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# Searching for genotype-by-environment interactions at the SNP level in Holstein dairy traits recorded in both China and UK

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# Motivation

- Genotype-by-environment interactions (GxE) have been widely studied in recent years with mature methodology
- Basic question – how does the same genotype perform in differing environments? Can we use this information to improve selection, management , etc.?
- Often thought of as between breed choices in different climates.
- More recent developments looked at random regression approach of individual genotypes (sires) on measureable differences between environments
- The use of SNP chips allows us to ask the question – how do animals with a particular SNP genotype perform in different environments – Equivalent of different QTL polymorphisms.

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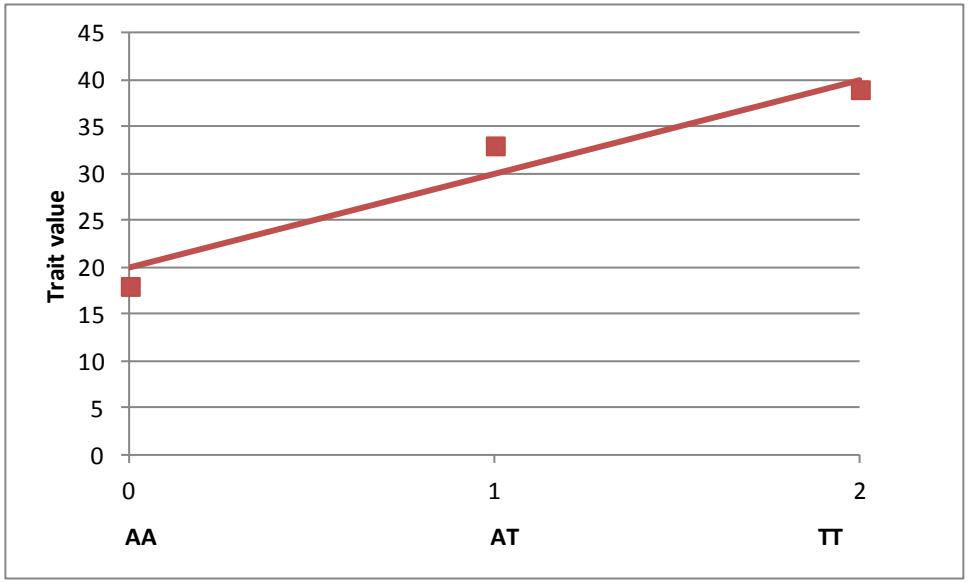
# GxE and SNP genotypes

- At each SNP on a chip we expect to see one of three possible genotypes in a population (say AA, AT, TT)
- Each allele may be in LD with an alternative form of a QTL
- Basic question – do the phenotypes of the 3 genotypes differ?  GWAS, GRAMMAR etc.
- GxE question -  do the phenotypes of the 3 genotypes perform differently in 2 or more environments?

# GxE and SNP genotypes - 2

- Under an additive model we would expect the phenotypic performance of AT to be (AA + TT)/2

- Using a regression approach, substituting 0 for AA, 1 for AT and 2 for TT, the slope of the regression line of phenotype on SNP genotype reflects the differences between the animals

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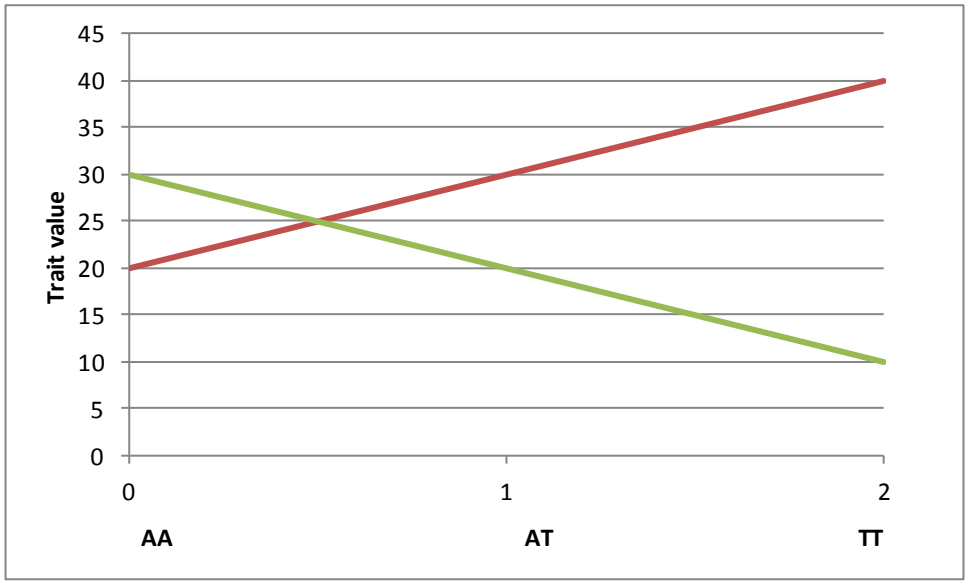
# GxE and SNP genotypes - 3

- In two environments, a comparison of the two within-environment regression slopes will tells us if the genotypes perform differently in each environment

- If they differ then this implies a GxE

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# Data

- Holstein cows recorded for milk, fertility and other performance characteristics in both UK and China (Wu et al., 2012; Brickell et al., 2009)

- DNA taken from ~250 cows per country and genotyped with Illumina 50K SNP chip – after QC, 36,025 SNP analysed on chromosomes 1 – 29.

- Three traits selected – heifer 305-d milk yield (MY305), first calving interval (CI) and age at first calving (AFC).

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# Analysis

- Environmental residuals derived for each trait (Amin et al., 2007) – residuals from fitting mixed polygenic model to data using ASREML
- Environmental residuals analysed by within-country regression of phenotype on coded genotype for each SNP
- Within-country regression slopes compared using Z score in PLINK ($[b_1-b_2]/s_{b1-b2}$; t test probability)

$b_1$ and $b_2$ are the two regression coefficients

$s_{b1-b2}$ is the standard error of the difference between the slopes

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# Trait statistics

| Trait | Heifer MY305 (kg) | First calving interval (d) | Age at 1st calving (mo) |
|---|---|---|---|
| UK | 8,631± 99.4 | 414 ± 8.64 | 26.5 ± 0.21 |
| China | 6,299 ± 97.2 | 526 ± 6.96 | 28.6 ± 0.26 |

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# Mixed models and polygenic results

All models (MY305, CI, AFC) included:

- Herd-year-season
- Principal components of the kinship matrix
- Polygenic animal term

Model for MY305 included AFC

***Heritabilities***

| | |
|---|---|
| Heifer 305-d milk yield | 0.27 ± 0.14 |
| Calving interval | 0.08 ± 0.07 |
| Age at 1st calving | 0.21 ± 0.15 |

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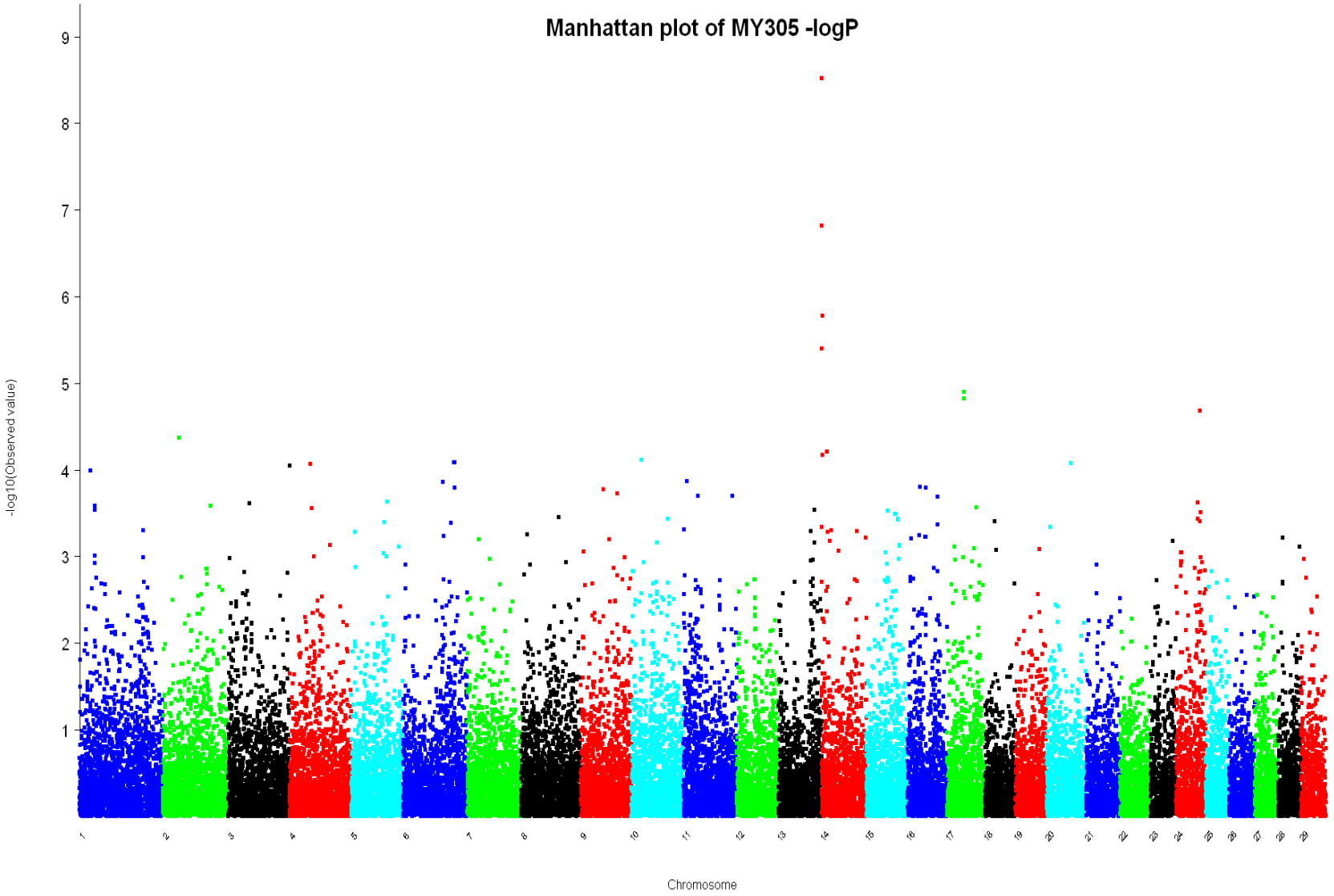
# Milk yield – SNP showing GxE

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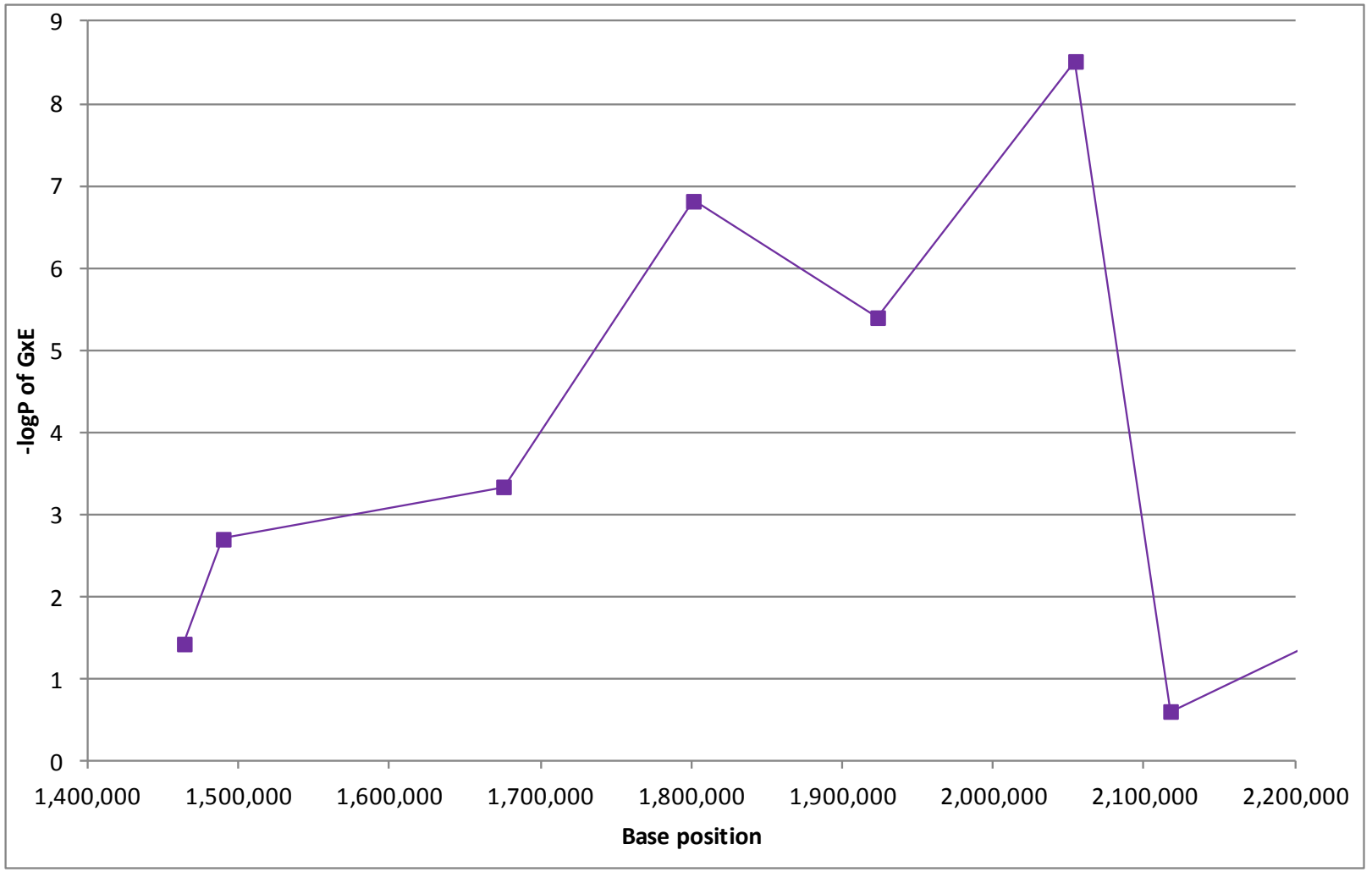
# Area on BTA 14 with high level of GxE




DGAT1 position – 1,795,425 -1,804,838bp

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# Genotype by country means and regression coefficients – MY305 residuals

| Genotype<br>ARS-BFGL-NGS-107379 | 11 | 12 | 22 | Regression coefficient |
|---|---|---|---|---|
| UK | -247.6 ± 232 | 2.1 ± 101 | 160.7 ± 81 | 192.3 ± 96.5 |
| China | -1637.1 ± 308 | -592.9 ±104 | 440.1 ± 71 | 1035.0 ± 104.3 |

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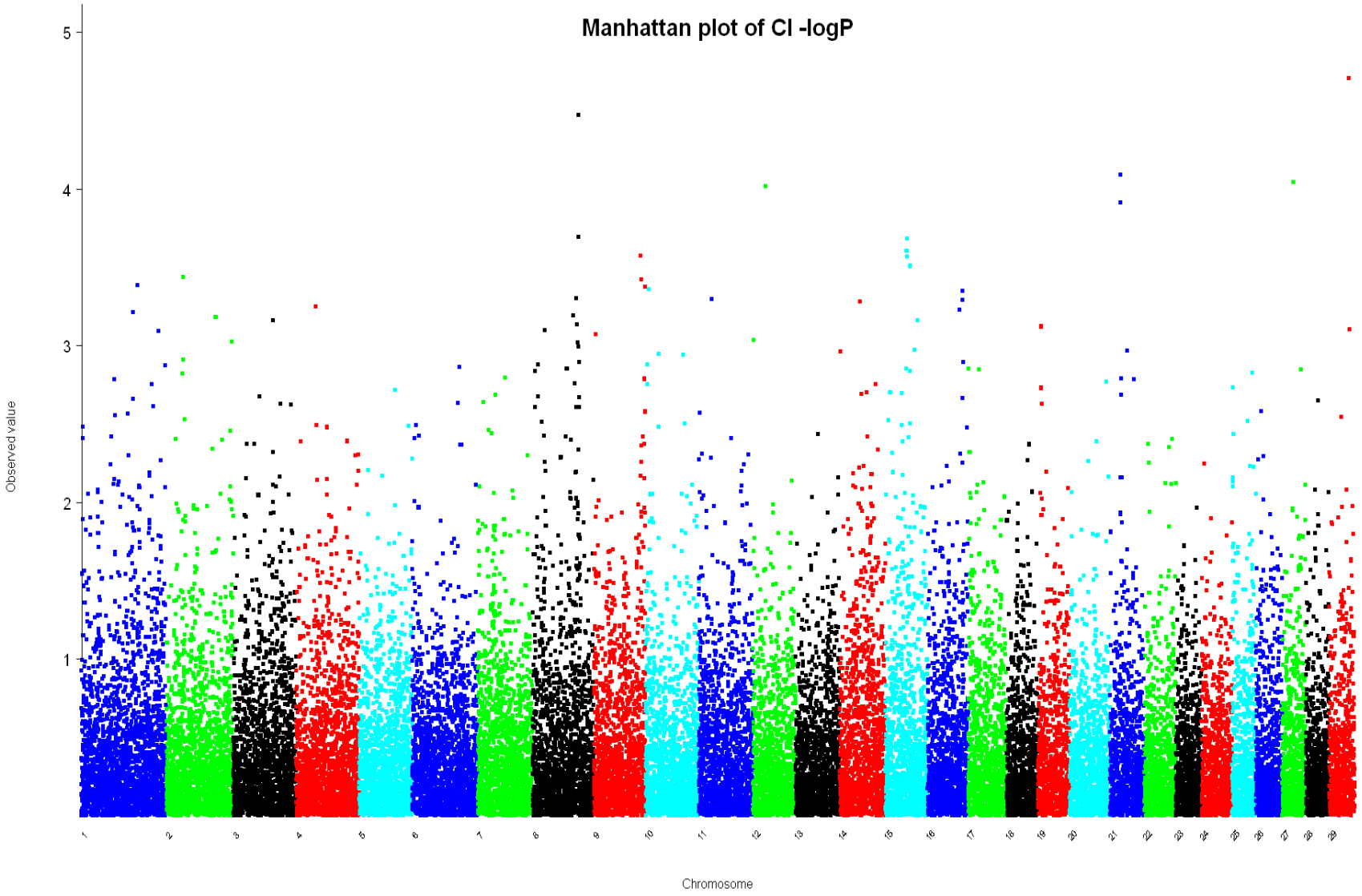
# Calving interval – SNP showing GxE



# Calving interval SNPs

None achieved genome-wide significance (-logP = 5)

BTA 29 – two adjacent SNPs, -logP = 1.45, 4.71

BTA 8 – four adjacent SNPs, -logP = 1.79, 4.47, 2.33,1.93

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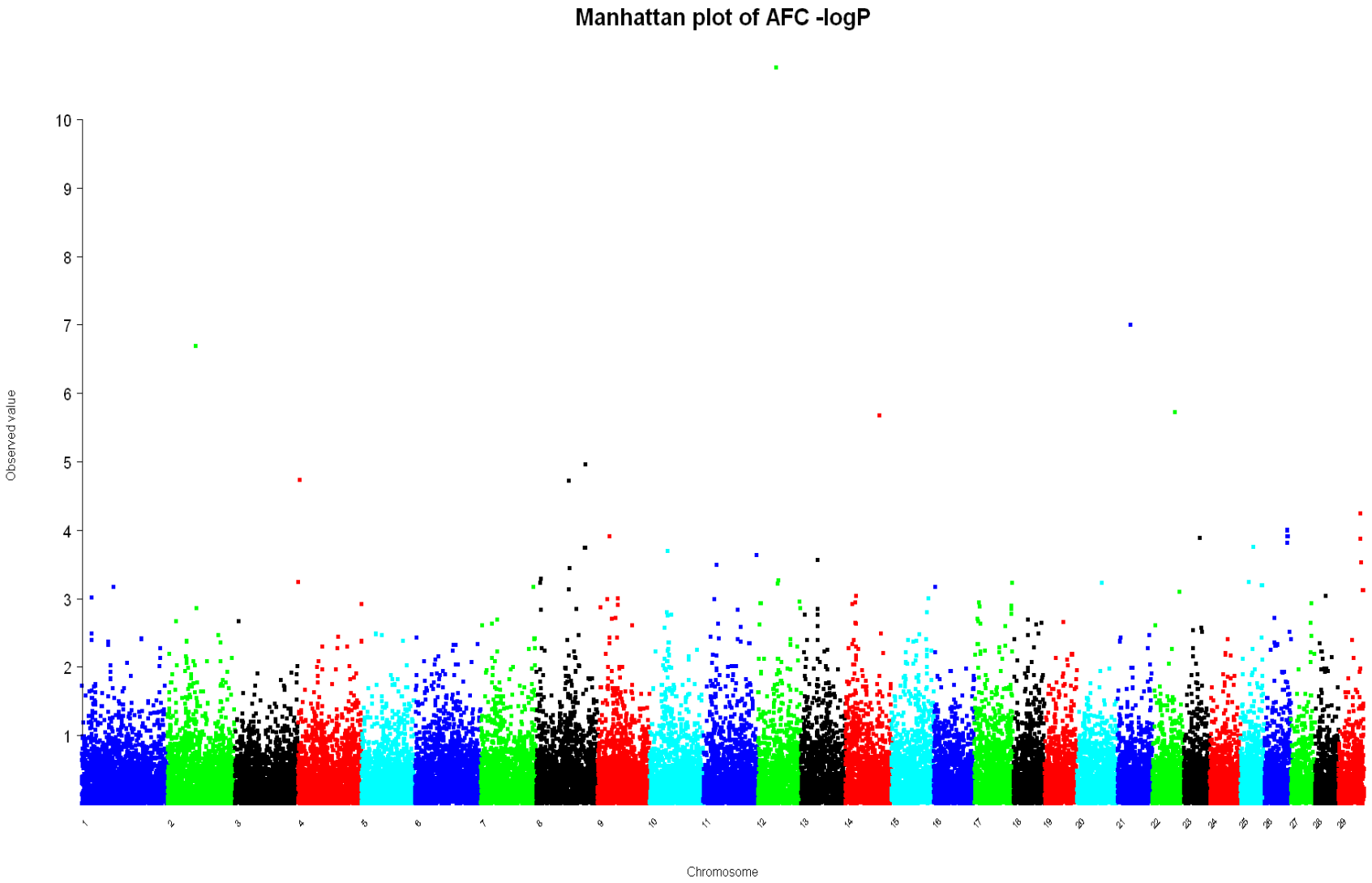
# Age at 1st calving – SNP showing GxE



# Age at 1st calving SNPs

BTA 2 – Single SNP P = 6.69

BTA 12 – Single SNP P = 10.75

BTA 21 – Single SNP P = 6.99

BTA 21 – Single SNP P = 5.71

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# Concluding remarks

Method works

Reveals some interesting results DGAT1

Larger numbers

More sophisticated models - dominance effects

- genotype as fixed effect

Functional genomics etc.

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# Acknowledgements

Collaborating farmers for their time, data and cooperation

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Thank you for your attention

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