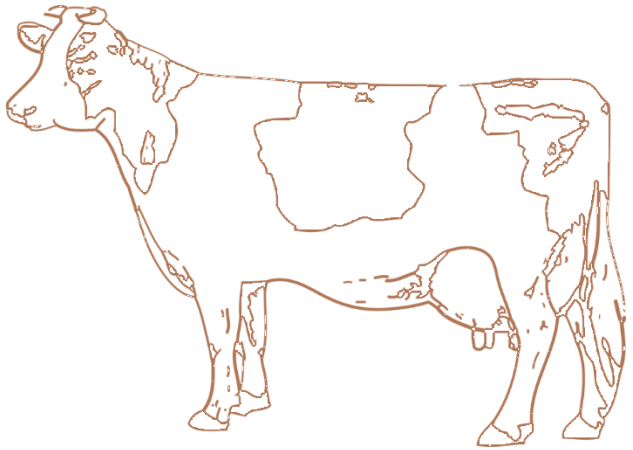
EAAP | 68th ANNUAL MEETING Tallinn, Estonia 2017

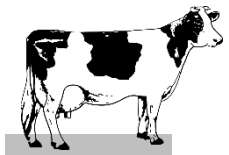
Unravelling the Genetic Background of Clinical Mastitis in Cattle Using Whole Genome Sequence

J.Szyda, M. Mielczarek, M. Frąszczak, G. Minozzi, R. Giannico, JL. Williams, K. Wojdak-Maksymiec

Objective

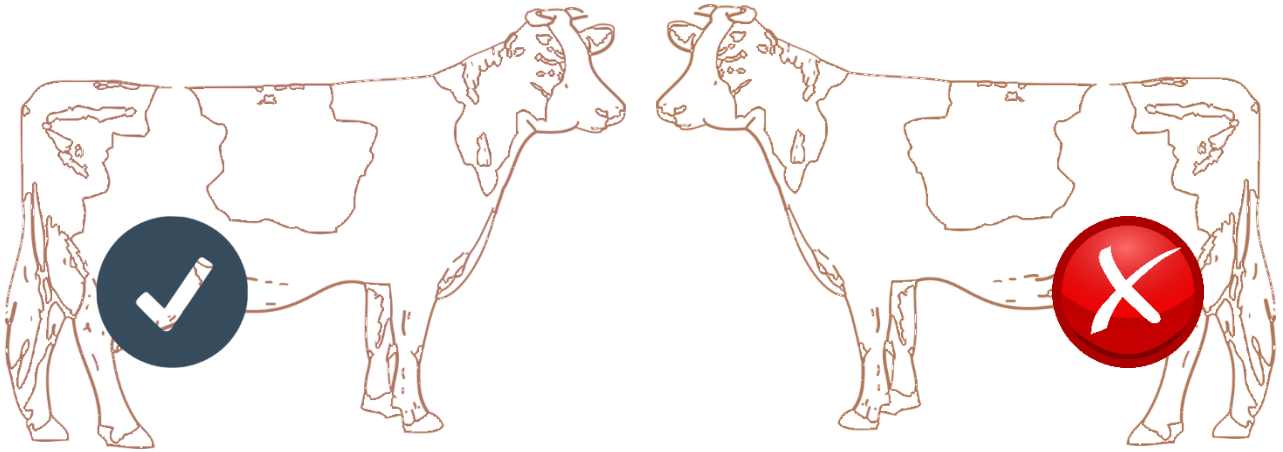
- characterize links between **SNPs** and **CNVs** and the incidence of **clinical mastitis**



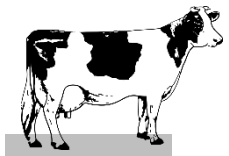


Dataset

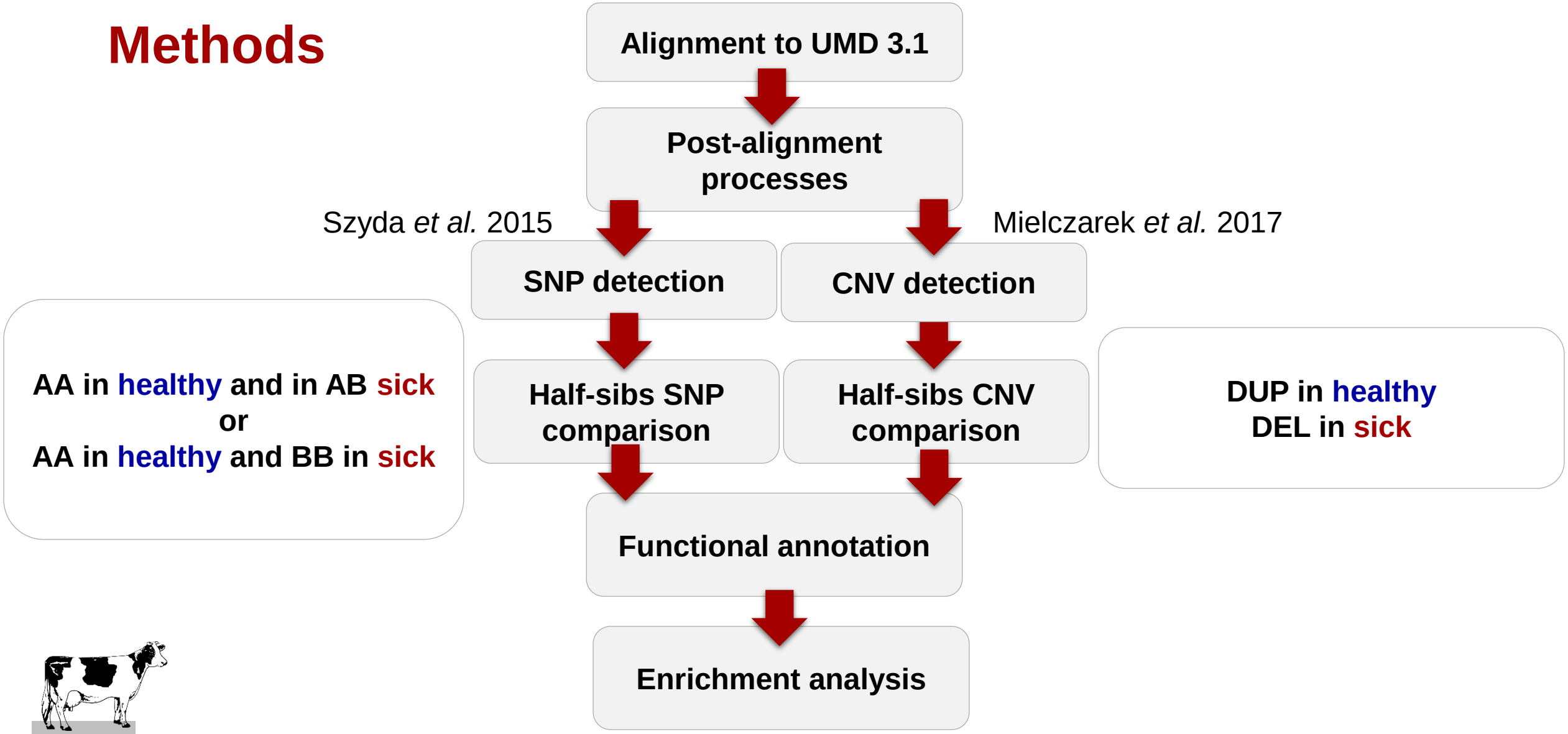
- 32 HF cows
- 16 paternal half-sibs
- Illumina HiSeq 2000 (WGS)
- Coverage 5x – 17x
- Accession → NCBI BioProject PRJNA359667



Healthy **Sick**



Methods


Alignment to UMD 3.1
Post-alignment processes
Szyda *et al.* 2015
Mielczarek *et al.* 2017
SNP detection
CNV detection
AA in healthy and in AB sick
or
AA in healthy and BB in sick
Half-sibs SNP comparison
Half-sibs CNV comparison
DUP in healthy
DEL in sick
Functional annotation
Enrichment analysis

Results: Association of **SNPs** with CM

SNP detection

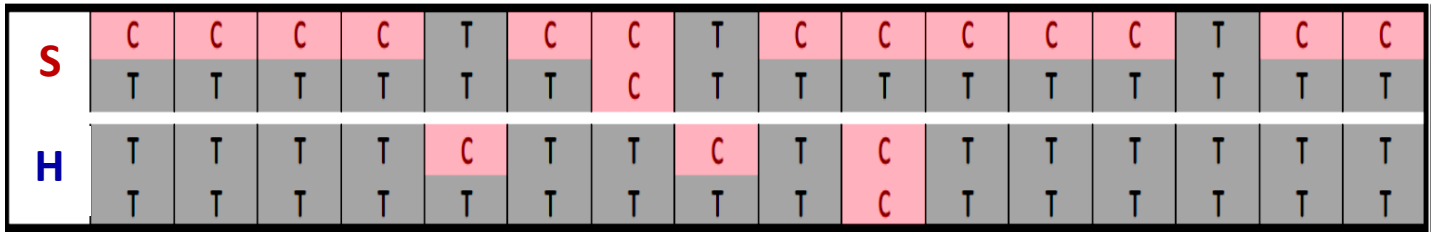
↓

Half-sibs SNP comparison

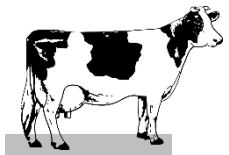
↓

Functional annotation

- 13,827,620 SNPs
- 35 SNPs AB or BB in at least 12 (16) **sick** sibs
- 1 SNP (rs379753215) on BTA3 **exon** of ENSBTAG00000046293



- ADAM30 a role in inflammatory bowel disease (Jostins *et al.* 2012)



Results: Association of **duplications** with CM

CNV detection

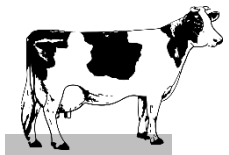
↓

Half-sibs SNP comparison

↓

Functional annotation

- 1,694 - 5,187 duplications per cow
- 36 regions duplicated in at least 9 (13) **healthy** sibs
- 2 overlapped with **exons:**
  - cholinergic receptor nicotinic alpha 10 subunit (BTA15)
  - novel ENSBTAG00000008519 (BTA27)



Results: Association of **deletions** with CM

CNV detection

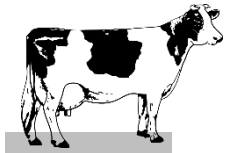
↓

Half-sibs SNP comparison

↓

Functional annotation

- 13,149 and 22,496 deletions per cow
- 192 regions deleted in at least 9 (13) **sick** sibs
- 1 overlapped with 2 lncRNAs on BTA12 (Koufariotis *et al.* 2015)
- 191 overlapped with exons of 46 genes
  - **7 potential causal influence on CM**



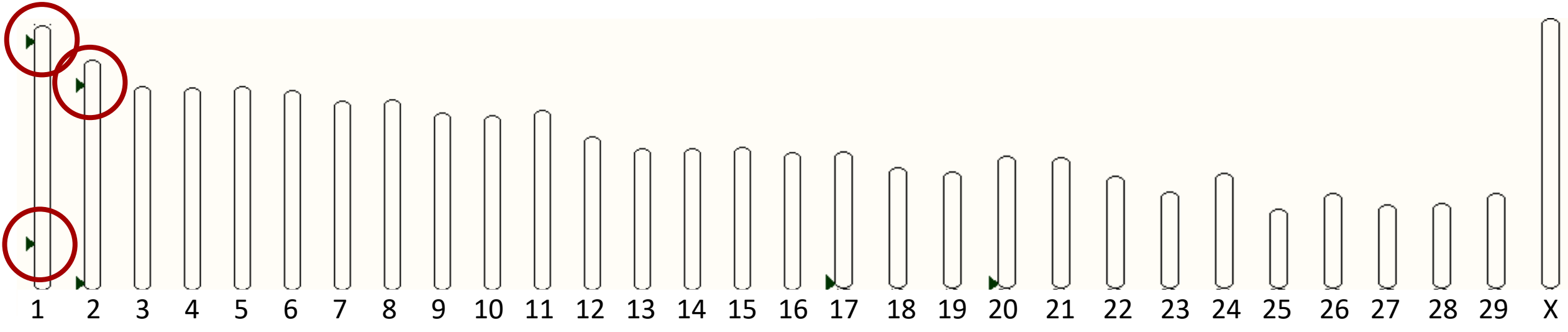
Results: Association of **deletions** with CM

APP: **amyloid beta precursor**
● bactericidal and antifungal activities in human
● molecular markers for a SCM in ruminants (Miglio *et al*. 2013)

FOXL2: forkhead box L2
● role in inflammation processes (Moumné *et al.* 2008)

SSFA2: sperm specific antigen 2
● associated with SCS = indicator of CM (Strillacci *et al.* 2014)
● overlapps with QTL for bovine immunoglobulin G (QTL ID: 20470)

novel **novel** **novel**



Results: Association of **deletions** with CM

OTUD3: **deubiquitinase 3**
● associatied with inflammatory bowel disease in humans (McGovern *et al.* 2010)

Keel *et al.* 2017

ADORA2A: adenosine A2a receptor
● modulating tissue response to inflammation (Salmon *et al.* 1993)
● in mice highly expressed in mammary gland (Yue *et al.* 2014)

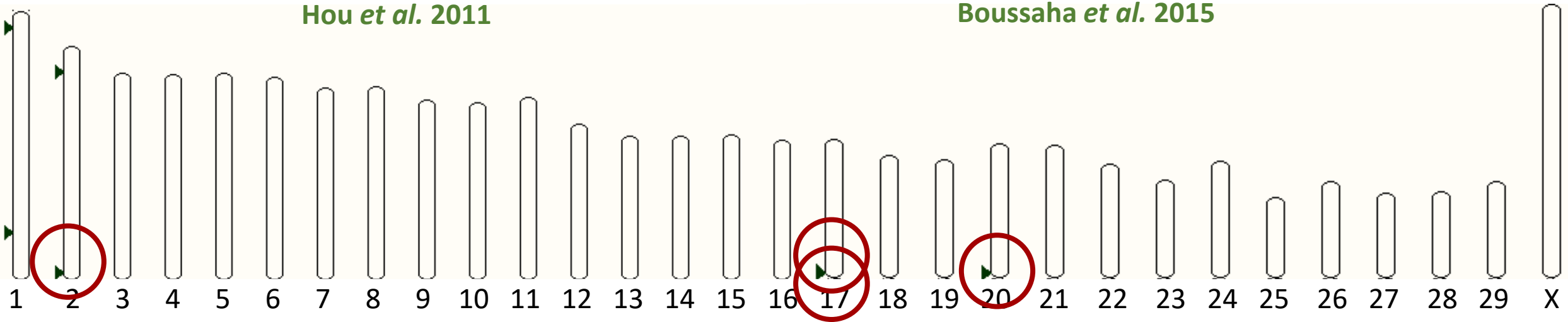
Hou *et al.* 2011

TXNRD2: thioredoxin reductase 2
● candidate for influencing susceptibility *to S.aureus* (Ghorbani *et al*. 2015)

Hou *et al.* 2011

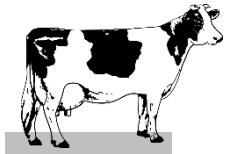
NDUFS6: NADH:ubiquinone oxidoreductase subunit S6
● QTL for SCS = indicator of CM (Durán *et al.* 2016)

Boussaha *et al.* 2015



Results: Enrichment analysis

- No significantly enriched Reactome-, KEGG- pathways, nor GO terms associated with genes underlying the SNP and CNVRs were reported



Conclusions: Technical

A small number of phenotyped animals enahnced with:

- a carefull experimental design

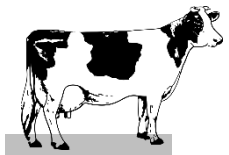
- a bp genomic resolution

- Allowed for functional inferences on clinical mastitis ☺

  → promising genes identified

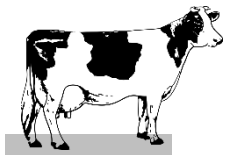
- Did not allow for statistical analysis ☹

  → no population-wide conclusions available



Conclusions: Biological

- CNVs play an important role in susceptibility to clinical mastitis
- Identified genes are involved in immune response
- Deletions – more severe consequences on reducing resistance against clinical mastitis, than
- Duplications – on increasing resistance to clinical mastitis



Submitted to:
frontiers in Genetics

Acknowledgements

The Network of Animal Disease Infectiology Research Facilities

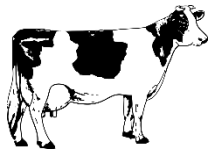
Polish National Science Centre

Leading National Research Centre in Poland

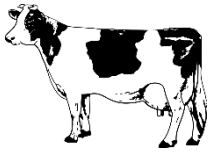
Poznan Supercomputing and Networking Center

Conclusions: Biological

- CNVs play an important role in susceptibility to clinical mastitis
- Identified genes are involved in immune response
- Deletions – more severe consequences on reducing resistance against clinical mastitis, than
- Duplications – on increasing resistance to clinical mastitis



Thank you!



Submitted to:

frontiers in Genetics