# Genome-wide association study of the de novo synthesized milk fatty acids based on the Dutch, Danish and Chinese Holstein

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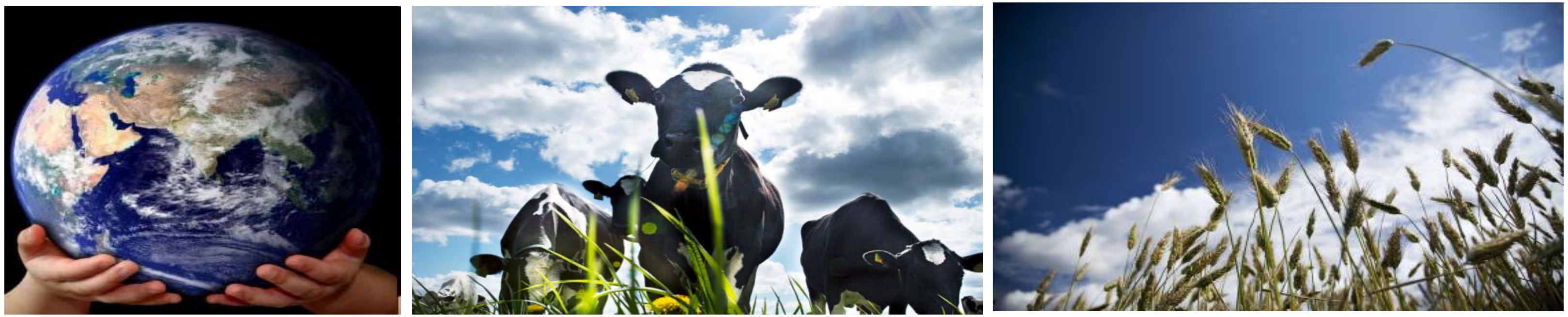


WCGALP 2018

# Background

- Fatty acids (FAs) in milk originate through:
  - Direct transfer from the feed
  - Mobilization of body fat reserve
  - De novo synthesis in the mammary gland
- Substantial genetic variation in de novo synthesized FAs
- Identifying genomic regions essential step for better understanding of the underlying genetics

# Background….

- Expensive to measure traits
- In GWA studies, small data => low power
- Combine data from different population?
- “Mega-analysis” in association studies for human diseases
- Challenges
  - Difference in LD structures?
  - GxE?

# Objectives

- Identify genomic regions for de novo synthesized milk FAs in the Dutch, Danish and Chinese Holstein
- Advantages and challenges of combining datasets for joint GWA studies

# Samples and methods

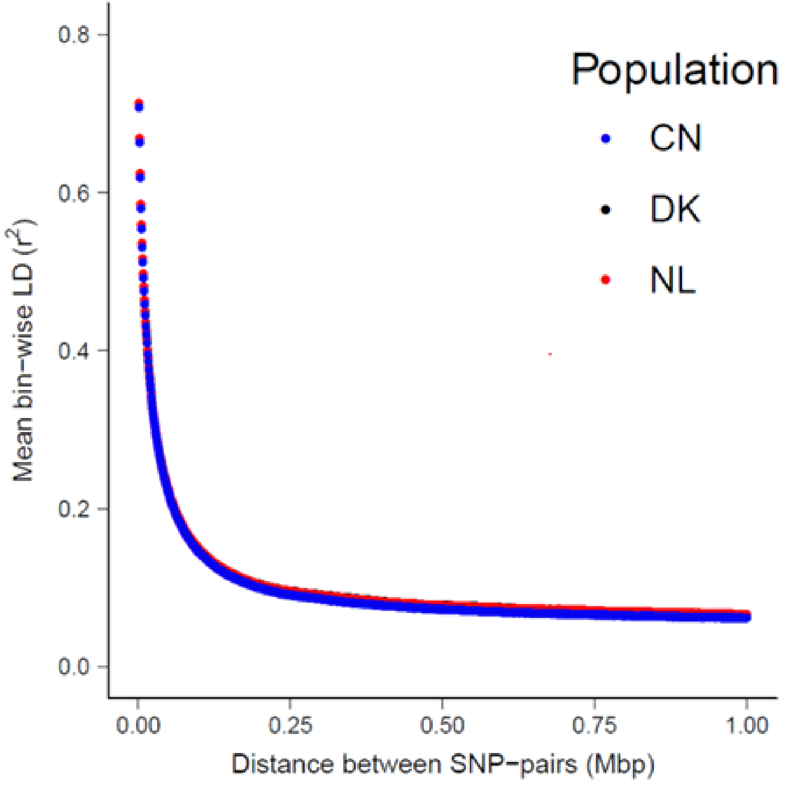
- GC samples on C8:0, C10:0, C12:0, C14:0 and C14:1
- 600 Danish, 1600 Dutch and 700 Chinese Holstein cows
- Bin-wise LD ($r^2$) for pair of SNPs in 1Mbp bin for LD consistency
- Linear mixed model (GCTA program)
  - $y_{ijkl} = \mu + par_i + herd_j + b_1 * DIM_{ijkl} + b_2 * SNP_k + g_l + e_{ijkl}$
- FDR < 5% (~ -log10p-value 5.0)
- Determine multiple regions in a chromosome fitting “LeadSNPs” as fixed effect

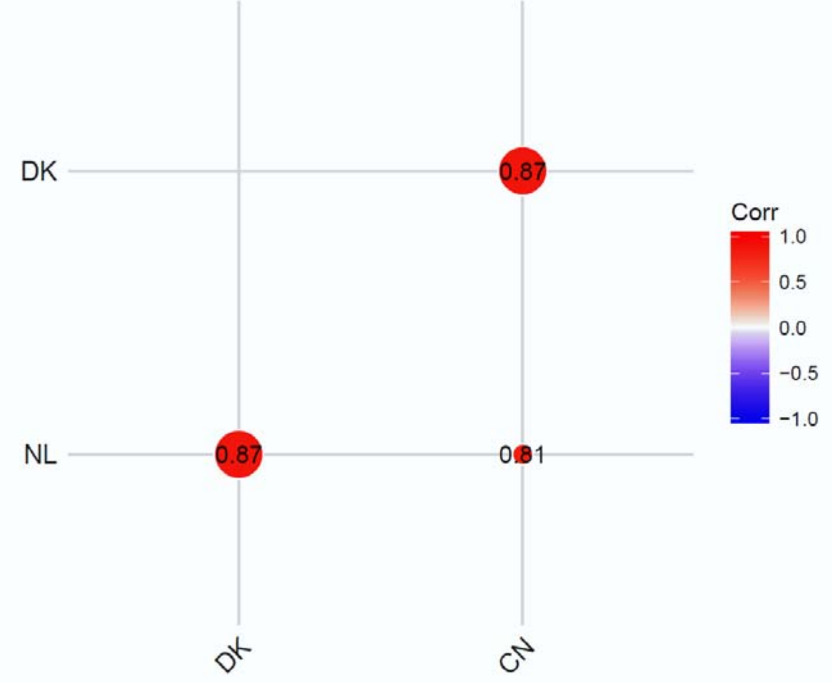
# Results

## Phenotypic means

| Trait | NL | DK | CN |
|---|---|---|---|
| C8:0 | 1.31 | 1.47 | 0.58 |
| C10:0 | 2.87 | 3.22 | 2.22 |
| C12:0 | 3.79 | 3.69 | 2.94 |
| C14:0 | 11.1 | 11.6 | 10.0 |
| C14:1 | 1.38 | 1.01 | 0.86 |

# LD and MAF correlations

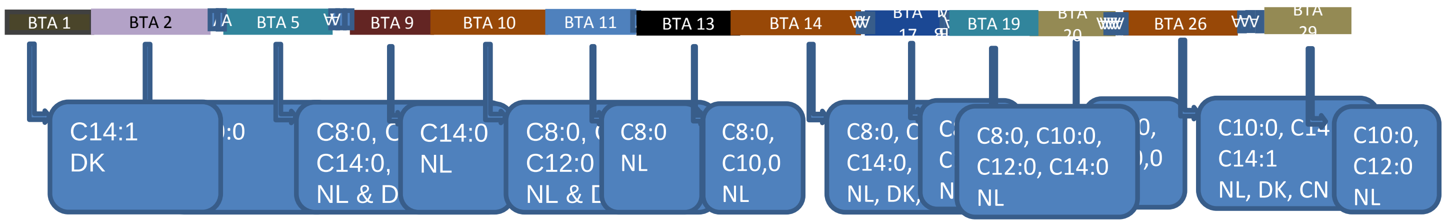




Correlation in MAF

# Population-specific GWAS

- Several regions with significant association (mainly Dutch sample)



BTA 1
BTA 2
BTA 5
BTA 9
BTA 10
BTA 11
BTA 13
BTA 14
BTA 17
BTA 19
BTA 20
BTA 26
BTA 29

C14:1
DK

:0

C8:0, C
C14:0,
NL & D

C14:0
NL

C8:0,
C12:0
NL & D

C8:0
NL

C8:0,
C10,0
NL

C8:0, C
C14:0,
NL, DK,

C8:0, C10:0,
C12:0, C14:0
NL

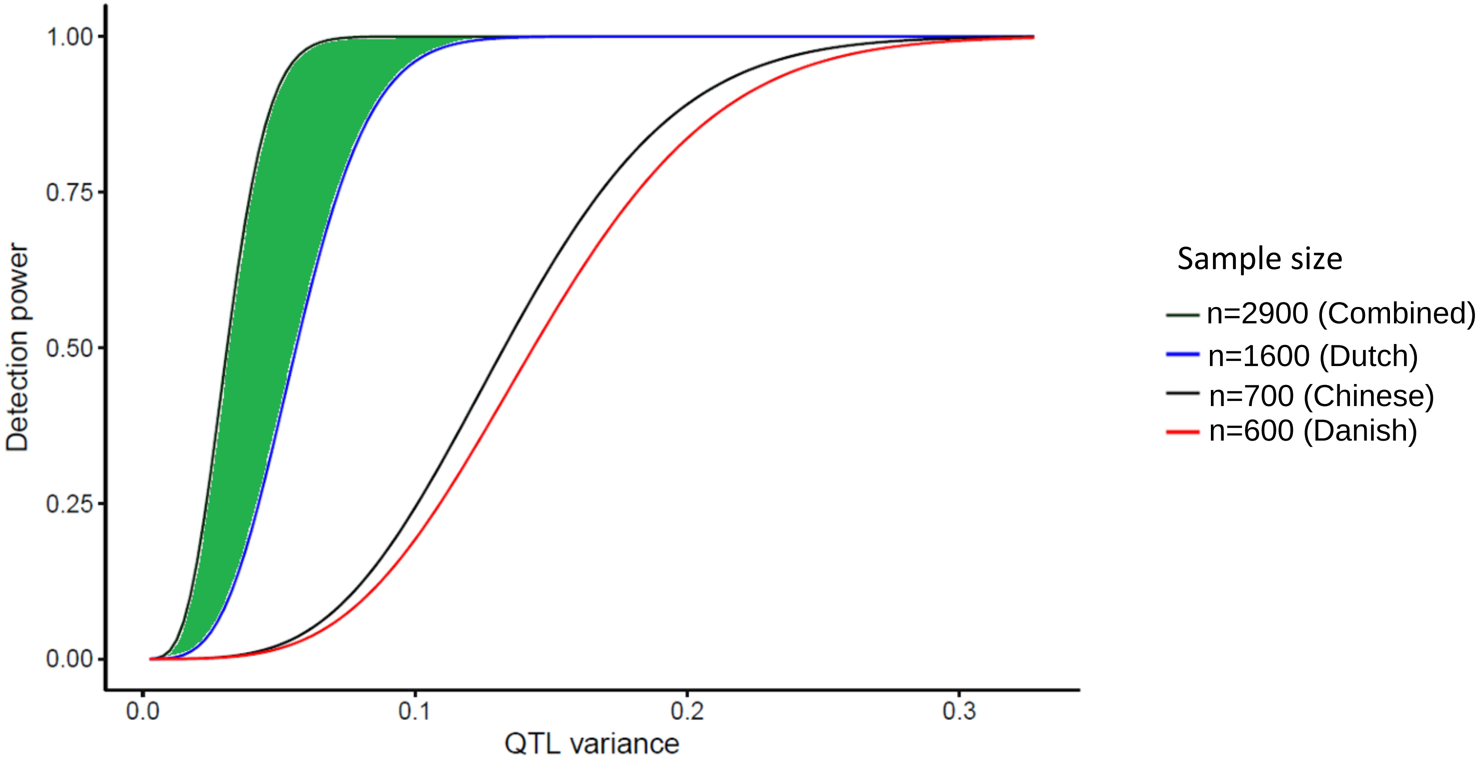
0,
,0

C10:0, C14
C14:1
NL, DK, CN

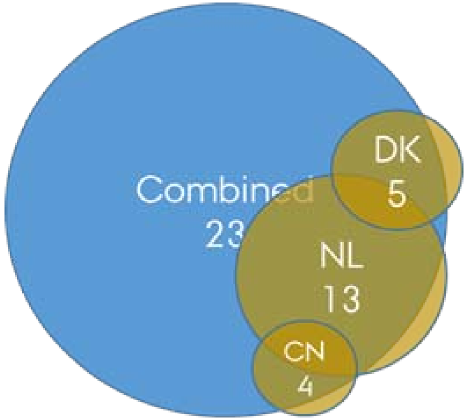
C10:0,
C12:0
NL

- In Chinese and Danish sample, significant association detected only for C14:1

# Additional regions from combined GWAS



# Additional regions from combined GWAS



- 11 additional regions detected from combined analysis
- More fatty acids also significantly associated for regions already detected in population-specific analysis

# Combined GWAS…

- Additional regions were on chromosomes 2, 5, 7, 12 and 15

- Regions on chromosomes 2 and 5:

| Region | Position (Mbp) | Associated fatty acids | Genes in region |
|---|---|---|---|
| **2a** | 12.5 – 19.8 | C8:0, C10:0 | *OSBPL6* |
| **2b** | 54.9 - 59.6 | C14:1 | |
| **2c** | 106.5 – 135.6 | C12:0 | *MECR*, *ACSL3*, *MOGAT1* |
| **5a** | 65.7 – 82.8 | C8:0, C10:0 | |
| **5b** | 87.4 - 99 | C8:0, C10:0, C12:0, C14:1 | *SMCO3*, *LRP6*, *MGST1* |

# Conclusion

- Several regions contribute to genetic variation in milk fatty acid composition
- Promising regions on chromosomes 2 and 5
- Combining related populations enabled detection of regions that couldn’t pass threshold in population-specific GWAS

EGS ABG

GenSAP

# Thank you

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