Effect of nutrient supply on mammary gland development and gene expression in pre-weaned calves

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Abstract #23492

Background

Experimental work

Implications

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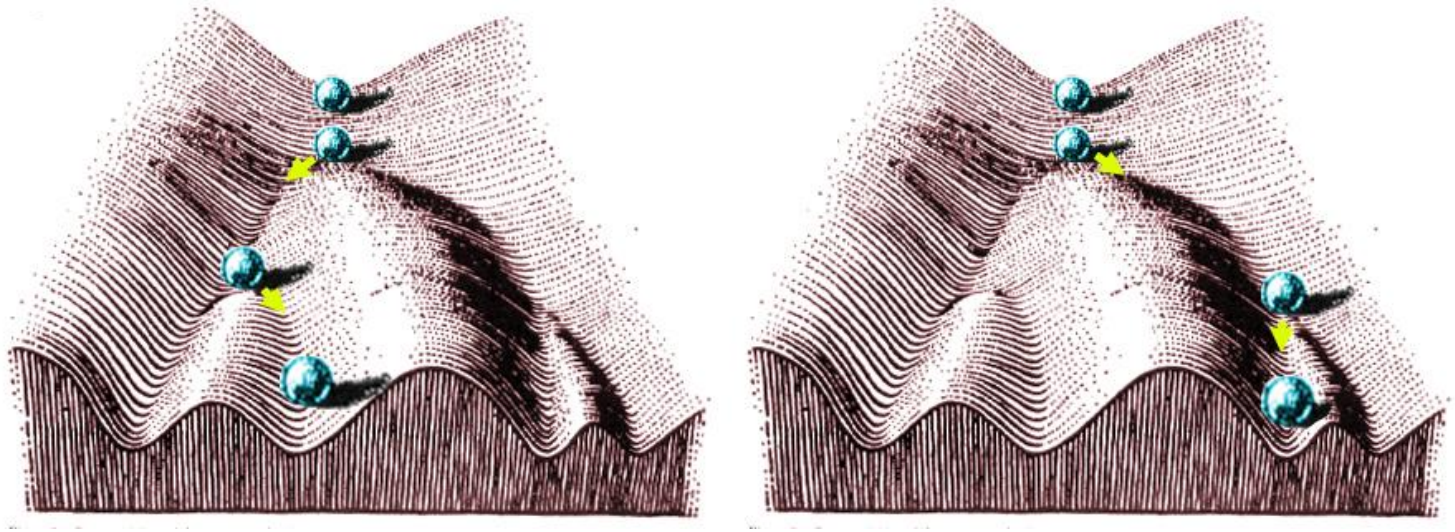
The metabolism can be programmed

"…**early adaptation to a nutritional stress** or stimulus that **permanently changes** the physiology and metabolism of the organism and continues to be expressed **even in the absence** of the stimulus/stress that initiated them…" (Patel and Srinivansan, 2002)



(Adapted from Conrad's Waddington epigenetic landscape)

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The metabolism can be programmed

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The metabolism can be programmed

Increased milk production [1, 2, 3, 5, 6]

Reduced age at 1st calving [1, 3]

Feed efficiency[4]

[1]Bar-Peled et al. 1998; [2]Drackley et al. 2007; [3]Raeth-Knight et al. 2009;
[4]Soberon et al. 2011; [5]Davis-Rincker et al. 2011; [6]Soberon et al. 2012

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Window of opportunity

Period 2-8 wks	Average		High	
ADG, g/day	400		670	
Period 9-14 wks	**Average**	**High**	**Average**	**High**
ADG, g/day	470	1060	400	1130
Final BW, kg	80	106	90	121
Parenchyma weight, g/100 kg BW	16	15	**24**	**23**
DNA, g/100 kg BW	44	42	**85**	**86**
RNA, g/100 kg BW	63	63	**103**	**108**

❖ Increasing protein and energy from 2-8wk increased mammary development

(Brown et al., 2005)

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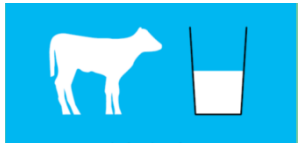
Enhanced milk supply and organ development



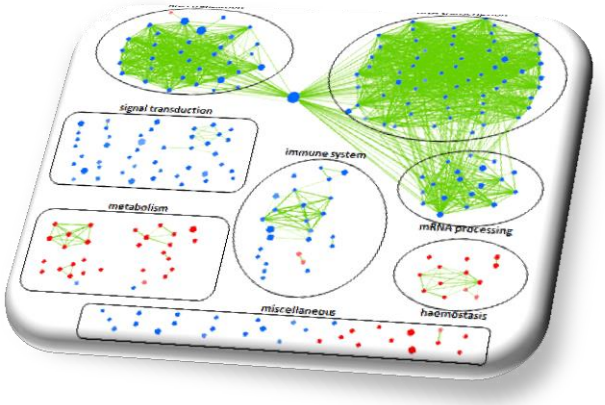
RESTRICTED: 0.6 kg/d MR

ENHANCED: 1.3 kg/d MR

	Restricted (n=6)	Enhanced (n=6)	*P* value
Birth weight, kg	39.2	39.7	0.90
Harvest weight, kg	61.0	83.2	< 0.01
Age at harvest, days	54.3	54.0	0.80
MJ above maintenance, MJ	3.7	15.7	< 0.01
ADG, kg	0.39	0.82	<0.01
Mammary gland, g	**75.48**	**337.58**	**< 0.01**
Parenchyma, g	**1.10**	**6.48**	**< 0.01**
Parenchyma, % of BW	**0.002**	**0.008**	**< 0.01**

(Soberon and Van Amburgh, 2011)

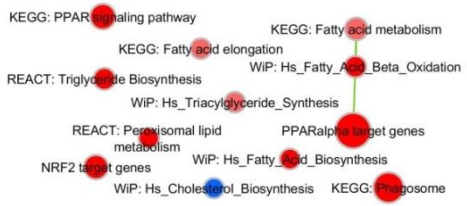
Gene expression profiles



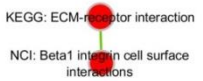
	Significantly changed genes in mammary gland (P<0.01)
Total	654
Up regulated	364
Down regulated	290
Up > 2 Fold change	48
Down < 2 Fold change	48

Gene expression – enrichment maps Cytoscape

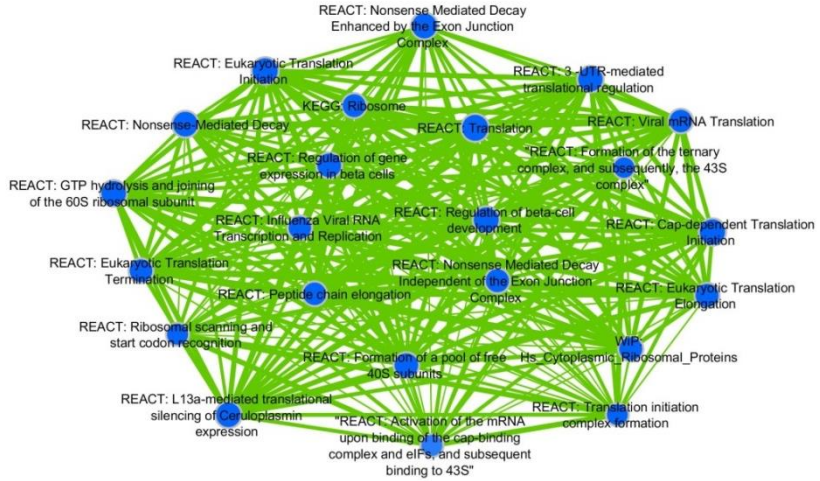
fat metabolism



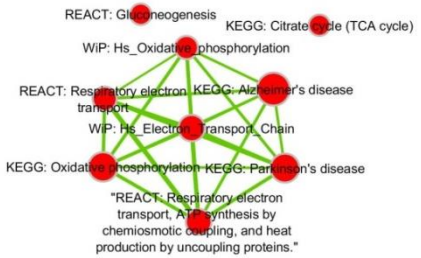
ECM interactions



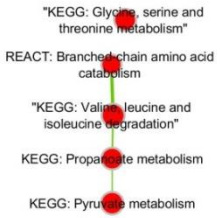
RNA translation



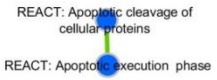
TCA cycle



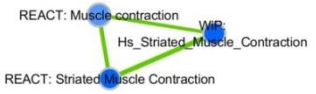
amino acid metabolism



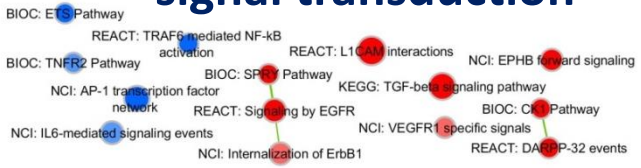
apoptosis



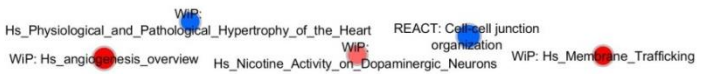
muscle contraction



signal transduction



miscellaneous



Enriched

Supressed

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↑ **Cell proliferation (epithelial cells)**

↑ **Triglyceride biosynthesis**

↑ **ECM interaction (cell proliferation)**

↓ **Apoptosis**

↑ **Metabolism**

Branched chain AA/oxidative energy metabolism

ENHANCED CALVES

↑ Milk intake
↑ BW
↑ Liver
↑ Mammary gland
↓ Dry feed intake

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Upstream regulator analysis (IPA)

Upstream regulator (P<0.01)	Activation Z-Score (> 2.00)	Predicted activation state	Effect in the tissue	References
TP63	2.26	Activated	Cell proliferation & diferentitation	1, 2
NFKB1	2.19	Activated	Cell proliferation, epithelial morphogenesis	3, 4, 5
TP53	2.04	Activated	Cell proliferation & diferentitation	6, 7
BCL6	- 2.00	Supressed	Cell diferentitation	8, 9, 10, 11
ESR2	- 2.19	Supressed	Cell proliferation	12, 13, 14

[1] Yang et al. 1999; [2] Senoo et al. 2007; [3] Hayden et al. 2008; [4] Brantley et al. 2000; [5] Brantley et al. 2001; [6] Cam et al., 2006; [7] Wang et al. 2015; [8] Ye et al. 2003; [9] Bos et al. 2003; [10] Logarajah et al. 2003; [11] Tran et al. 2010; [12] Weihua et al. 2001; [13] Weihua et al. 2002; [14] Imamov et al. 2012

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Take home messages

- Early life stimuli have long lasting effects
- Depends on the timing and intensity (early nutritional interventions)
- Elevated planes of nutrition substantially modified gene expression
- Differentiated mammary organogenesis

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Thank you for your attention

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