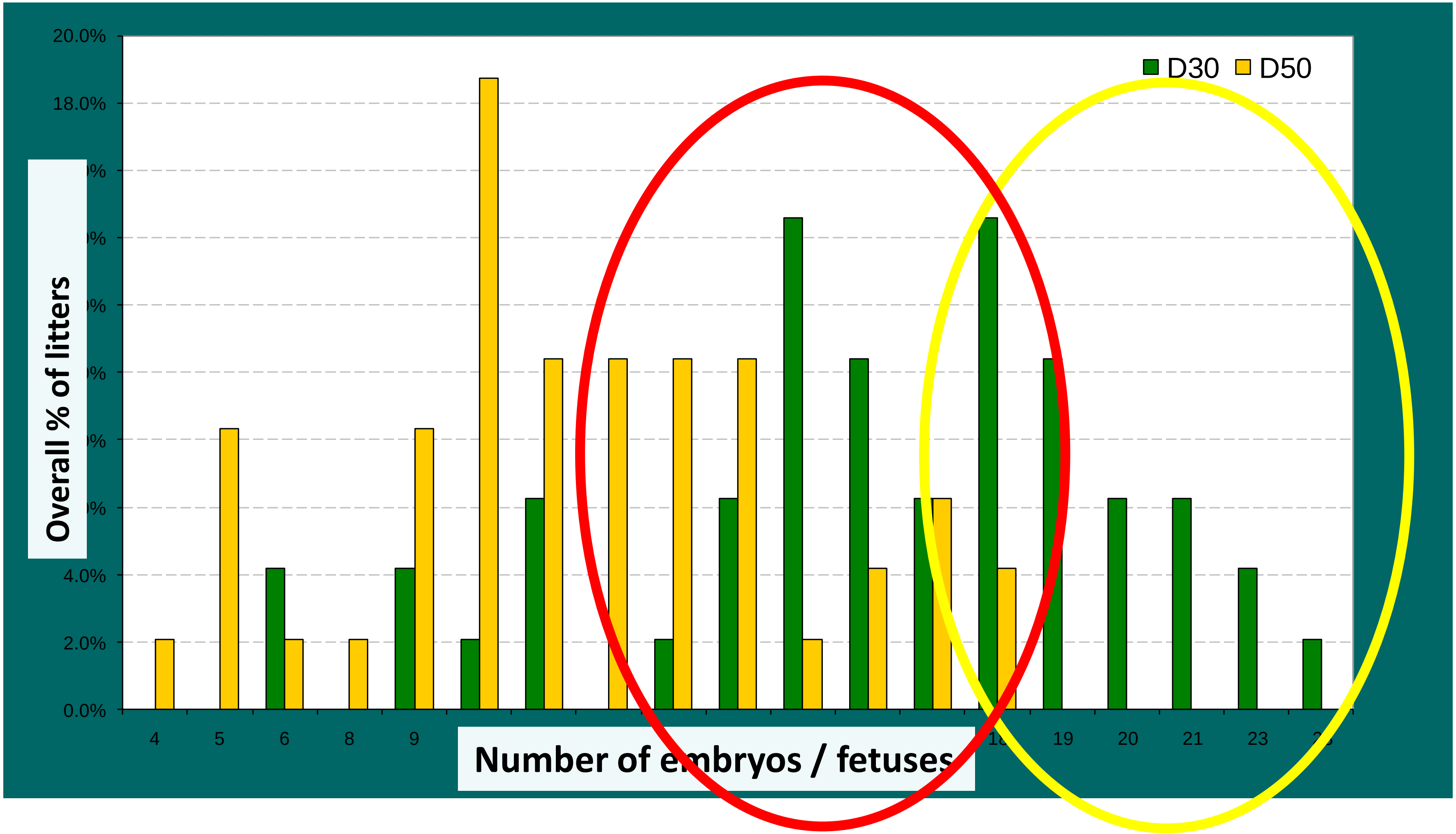
Studies with contemporary commercial sows

Ovulation rate x parity interactions in sows

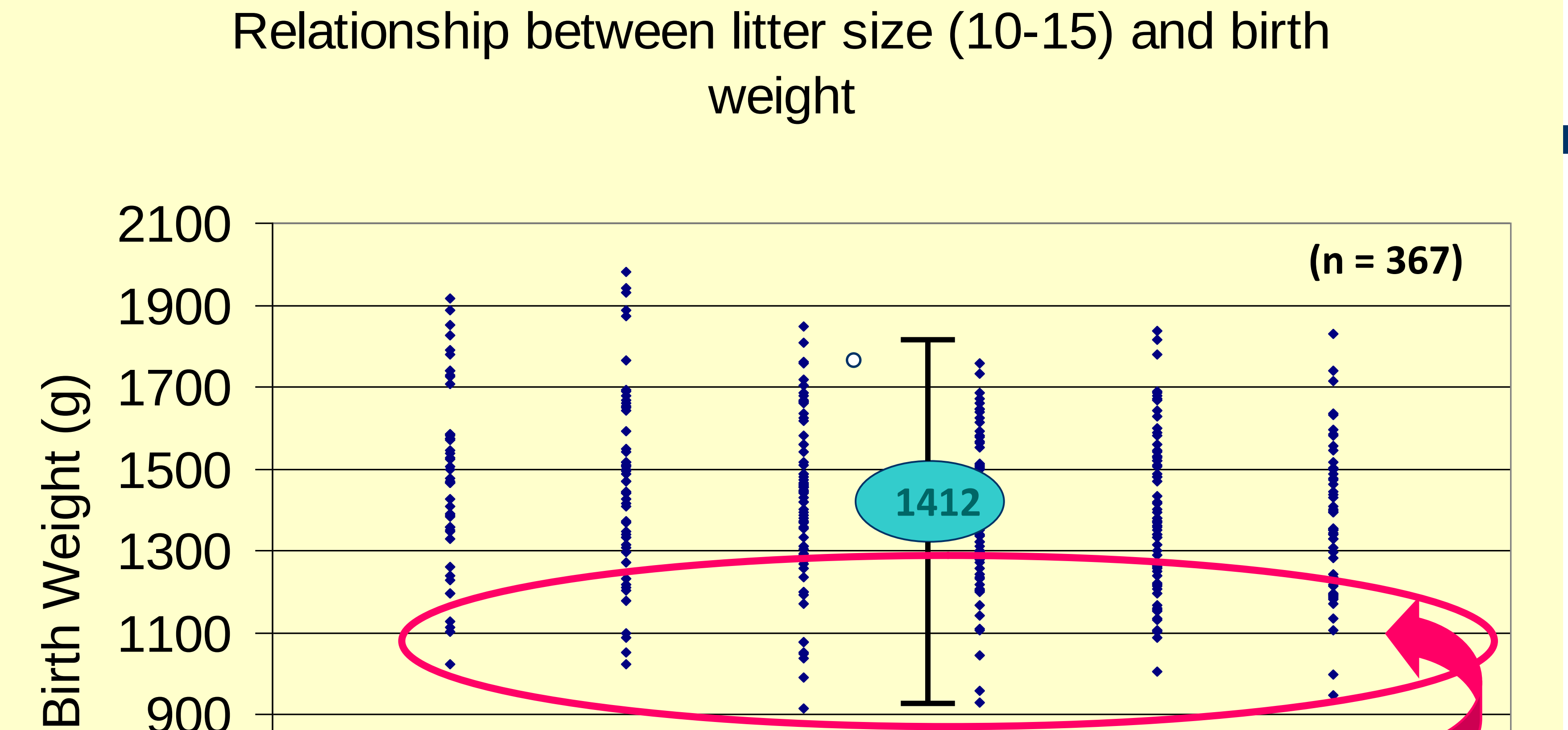


(Patterson et al., 2008:J. Anim. Sci., 86, 1996-2004)

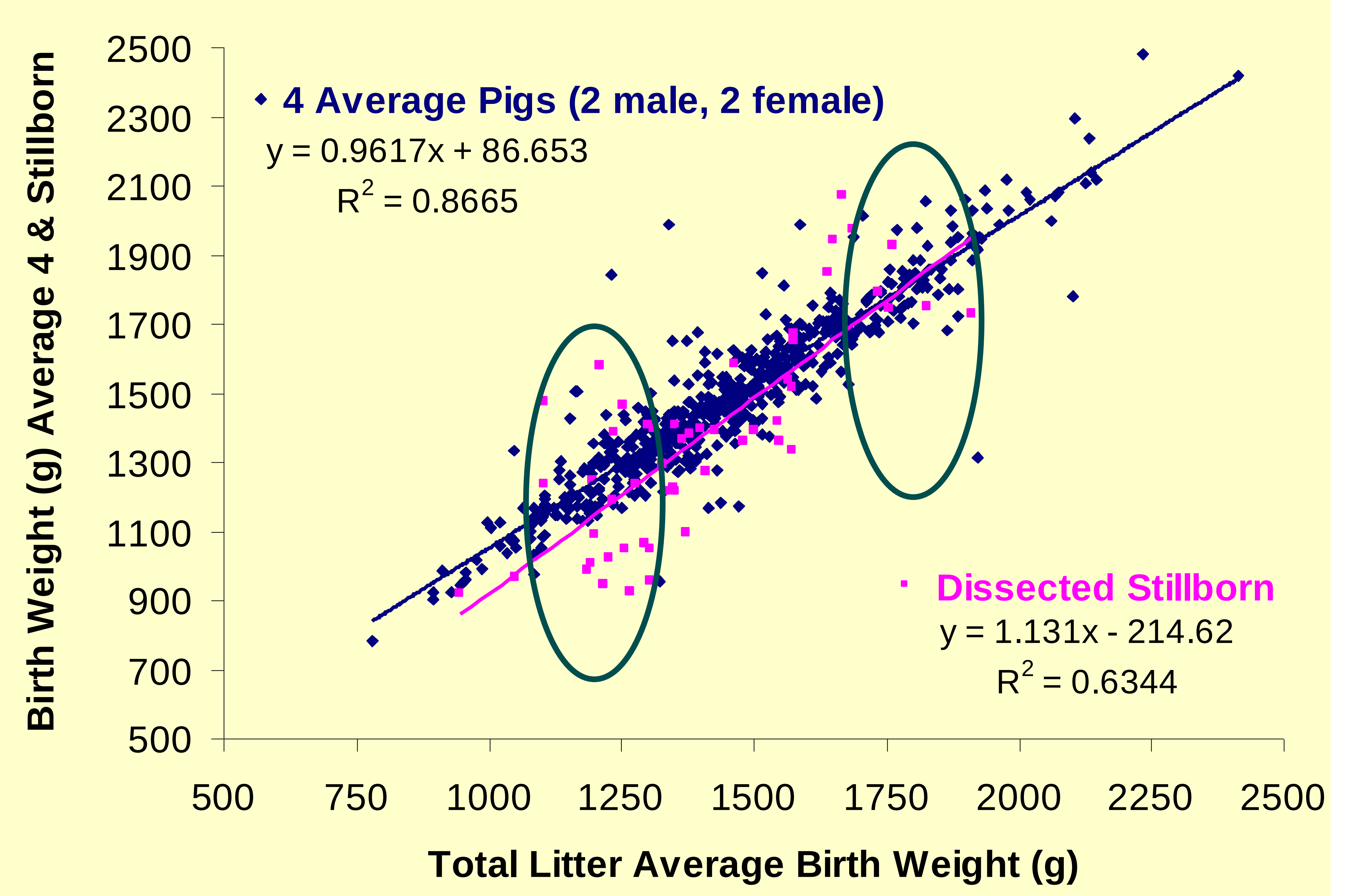
Evidence for early intra-uterine crowding and a wave of fetal losses by day 50



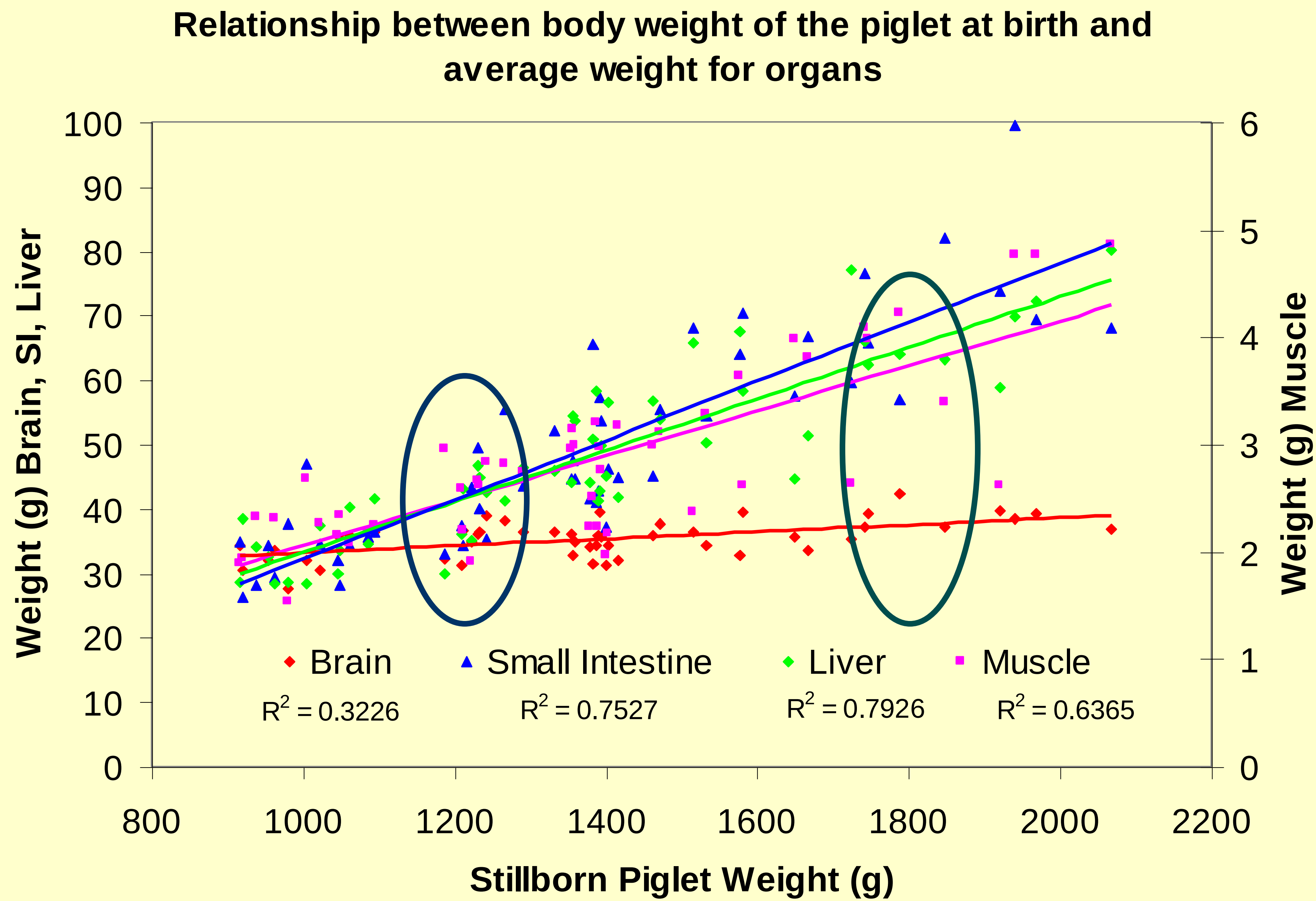
(From Patterson et al., 2008)



Hypothesis: Low average birth weight ***litters*** are a consequence of high ovulation rates, linked to early crowding of embryos *in utero* in early gestation and detrimental effects on placental development linked to IUGR later in gestation.



(SRTC – University of Alberta; unpublished data, 2007)



(SRTC – University of Alberta; unpublished data, 2007)

3. Metabolic (epigenetic) effects on prenatal development

“Nutrition and metabolic state of the lactating and weaned sow exerts lasting effects on the quality of the subsequent litter”

Characteristics of contemporary dam-lines:

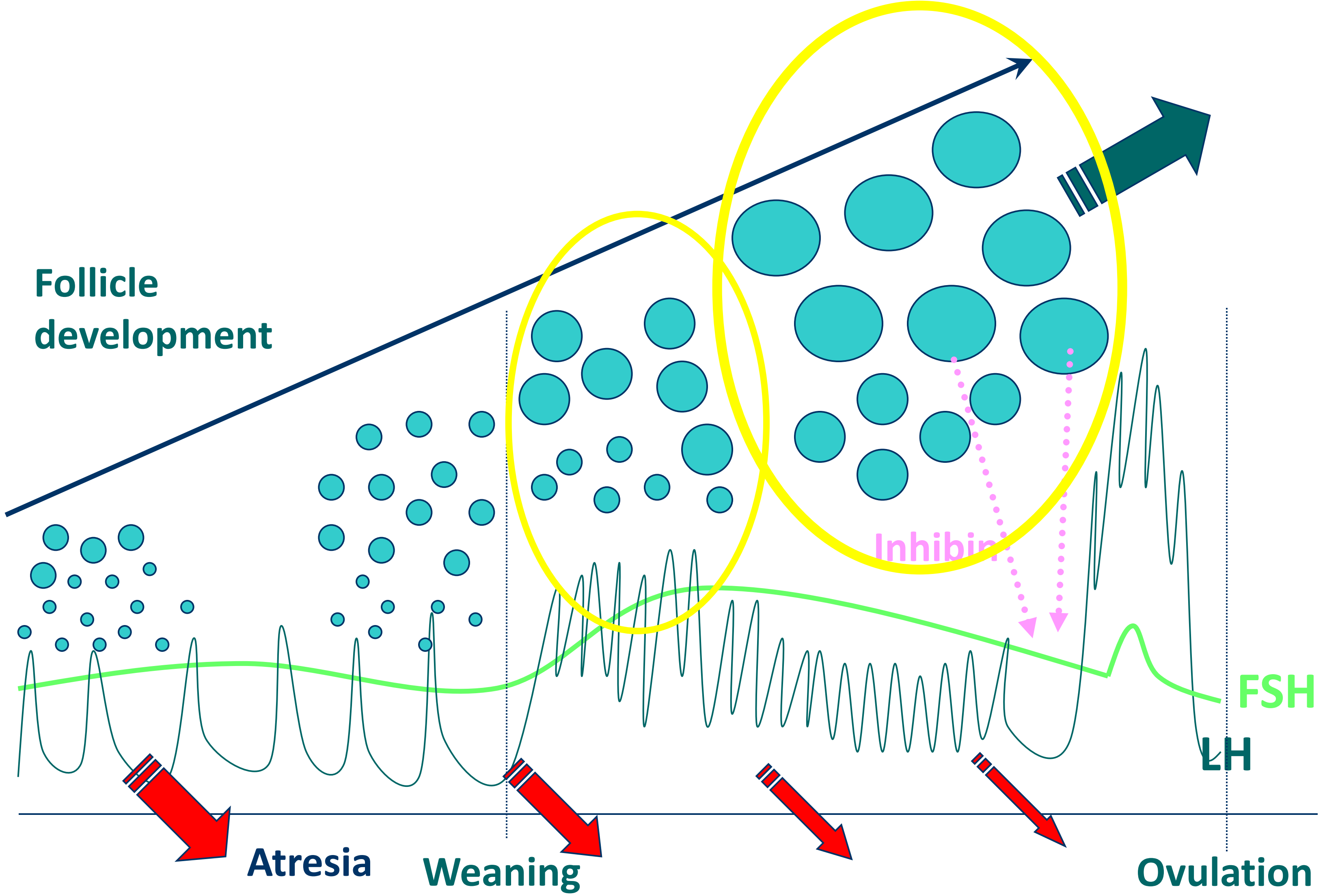
Little variance in Weaning-to-Estrus interval

Little time to allow "normal" follicular growth …

…. no effects on ovulation rate but effects on follicle size and quality

<u>Variability in embryonic survival/quality</u> are limiting for subsequent litters born

Earlier studies established that sow catabolism in late lactation affected follicular development and oocyte quality at weaning



Sow reproduction data – d30 gestation (LSM ± SEM)

Item	Control (n=16)	Restrict (n=17)	P value
Embryonic survival (%)	78.7 ± 6.7	67.6 ± 6.5	0.04
Number of Males	7.75 ± 0.59	7.53 ± 0.57	0.79
Number of Females	6.50 ± 0.57	4.71 ± 0.56	0.03

(Vinsky et al., 2006)

Embryonic & placental effects at d 30

	Control Males (n=124)	Restrict Males (n=128)	P	Control Females (n=104)	Restrict Females (n=80)	P
Embryo weight (g)	1.42 (± 0.29)	1.34 (± 0.30)	0.02	1.52 (± 0.02)	1.35 (± 0.03)	<0.001
Trophoblast volume (ml)	227.5 (± 8.2) (n=59)	231.7 (± 7.2) (n=58)	0.70	215.2 (± 8.7) (n=46)	236.6 (± 9.5) (n=39)	0.10

Main metabolic effect is directly on the embryo, in contrast to effects on placental development due to crowding

Are imprinted genes be involved ?

(Vinsky et al., 2006)

Are epigenetic mechanisms involved?

….. ideas from experimental studies on imprinting mechanisms and links to nutrition and metabolism

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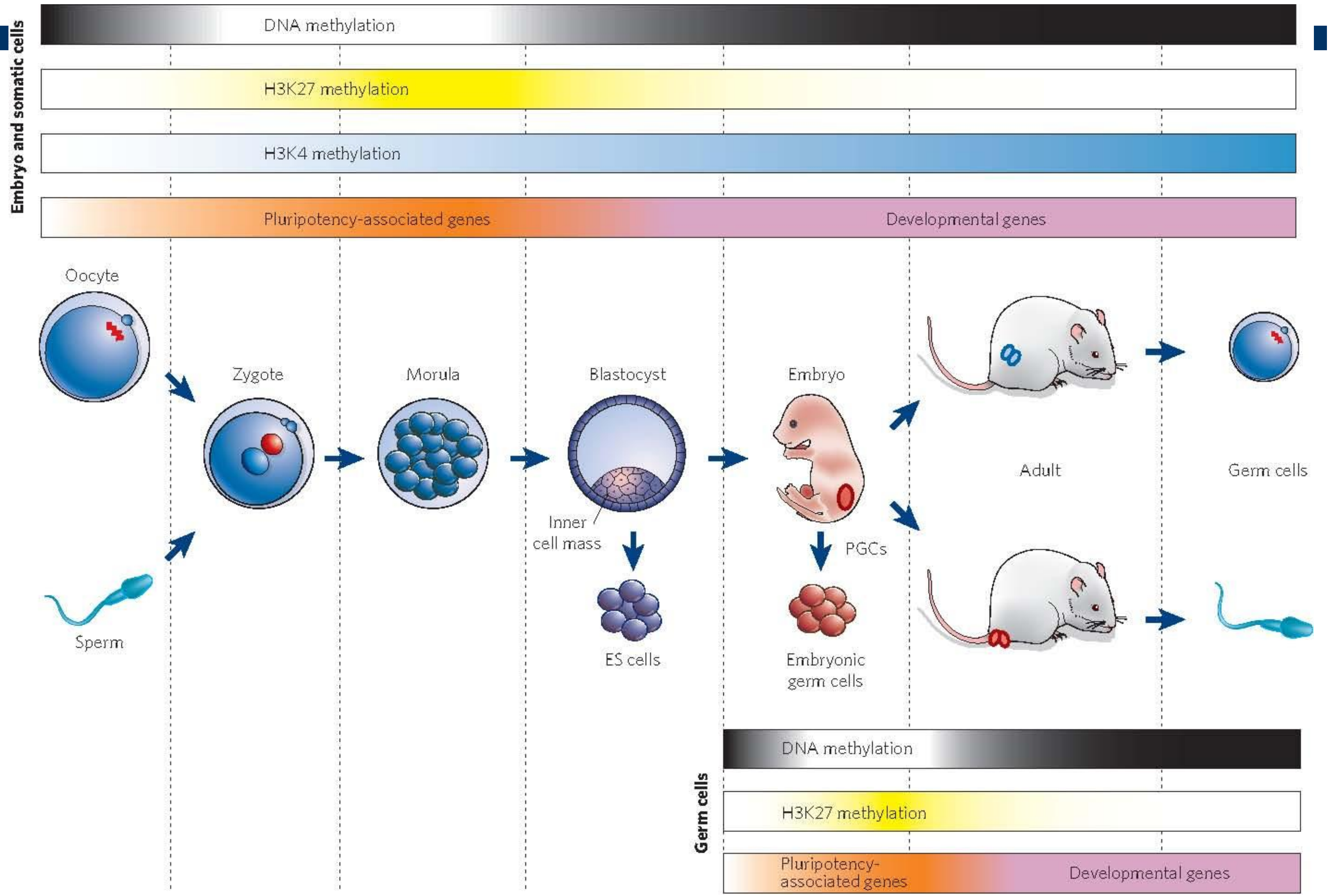
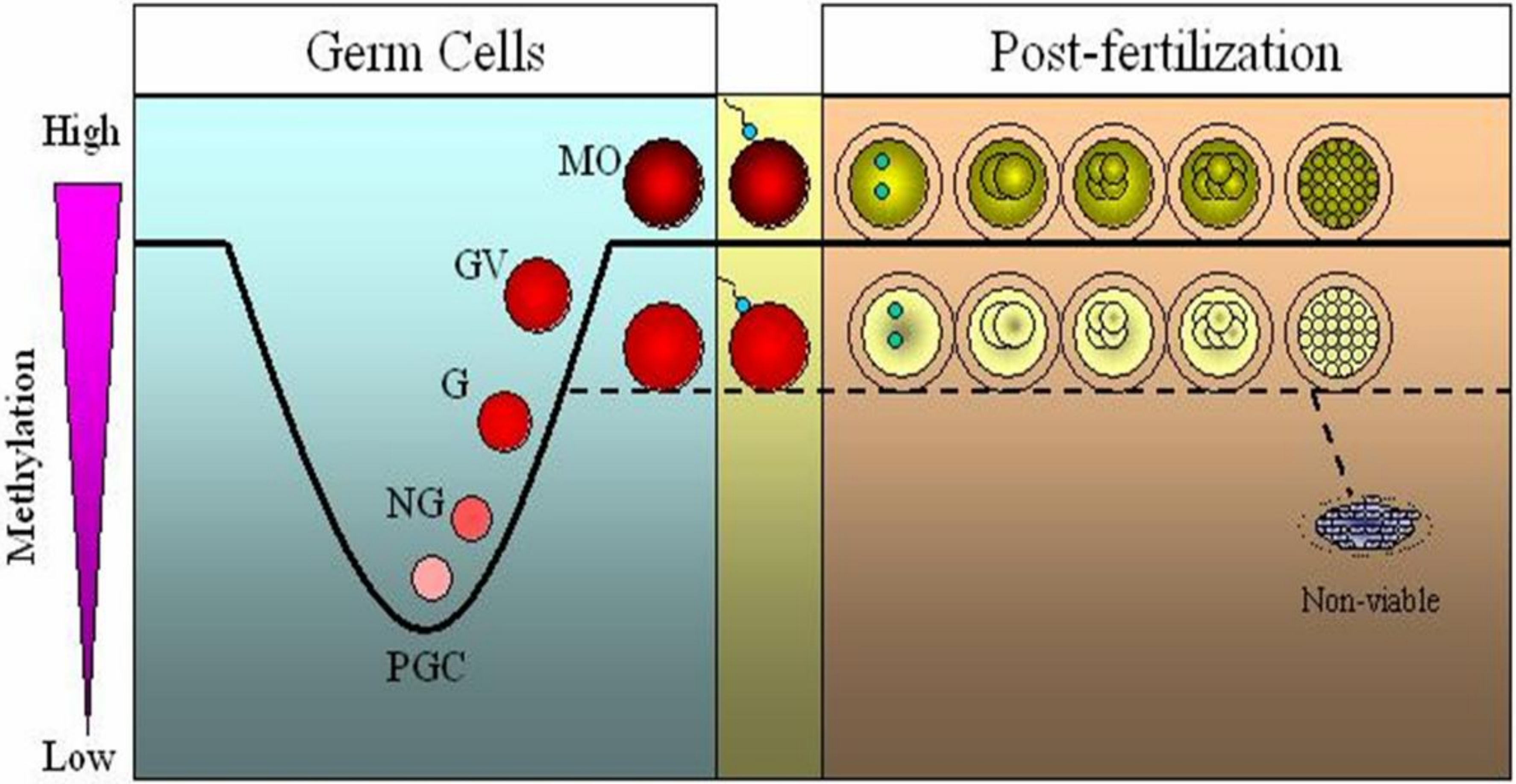
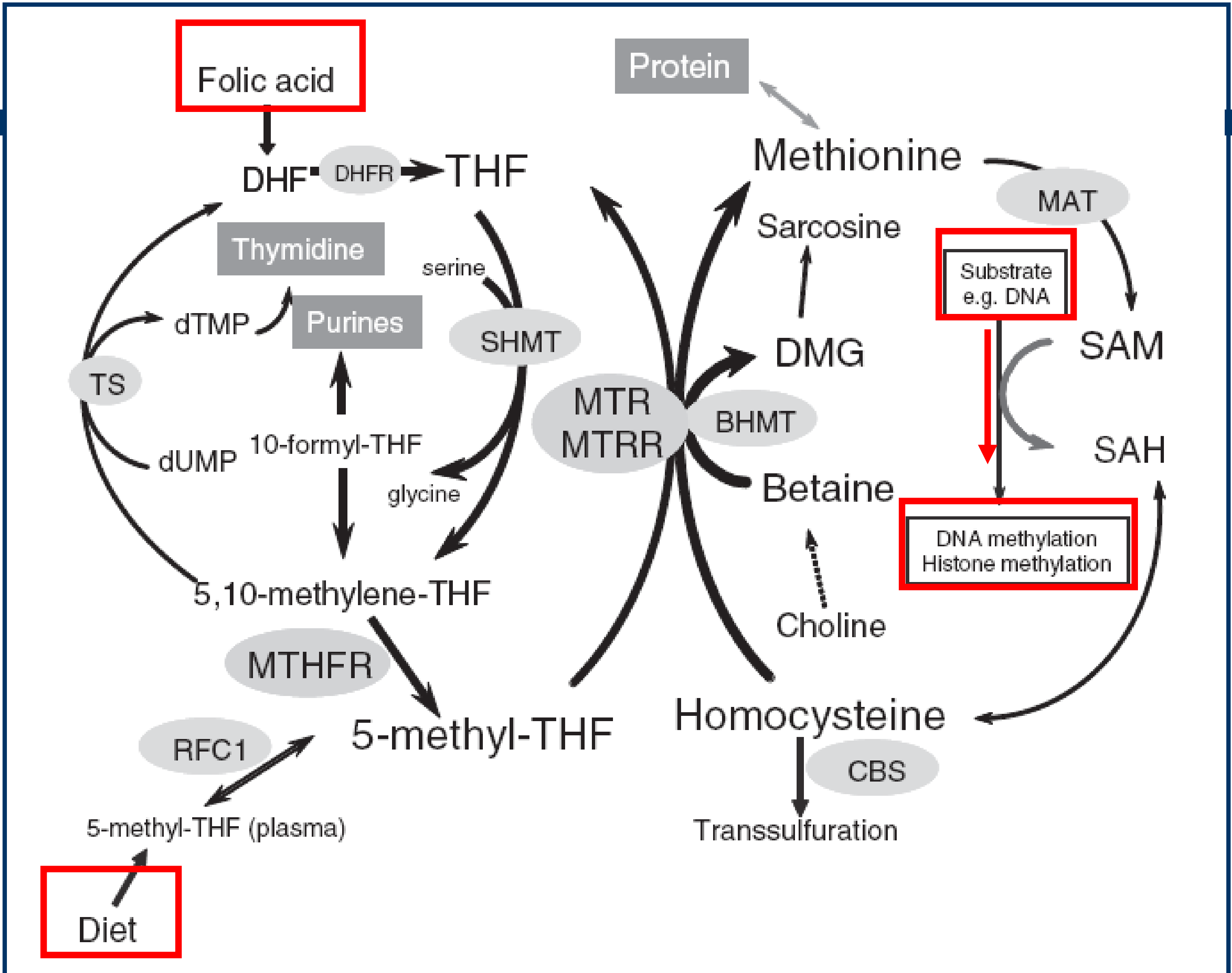
"Development is, by definition, epigenetic"



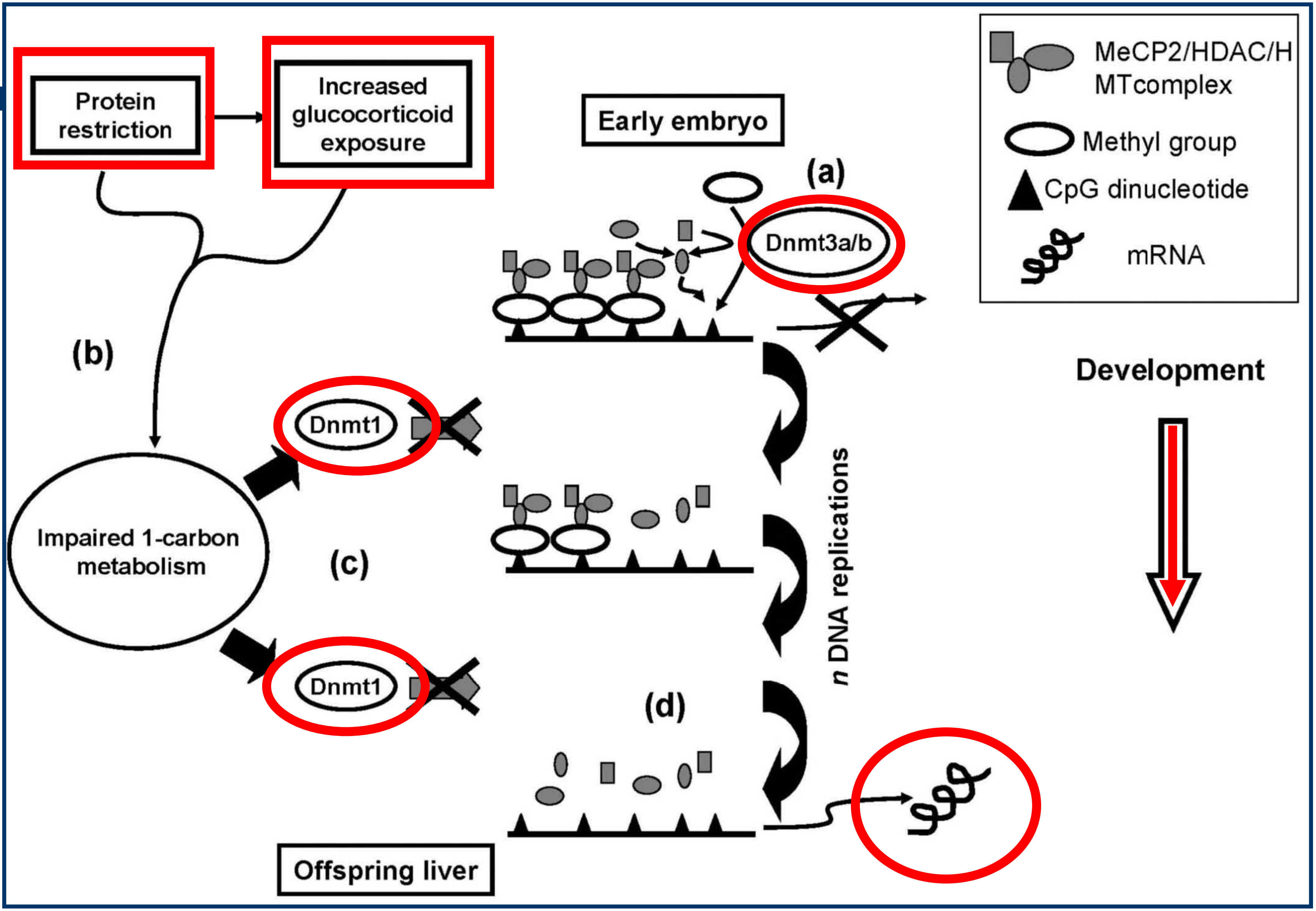
(From Reik 2007)

The final methylation state of imprinted genes in female mammals and is set in the late follicular phase.





(From Kelly and Trasler 2004)



(From Burdge et al. 2007)

Nutritional Restriction Prior to Conception in the Sow Alters Embryonic Development and Candidate Gene Expression in the Placenta and Endometrium

Susan Novak

Gina Oliver, Kristina Oxtoby, Alex Pasternak, François Paradis, Jenny Patterson, Michael Dyck, Walter Dixon and George Foxcroft

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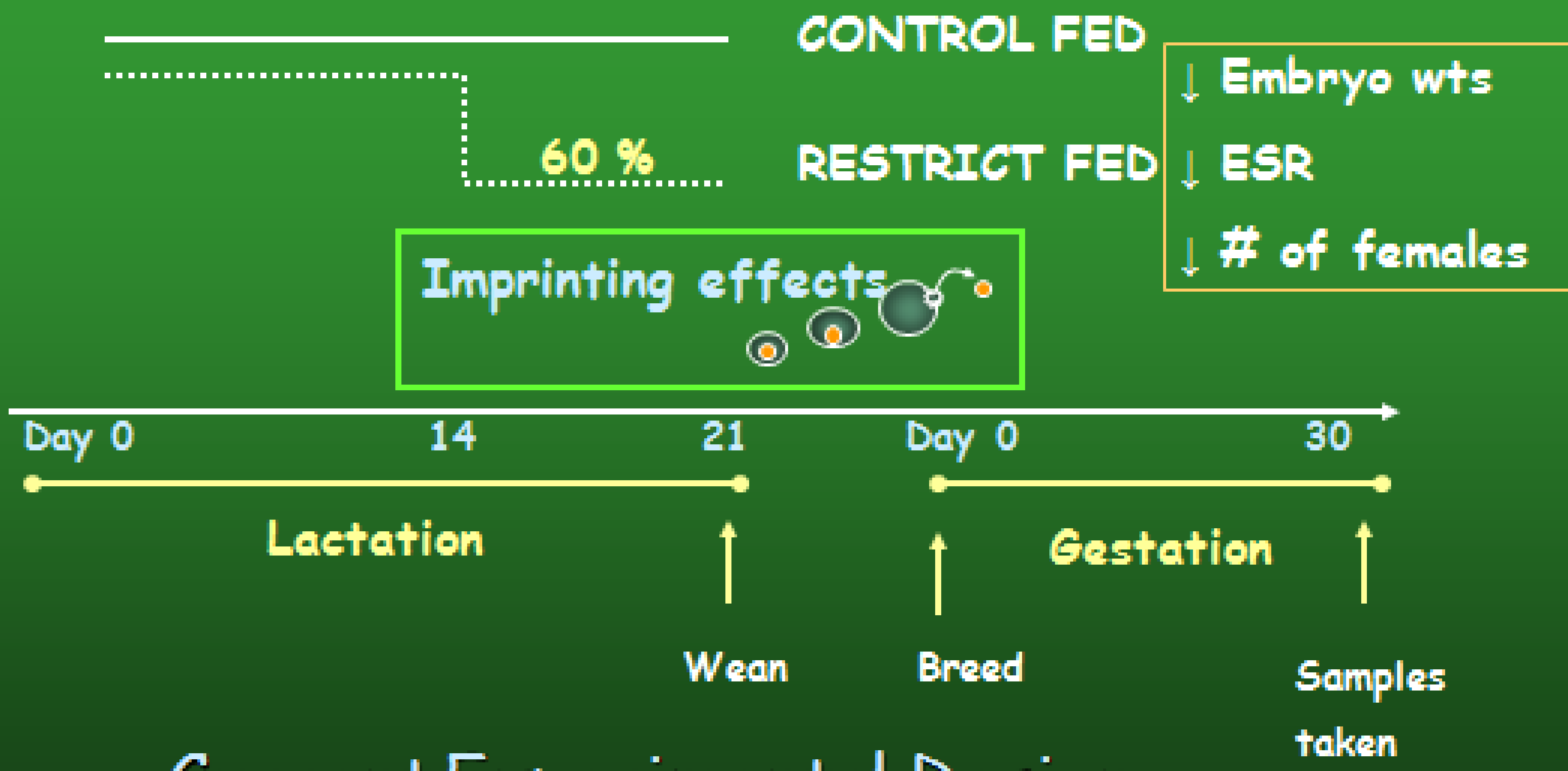


Current Experimental Design
(Vinsky et al., 2006 Reprod Fertil Dev

Objectives

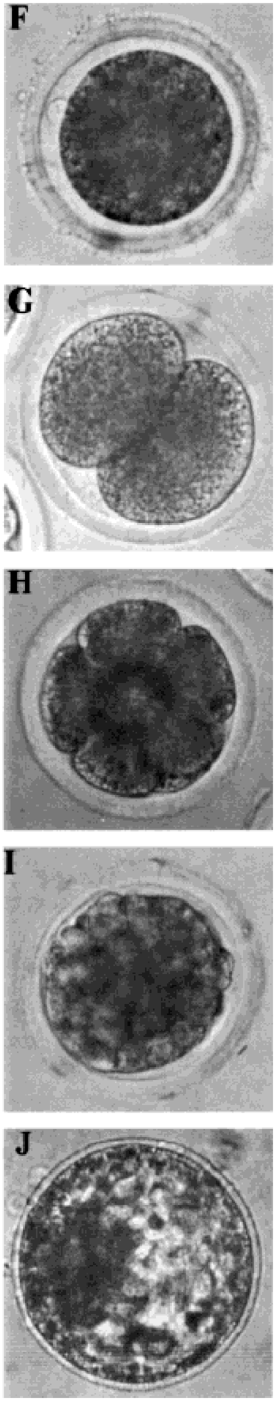
To examine the effects of lactational catabolism in the primiparous sow on :

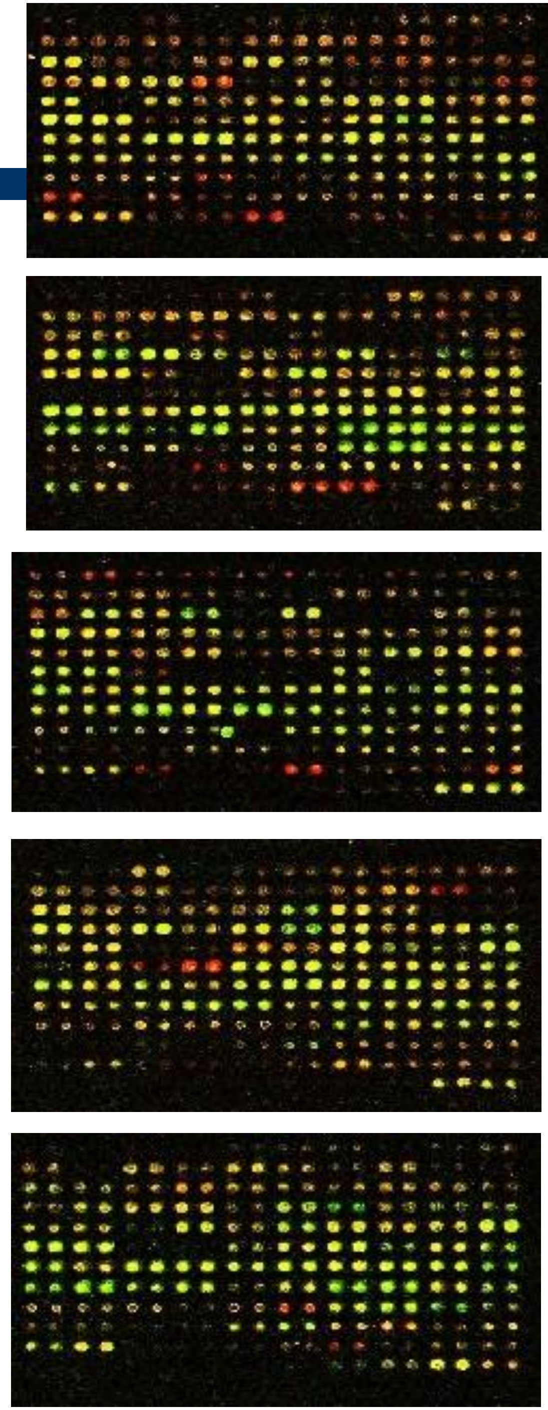
- Subsequent embryonic and placental development
- Sex ratio and embryonic survival
- Angiogenesis-related gene expression in both the placenta and the maternal endometrium
- Embryonic myogenesis-related gene expression
- Expression of potentially imprinted genes in the embryo and placenta

Fold-change over CON treatment

Gene	Day 30 EMBRYOS	P-value	Day 30 PLACENTAE	*P*-value
INSR	**1.39**	**0.034**	1.20	NS
IGF2	1.14	NS	1.06	NS
AIR	**1.19**	**0.025**	1.02	NS
IGF2R	**1.24**	**0.055**	1.06	NS
DNMT1	1.06	NS	-	-
ESR1	**0.57**	**0.029**	1.39	NS
ESR2	1.07	NS	-	-
PLAGL	1.08	NS	-	-

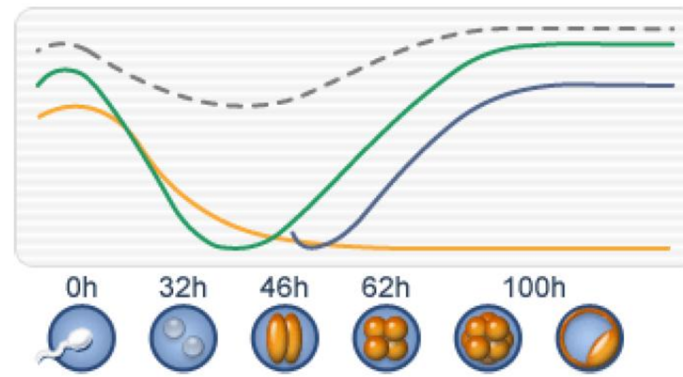
NS- Non-significant





EmbryoGENE
Genomics Epigenomics
Nutrition Environment

Expression profiles



Description of early embryonic development

4. Implications for management

Implications for selection traits:

1. Select for "uterine capacity":
   - Numbers born live, <u>not total born</u>
   - Mean litter birth-weight
   - Quality (survivability) of the pigs born

2. Include phenotypic data from litters of higher parity sows to guide selection for <u>*optimal lifetime productivity*</u>

Production strategies <u>at sow/litter level</u> :

1. **Segregate sows into farrowing rooms based on expected birth weight phenotype.**
2. **Segregate different birth-weight litters into different nursery/grow-finish flows.**
3. **Adjust nutrient requirements to reflect expected lean growth potential**
4. **Market progeny of different birth-weight litters at different market weights or different ages**

Characterization of growth performance of different phenotypes

Collaborations with Dr. Joel Spencer - JBS United Research Farms

- 1400 Multiparous PIC Camborough sows bred to PIC 337 boars
- Characterize sow's litter birth weight phenotype within 24-h of birth

Litter size	Low bw group (kg)	High bw group (kg)
9	< 1.34	> 1.80
10	< 1.34	> 1.92
11	< 1.30	> 1.78
12	< 1.31	> 1.73
13	< 1.28	> 1.72
14	< 1.22	> 1.62
15	< 1.20	> 1.60
16	< 1.26	> 1.58

Low = 1 SD below litter size mean   High = 1 SD above litter size mean

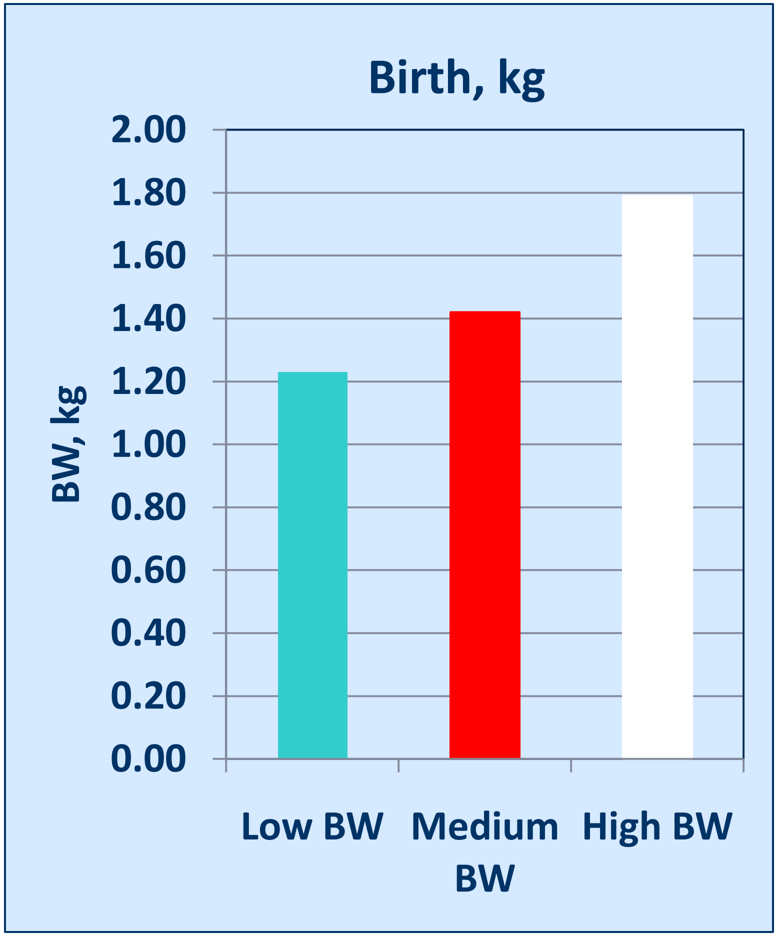
Characterization of growth performance

All pigs tagged and weaned into conventional nursery

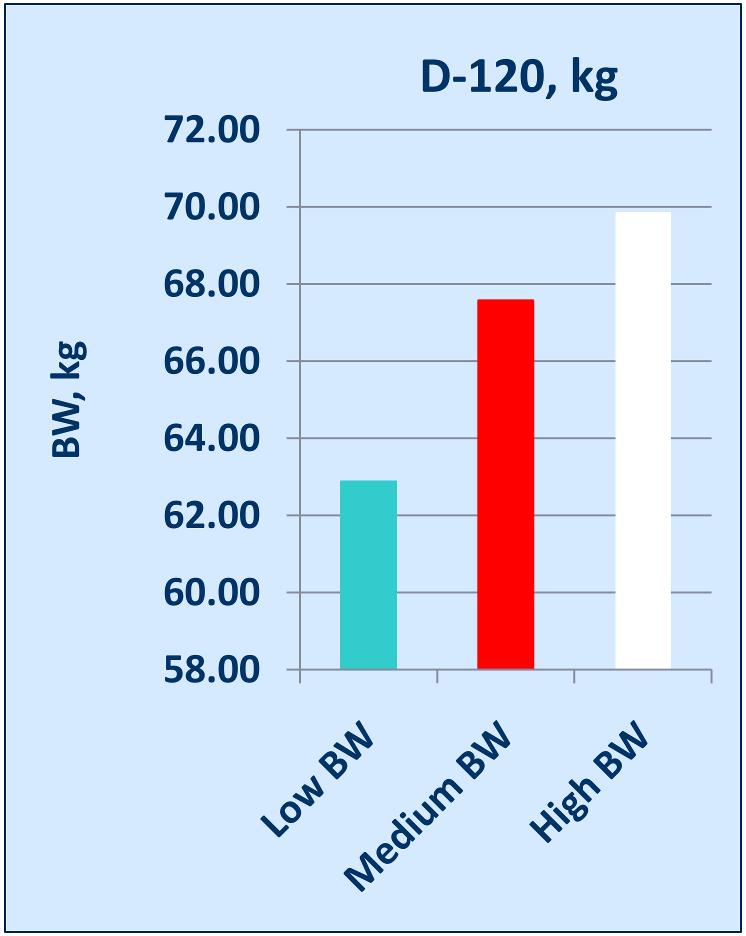
- Pigs penned by entire litter phenotype classification
- At least 10 pens per phenotype
- 26 pigs/pen (mixed sex)
- Common feeding program
- Nutrients above determined herd requirements
- Pen weights and pen intakes throughout growth period
- Individual pig weights at weaning and at market
- Pen and individual carcass metrics at commercial processor (Tyson Fresh Meats; Logansport, IN).

Preliminary trial data: Body weight to 120 days of age

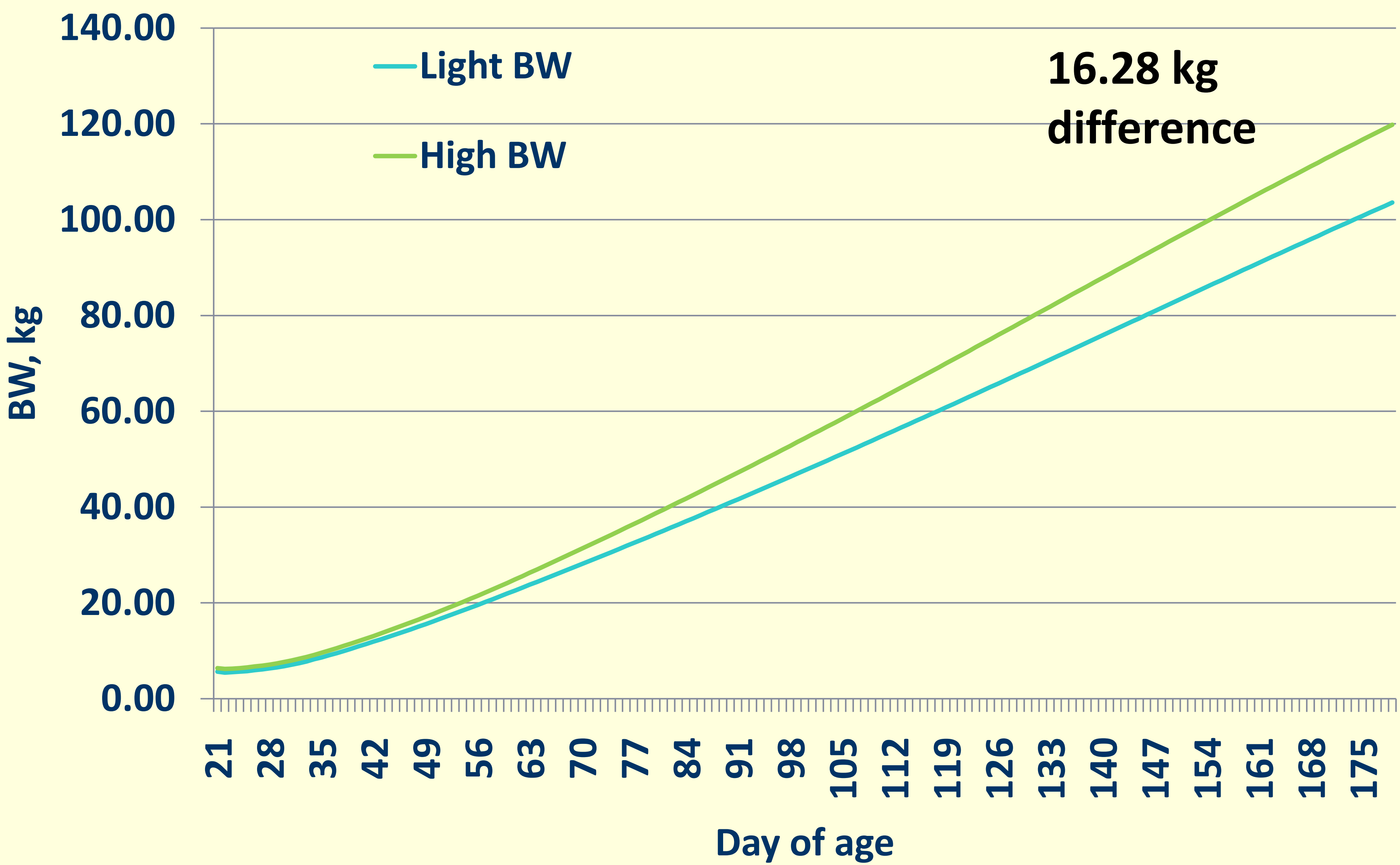
0.56 kg difference



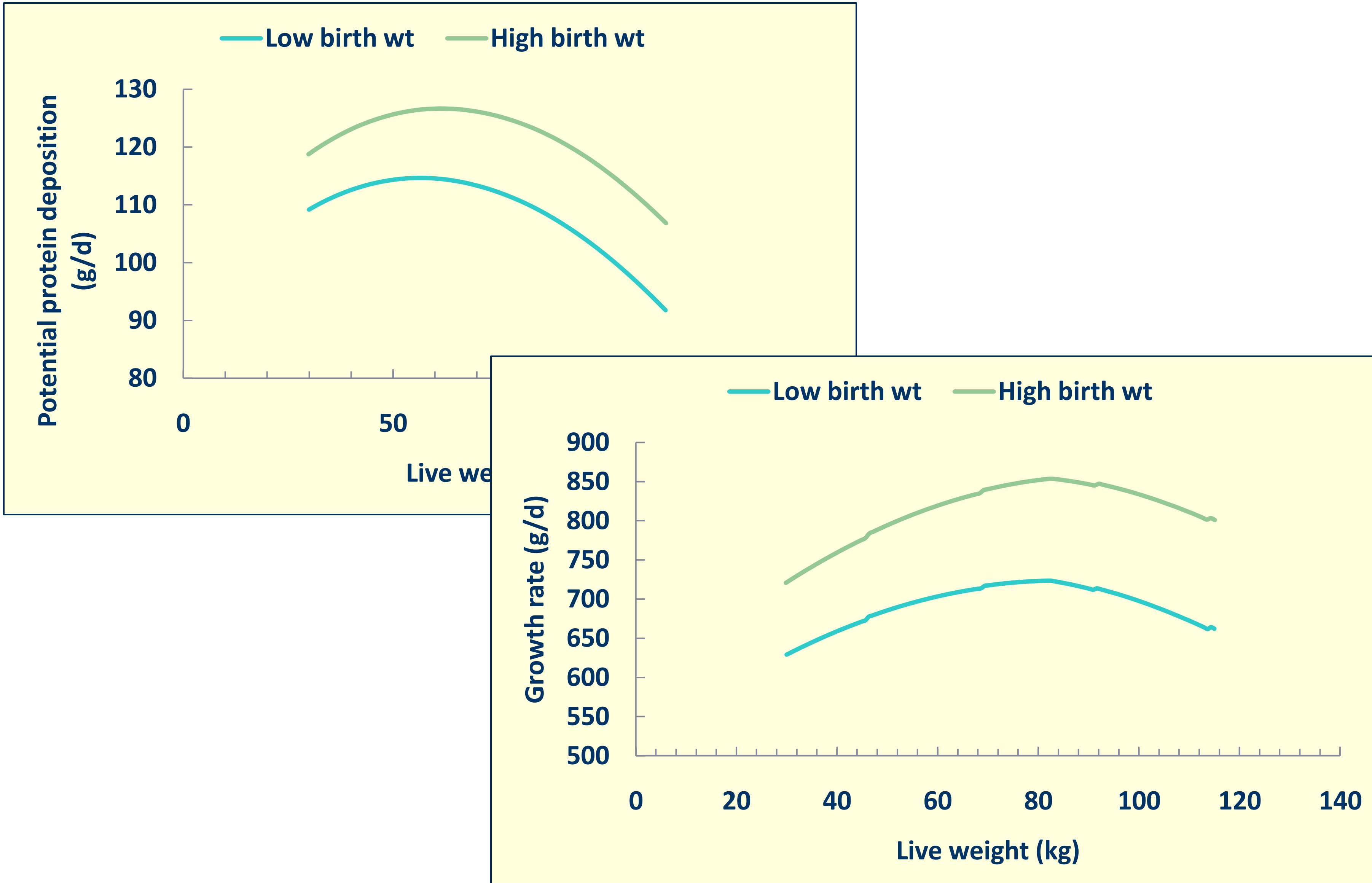
6.99 kg difference



Projected body weight at 179 days of age *(Based on 120 day of age data)*

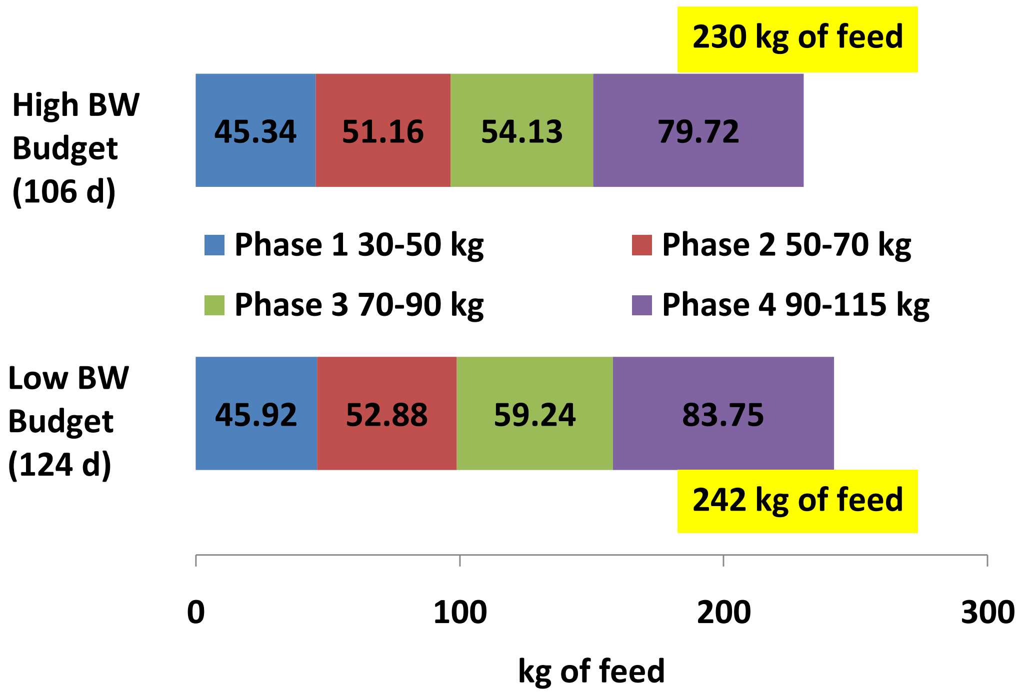


Modeled growth and protein accretion of low and high birth weight pigs



Possible feeding strategies based on birth weight phenotype?

Projected amount of feed needed per phenotype to 115 kg BW



$42.15/pig

<u>$44.18/pig</u>

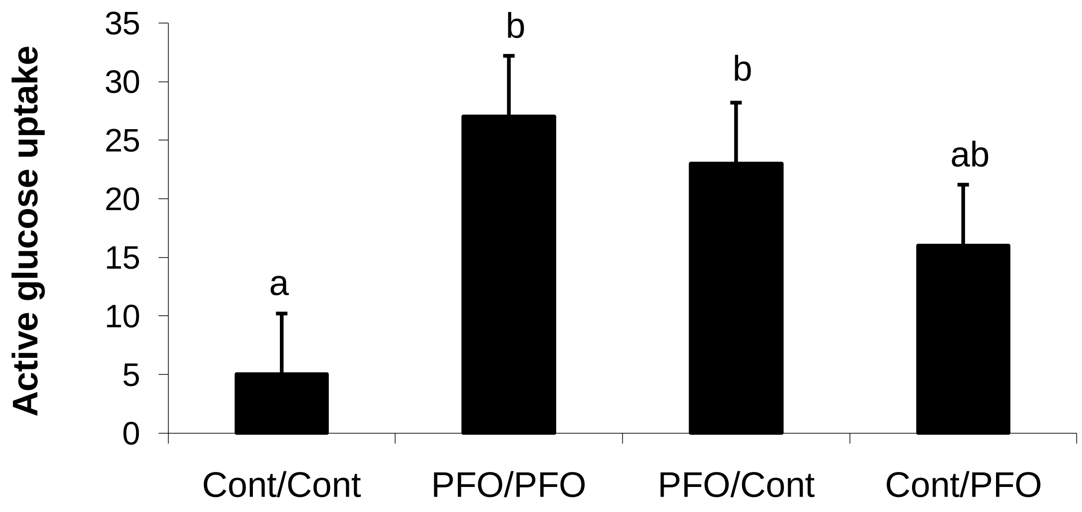
($2.03/pig)

Nutrition targeted at low birth weight litters?

Q: Will n-3 (DHA) supplementation during gestation and lactation improve performance of low birth weight litters?

- Collaborative trial – JBS United/Univ. Alberta
- Ranked sows based on average birth weight of past 3 litters.
- At weaning ranked sows pair-matched and fed diets with or without n-3 PUFA (Gromega/Sow Fat Pak - High in DHA).
- Evaluate offspring performance to market and carcass merit of low average birth weight litters

n-3 Fatty Acids Increase Intestinal Glucose Transport at Weaning

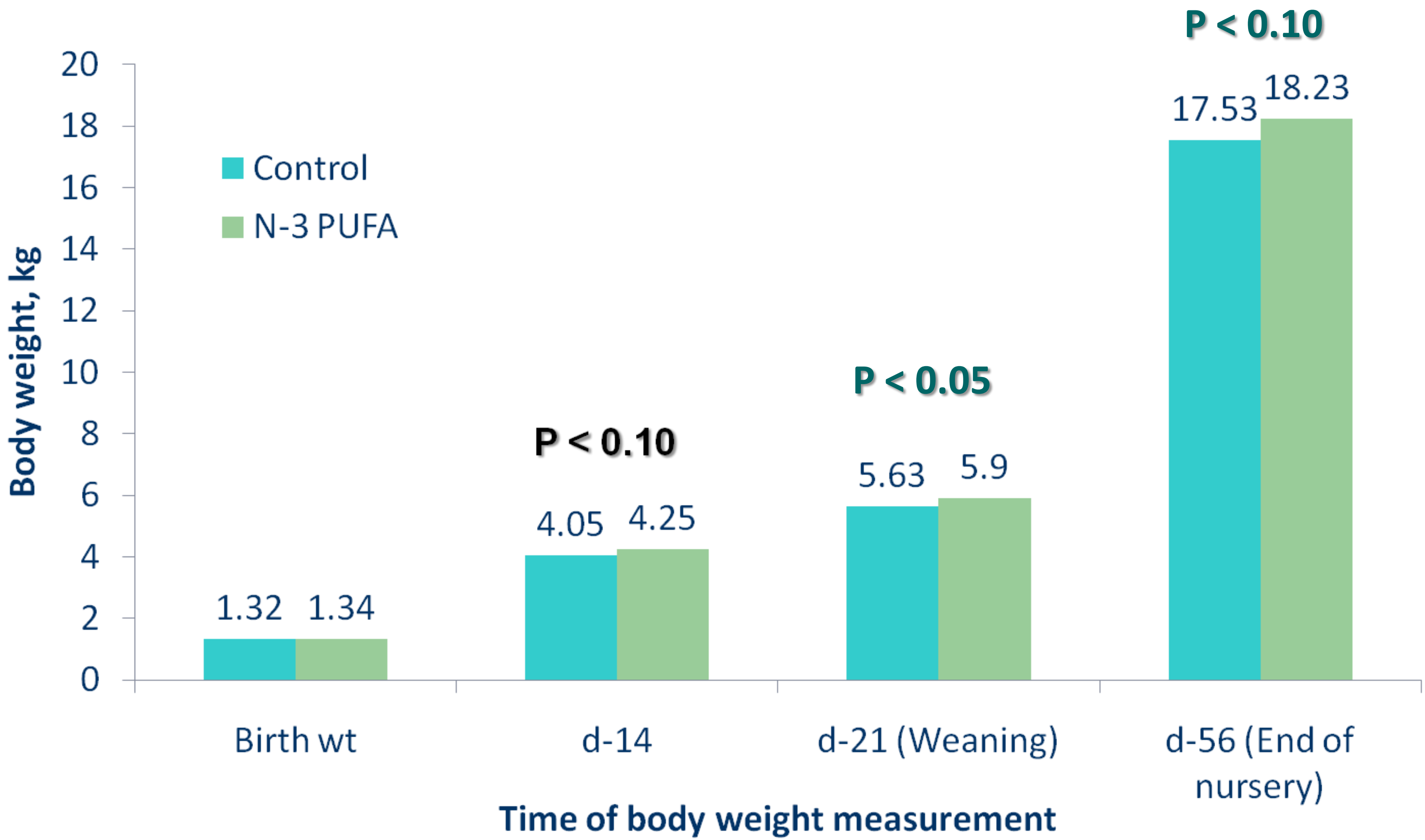


Different letters a,b represent significant differences between treatments ($P<0.05$)

Means±SEM, n = 5 piglets/treatment

Gabler et al., 2009. J. Nutr. Biochem. 20:17-25.

Effects of supplementation of omega-3 fatty acids to gilts on growth performance of their litters and subsequent reproductive performance



(Smit et al., 2010, Univ. Alberta, unpublished data)

Ongoing collaborative trials

- Can we improve the performance of these low birth weight litters with n-3 PUFA to the sow?
- Immunologically
  - Immunoglobulins , inflammation
- Protein deposition
  - Growth rate and Feed efficiency
  - Recover lost growth of this population due to uterine crowding

Additional characterization of growth so economic models can be generated to increase profits.

Thank you for your attention