

Gene expression patterns in Anterior Pituitary associated with quantitative measure of oestrous behaviour in dairy cows

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Introduction

- Fertility traits declining in dairy cattle
- Faster genetic gain by using genomic techniques
- Genomic factors underlying fertility poorly known
- Oestrous behaviour → gene expression in
Anterior Pituitary

Objective

- Identify genes expressed in the **Anterior Pituitary** that are associated with **Oestrous behaviour** at different phases of oestrous cycle: **Oestrus** (Day0) and **Luteal** (Day12)

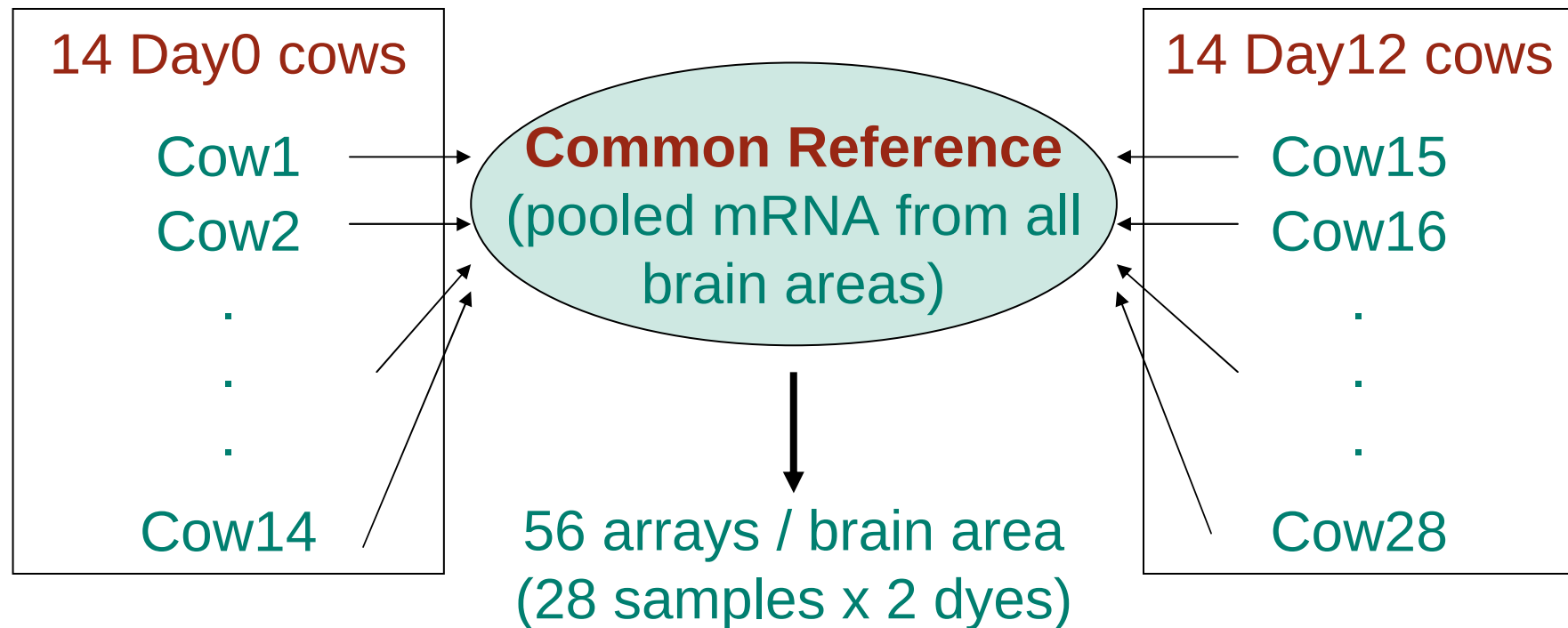
Materials and Methods

- 28 primiparous HF cows
- Phenotypic traits recorded
 - from 30 DIM for at least 2 oestrous cycles till offered for gene expression study
 - Milk yield, milk progesterone
 - Ovarian structure - ultrasonography
 - Oestrous behaviour: heat score (Van Eerdenburg, 2006)
- Gene expression in brain studied
 - Tissues collected at Day0 and Day12
 - Anterior Pituitary, Amygdala, Hippocampus, Dorsal and Ventral Hypothalamus



Gene expression study

- Microarray experiment setup:
 - Completely balanced common reference design
 - 24K bovine oligonucleotide array (BOMC, USA)



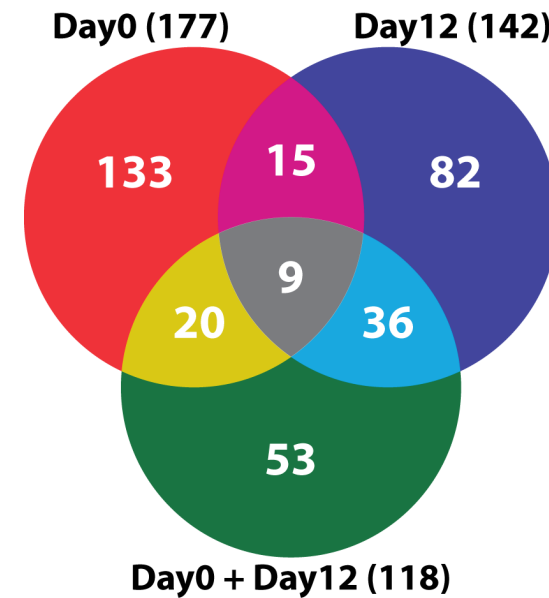
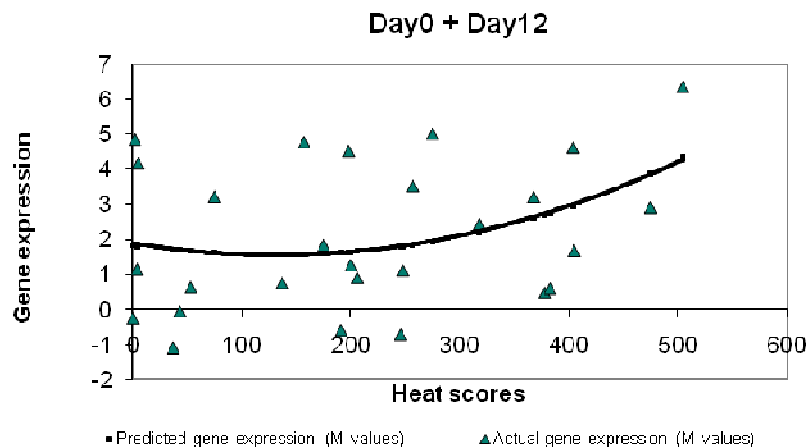
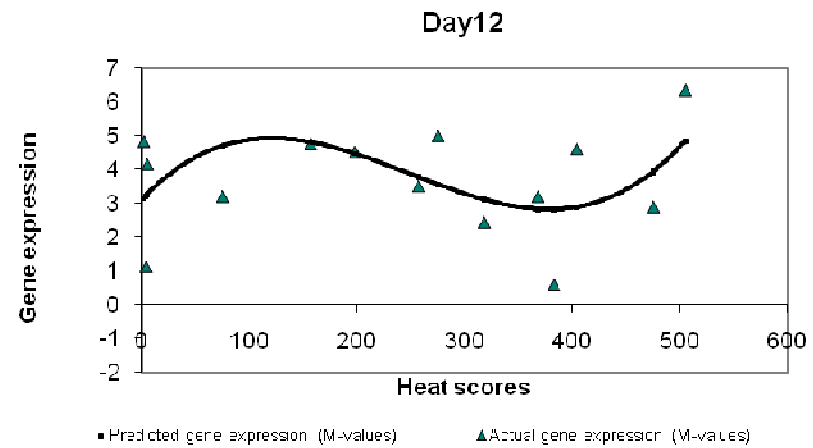
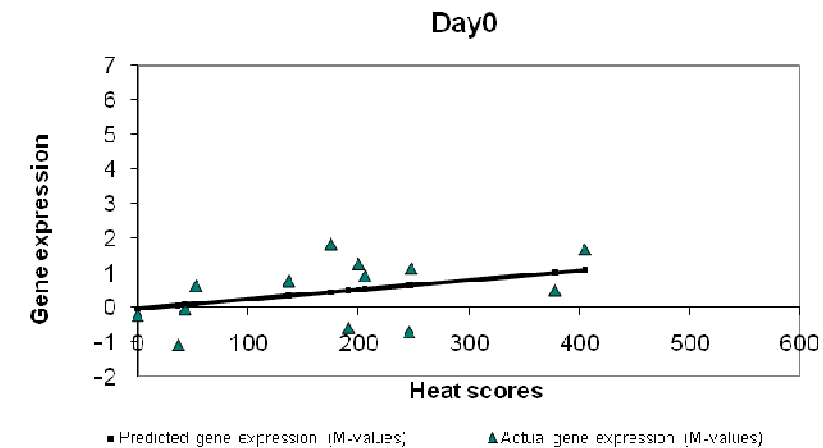
Two step analysis

- Microarray pre-processing
 - Gene expression ratios (M-values): LIMMA
(Smyth, 2005)
- Identify gene expression patterns associated with oestrous behaviour
 - Bayesian hierarchical mixed model (Jia *et al.*, 2008)
 - To identify Linear / non-linear patterns, Heat scores → Orthogonal polynomials
 - Algorithm implemented in SAS

Association analyses: Anterior pituitary

- Data for analyses:
 - M-values from Anterior Pituitary per cow
 - Average heat score (of previous cycles) per cow
- 3 separate analyses:
 - To identify genes associated with heat score
 - at oestrus : data of Day0 cows
 - at mid-cycle : data of Day12 cows
 - regardless of phase : data of Day0 + Day12 cows

Results: Patterns of association



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Results: Associated genes

Gene	Day 0	Day 12	Day0+ Day12	Remarks
<i>PRL</i>	✓			Neg. effect on sexual behaviour
<i>ATP1A3</i>	✓			Implicated in rapid-onset dystonia parkinsonism
<i>PIT1</i>	✓	✓		TF for <i>PRL</i> , <i>GH</i>
<i>MCH</i>	✓	✓		Stimulates sexual behaviour in rats
<i>FSHB</i>	✓	✓	✓	Regulates oestrous cycle
Ig	✓	✓	✓	Facilitates re-modelling of synaptic networks



Results: Gene ontology terms

Day0

- Behaviour
- MHC class I receptor activity
- Nervous system development

Day12

- Calmodulin binding
- Hormone activity

Day0 + Day12

- Pattern binding
- Rhythmic process



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Conclusions

- Method successfully predicted **oestrous behaviour** associated genes in the **anterior pituitary**
 - Limited annotation: Some genes with known relation to oestrous and oestrus behaviour
 - Biological interpretation → a step towards understanding genomic regulation of oestrous behaviour and fertility
- Associated genes also found at mid-cycle
 - May be important for proper expression of next oestrus