Genome wide association study for calving performance in Irish cattle

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Introduction

- Focus on two traits

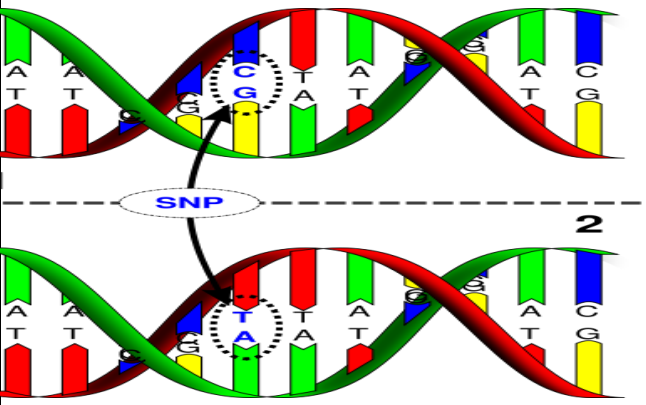
  1. Dystocia (CD)

  2. Perinatal Mortality (PM)

- Complex quantitative traits influenced by genetics
- Lowly heritable

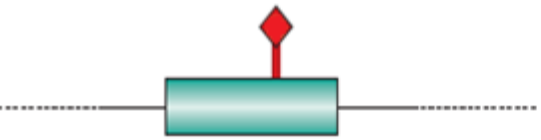
	Dystocia	Perinatal Mortality
Direct	0.19	0.02
Maternal	0.01	0.01

Genome Wide Association Study

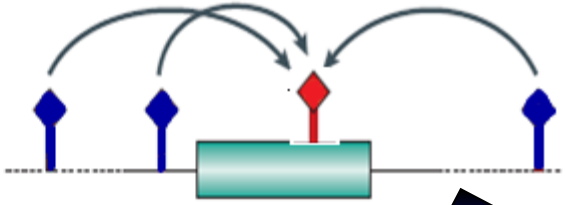


Single **N**ucleotide **P**olymorphisms

SNPs



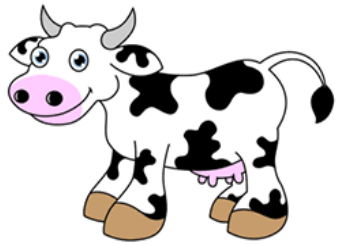
Direct Association



Indirect Association

SNP1A

SNP1G



Materials & Methods

- 4,683 Holstein-Friesian sires genotyped using Illumina Bovine SNP50 Beadchip
- SNP edits were applied

43,204 SNPs remained

- PTAs for calving difficulty and perinatal mortality
  - Deregressed
  - Animals with >40% reliability

1,970 animals for Calving Difficulty

740 animals for Perinatal Mortality

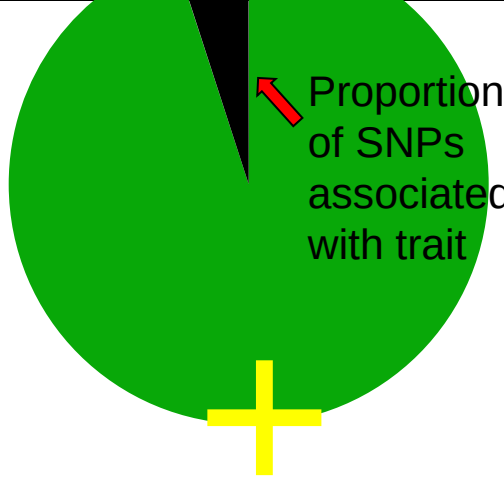
>1 million progeny

- Pathway analysis

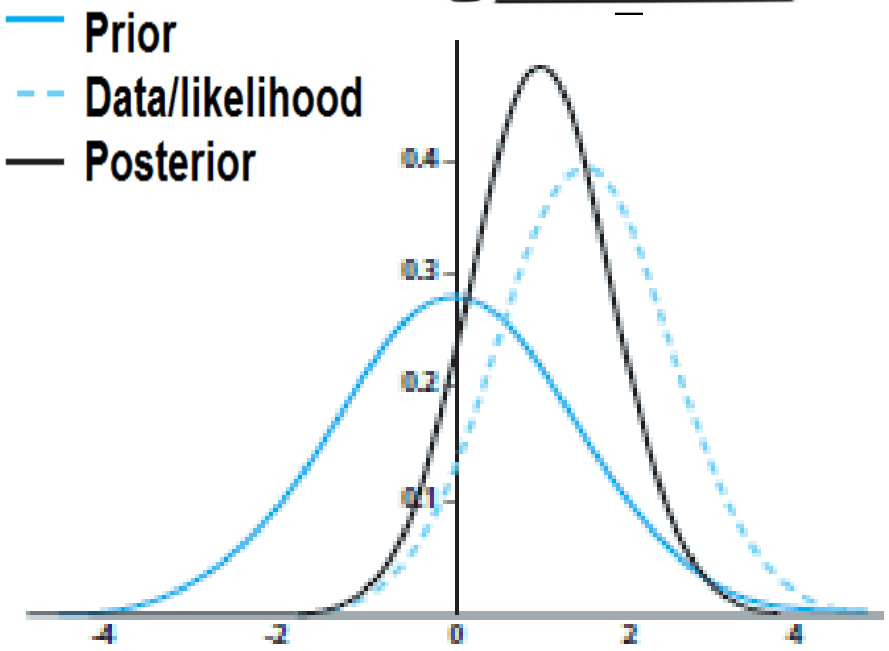
Bayesian Approach

1. Bayesian approach uses prior knowledge
2. Likelihood inference from data
3. Fits SNPs simultaneously
4. Calculates Posterior distribution

Priors



Data

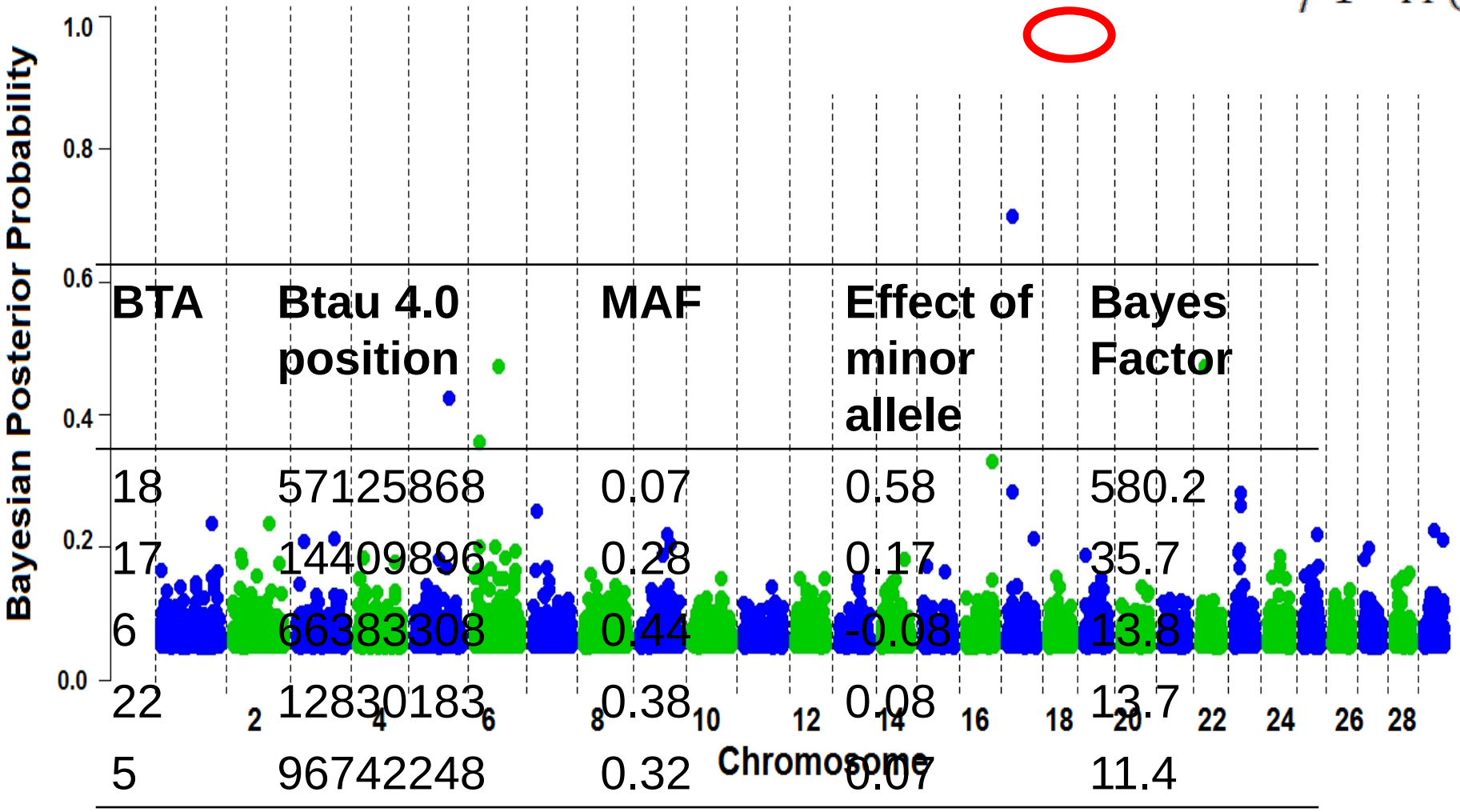


Model Statistics

Trait	Prop of SNPs assoc with trait (1-π) %	Genetic variance accounted for by SNPs %	Number of SNPs (Posterior Probability)		
			>0.95	0.50 - 0.95	0.15-0.50
Direct Calving Difficulty	7	93	1	1	77
Maternal Calving Difficulty	6	96	0	3	55
Perinatal Mortality	4	96	0	0	5

Direct dystocia GWAS

$$Bayes\ Factor = \frac{\Pr(H_1|y)}{1-\Pr(H_1|y)} \Big/ \frac{\Pr(H_1)}{1-\Pr(H_1)}$$



BTA	Btau 4.0 position	MAF	Effect of minor allele	Bayes Factor
18	57125868	0.07	0.58	580.2
17	14409896	0.28	0.17	35.7
6	66383308	0.44	-0.08	13.8
22	12830183	0.38	0.08	13.7
5	96742248	0.32	0.07	11.4

Genes of interest for direct calving difficulty

45 SNPs showed '**substantial evidence**'

- 538 gene/gene-products within 500kb of these

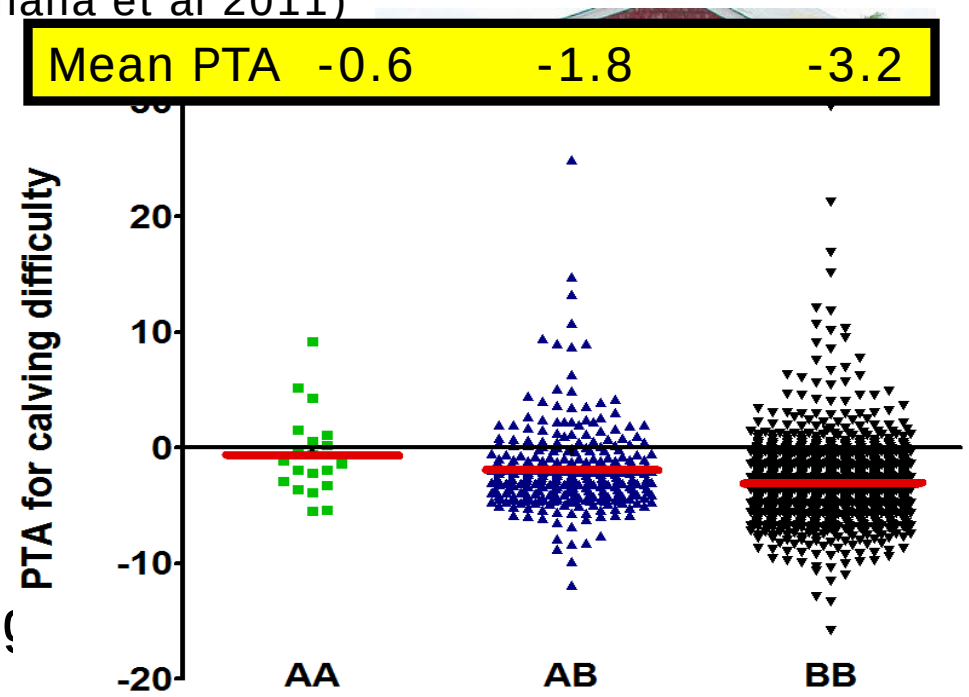
Chromosome 18

- SNP ss8632477 explained 2.1% of the genetic variation
- **Siglec-5** (Cole et al., 2009, Sahana et al 2011)
- Delay parturition
- Favourable allele selected

Chromosome 17

- **HHIP**; stature
- SS86289496 & Zinc finger protein 827; skeletal growth

Riboflavin metabolism signallin



Maternal Calving Difficulty GWAS

BTA	Btau 4.0 position	MAF	Effect of minor allele	Bayes Factor
28	24176808	0.27	0.25	44.8
12	57275021	0.34	0.16	19.6
11	882225	0.41	0.12	19.3
9	66769980	0.20	0.14	16.2
12	57357710	0.35	0.07	7.3

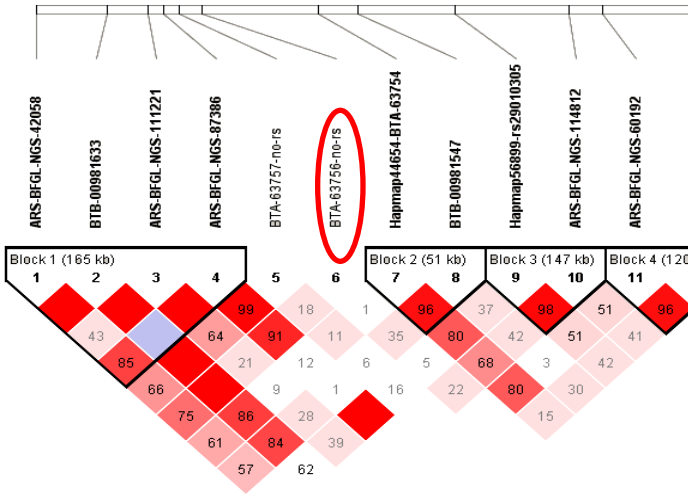
Genes of interest for maternal calving difficulty

42 SNPs showed '**substantial evidence**'

- 313 genes/gene-products within 500kb

Chromosome 28

- SNP rs416524683 explained 0.69% of the variation
- Not in a LD block
- Closest genes; SNORA36 & Graves disease carrier protein



Chromosome 12

- BTA-mir-1256; stemloop microRNA

Glycosaminoglycan degradation pathway

Perinatal Mortality GWAS

Bayesian Posterior Probability

0.15

0.10

0.05

2 4 6 8 10 12 14 16 18 20 22 24 26 28

Chromosome

BTA	Btau 4.0 position	MAF	Effect of minor allele	Bayes Factor
14	71416566	0.42	-0.02	6.2
16	74940930	0.49	-0.02	5.3
10	12799367	0.48	-0.02	5.1
18	57125868	0.07	0.04	5.0
4	25183065	0.17	0.02	4.6

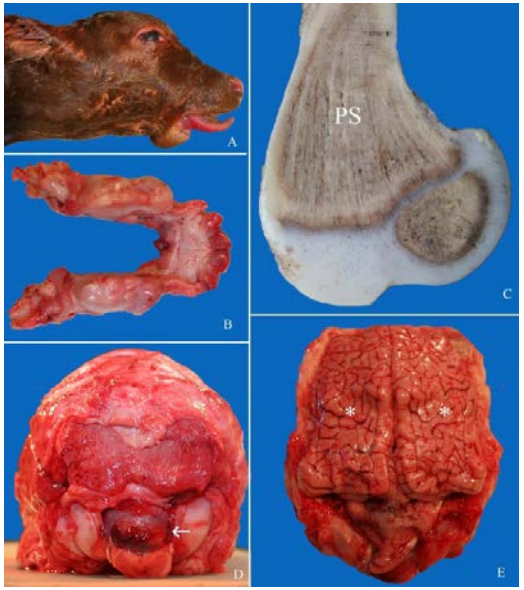
Genes of interest for perinatal mortality

17 SNPs showed '**substantial evidence**'

- 200 genes/gene-products within 500kb

Chromosome 14

- Ss86296129 in high LD with SLC26A7
- SLC26A7 colocalizes with SLC4A2
- Associated with osteoporosis and mortality



Chromosome 2

- Associated with birth weight
- ss86303585 in close proximity to QTL that accounts for 2.8kg difference (Grosz & MacNeil,2001)

Systemic lupus erythematosus pathway

Conclusions

- Several novel and previously reported QTLs were associated with calving performance traits
- QTLs associated with only one trait have been identified
- Siglec-5 and SLC26A7 of particular interest

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Questions??

Thank you for your attention