



# Using whole genome sequences to identify QTL for udder health and morphology in French dairy cattle

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## *Material & methods: animals*

**2,588**

Montbéliard bulls

**MON**



**2,319**

Normand bulls

**NOR**



**6,333**

Holstein bulls

**HOL**

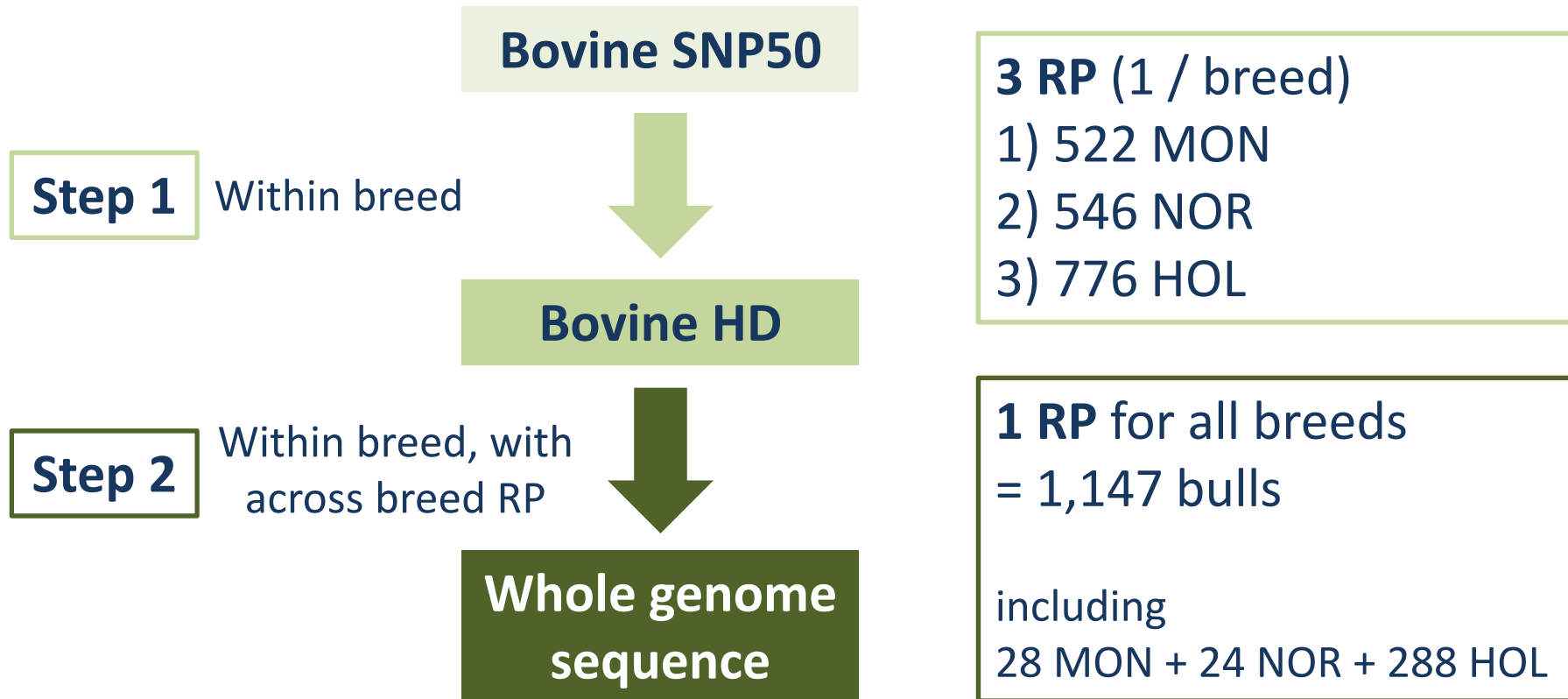


genotyped with the 50k or 800K Beadchips

# Material & methods: genotypes & imputation

*Imputation in two steps with Flmpute (Sargolzaei et al., 2014)*

*Reference populations (RP)*

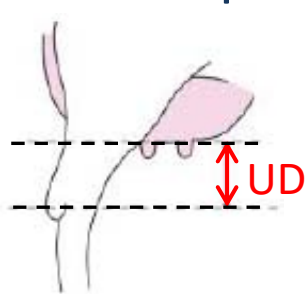


**27 millions of sequence variants**

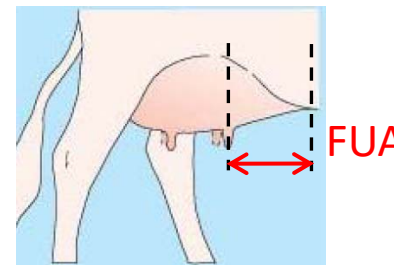
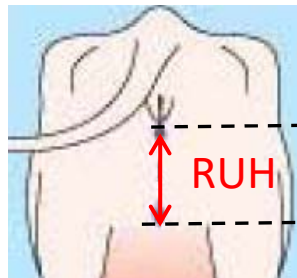
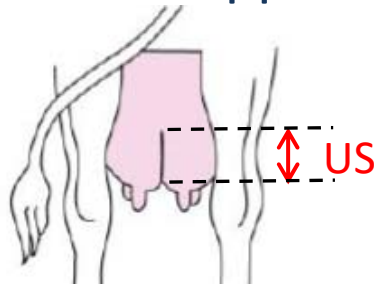
# Material & methods: phenotypes

- 2 udder health traits: - Clinical Mastitis before day 150 of lact. (**CM**)  
- Somatic Cells Count in milk (**SCC**)

- 6 - 11 udder conformation traits (*dep. pop.*), correlated with health:
  - udder depth (**UD**), udder support (**US**), fore udder attachment (**FUA**)



rear udder height,  
(**RUH**)



+ teat length, thickness, position, ...

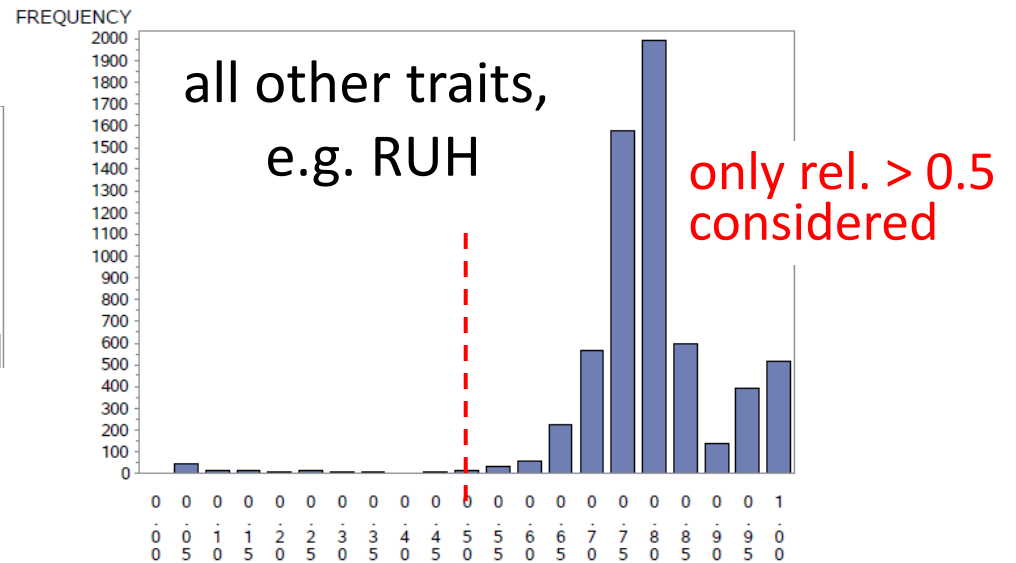
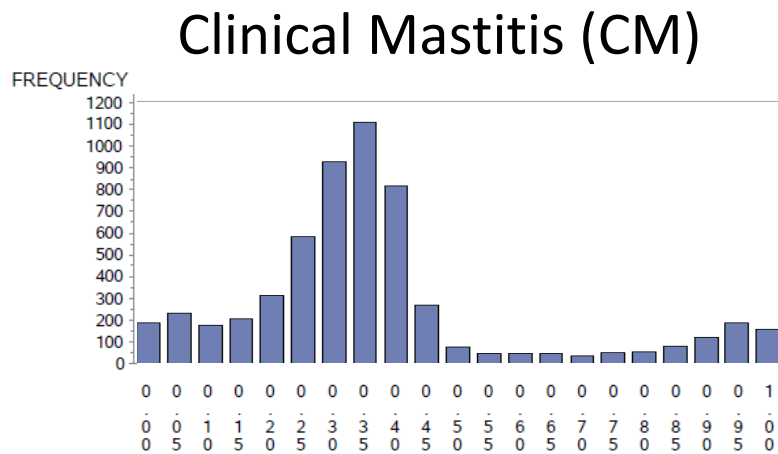
- milking ease (**ME**)

# Material & methods: phenotypes

Phenotypes recorded on females

→ use of **Daughter Yield Deviations (DYD)** of the bulls as response variables for association testing

Distribution of DYD reliability ( $r^2$ ): example for HOL bulls



→ Nb of bulls considered:

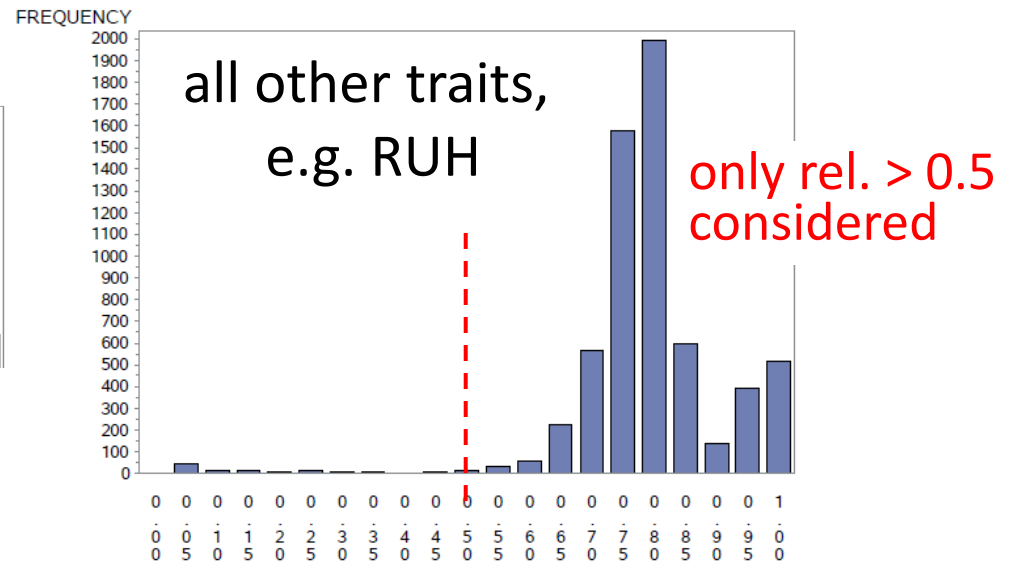
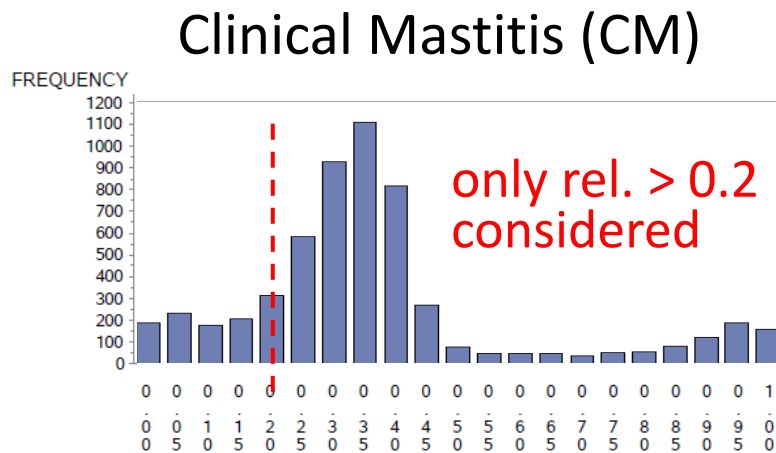
	population	Clinical Mastitis	other traits
MONTBELIARDE			2,438 to 2,515
NORMANDE			2,020 to 2,203
HOLSTEIN			5,959 to 6,321

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→ Nb of bulls considered:

	population	Clinical Mastitis	other traits
MONTBELIARDE		1,857	2,438 to 2,515
NORMANDE		1,427	2,020 to 2,203
HOLSTEIN		4,959	5,959 to 6,321







# Results: Number of QTL per trait & population

Genome-wide significance : 5% or better

Trait	MON	NOR	HOL	distinct QTL
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Nb of distinct QTL	10	5	20	<b>31</b>
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# Results: Number of QTL per trait & population

Genome-wide significance : 5% or better

Trait	MON	NOR	HOL	distinct QTL
Clinical Mastitis				0
Somatic Cell Count	2		2	4
Rear Udder Height	1	4	2	7
Udder Depth	2		6	6
Fore Udder Attachment	1		3	4
Milking Ease	2		2	3
Udder balance	1		2	3
Udder Support	1	1	1	2
Other traits				0 or 1
<b>Nb of distinct QTL</b>	<b>10</b>	<b>5</b>	<b>20</b>	<b>31</b>

From 0 to 6 QTL per trait within population

## **Results:**



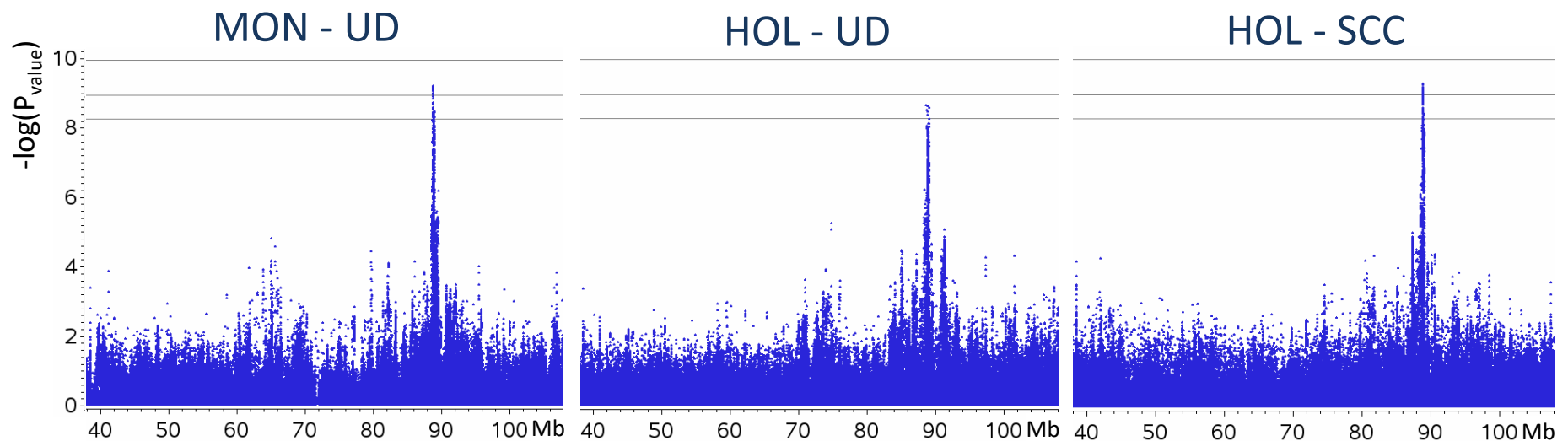
Most of the time:

no **significant** QTL shared between different traits / different breeds ...

***Focus on some QTL detected in 2 or 3 breeds or for several traits***

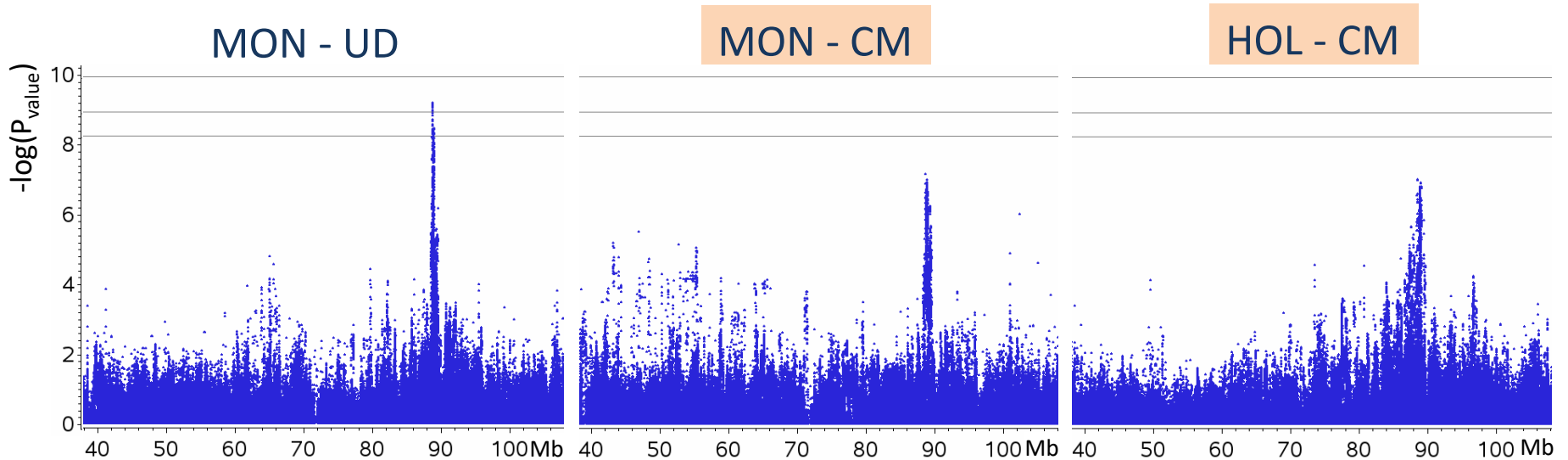
## Results: QTL *bta6* ~88.8 Mb

breed	Trait	Top variant (bp)	$-\log_{10}(P_{\text{value}})_{\text{max}}$
MON	Udder Depth	88,744,985	9.16 < 1%
HOL	Udder Depth	88,697,293	8.61 < 5%
HOL	Somatic Cell Count	88,881,928	9.21 < 1%



# Results: QTL *bta6* ~88.8 Mb

	breed	Trait	Top variant (bp)	$-\log_{10}(P_{\text{value}})_{\text{max}}$
	MON	Udder Depth	88,744,985	9.16 < 1%
→	HOL	Udder Depth	88,697,293	8.61 < 5%
	NOR	<i>Udder Depth</i>	<i>88,918,554</i>	<i>6.83 (NS)</i>
	HOL	Somatic Cell Count	88,881,928	9.21 < 1%
→	MON	<i>Somatic Cell Count</i>	<i>88,512,675</i>	<i>6.13 (NS)</i>
→	MON	<i>Clinical Mastitis</i>	<i>88,677,080</i>	<i>7.13 (NS)</i>
→	HOL	<i>Clinical Mastitis</i>	<i>88,484,141</i>	<i>6.99 (NS)</i>

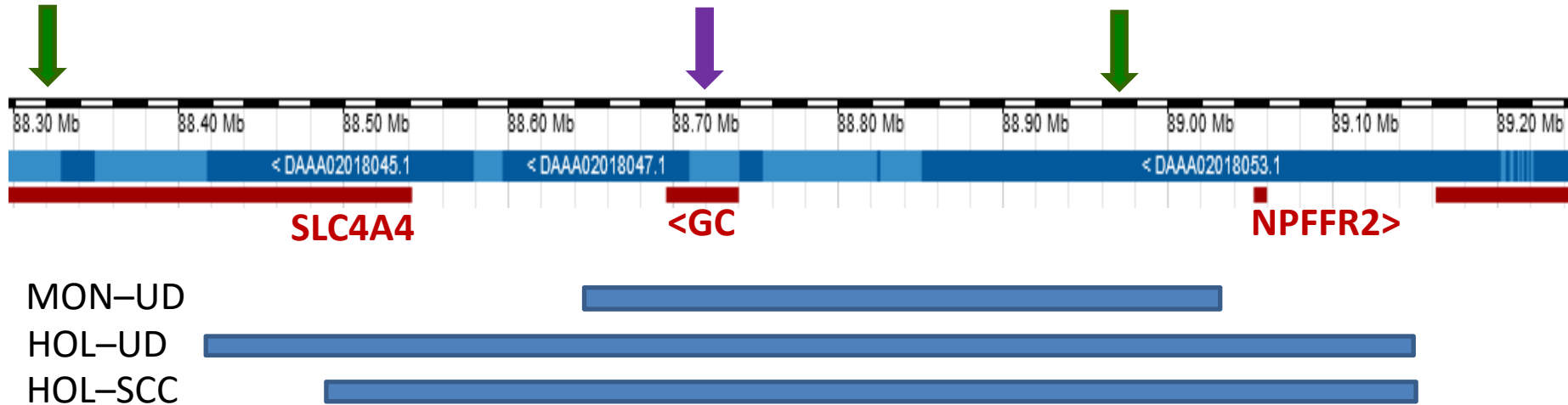


## Results: QTL *bta6* ~88.8 Mb

Sahana et al (2014)  
SCC in HOL

Pausch et al (2016)  
UD, FUL, CL in Flekvieh

Sahana et al (2014)  
CM in HOL & Nordic Red



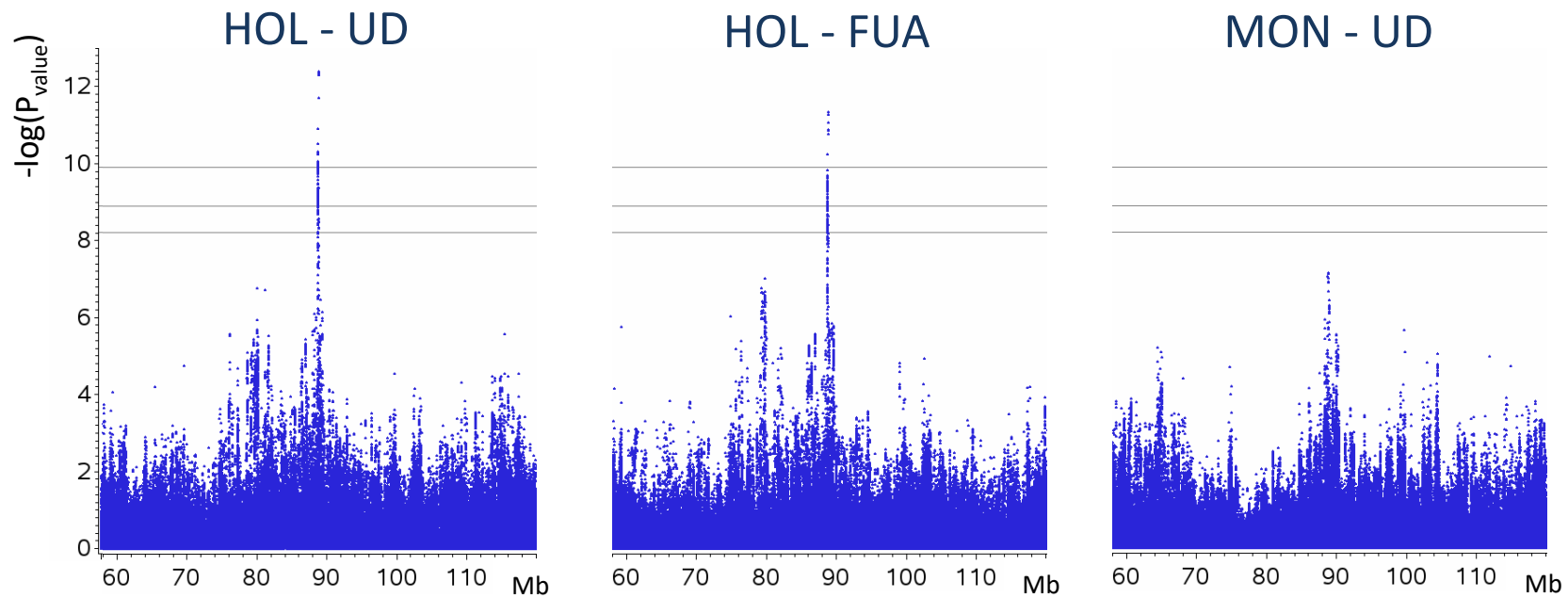
Among SNP with low P-value in confidence interval:

- **GC gene:** upstream region, introns
- **NPFFR2 gene:** upstream region, 1 missense, introns
- **SLC4A4 gene:** introns

**GC and NPFFR2 = good candidates** (*Pausch et al (2016), Sahana et al (2014)*)

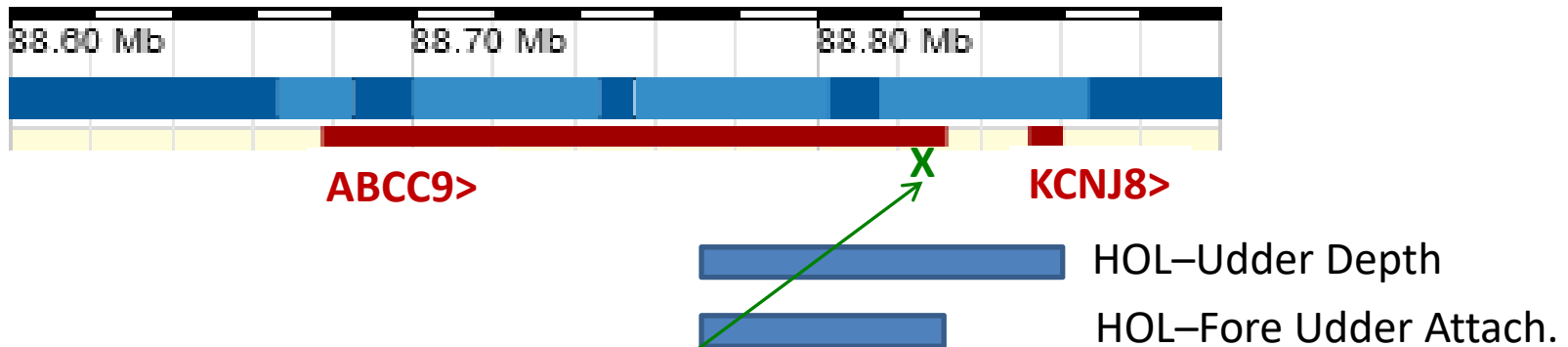
# Results: QTL *bta5* ~88.8 Mb

breed	Trait	Top variant (bp)	$-\log_{10}(P_{\text{value}})_{\text{max}}$
HOL	Udder Depth	88,800,994	12.39 < 1‰
MON	<i>Udder Depth</i>	88,862,821	7.167 (NS)
HOL	Fore Udder Attach.	88,800,994	11.33 < 1‰





## Results: QTL *bta5* ~88.8 Mb



SNP with low P-value in confidence intervals:

- ABCC9 gene

→ SNP pb88,823,164: splice region variant,

~top SNP for HOL-UD, MON-UD & HOL-FUA

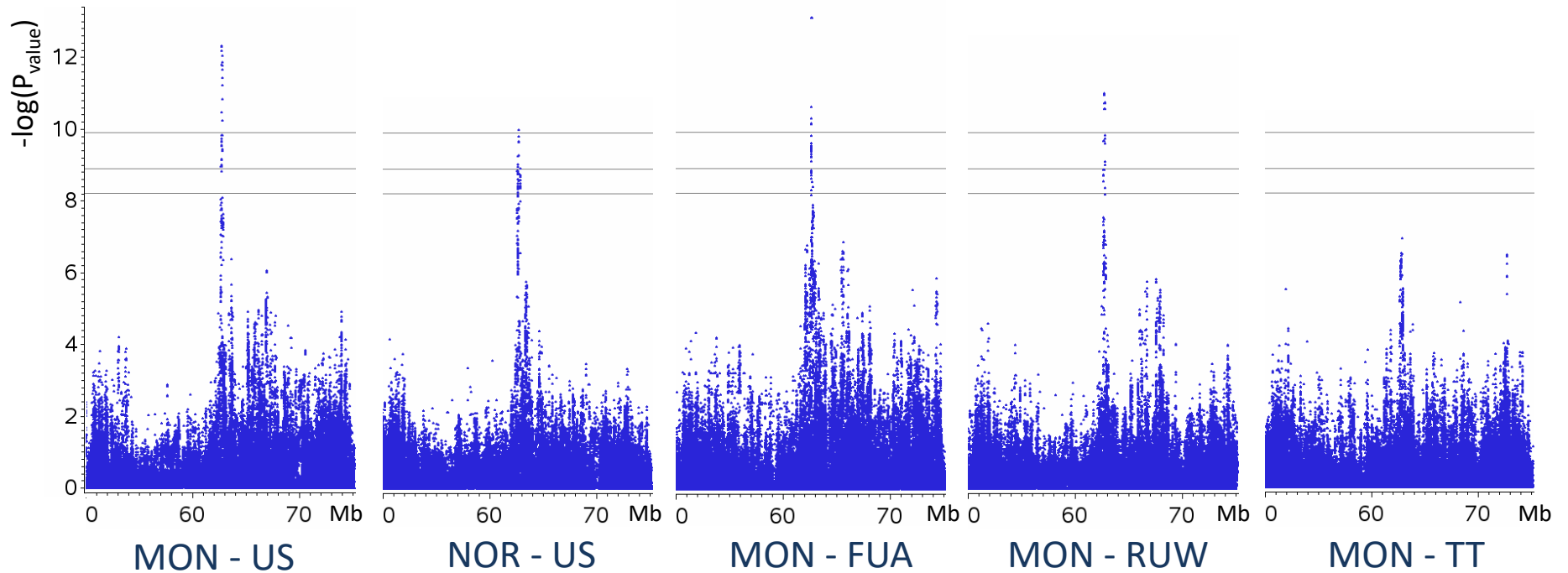
→ SNP in introns

- KCNJ8 gene

→ SNP in downstream region (HOL-FUA)

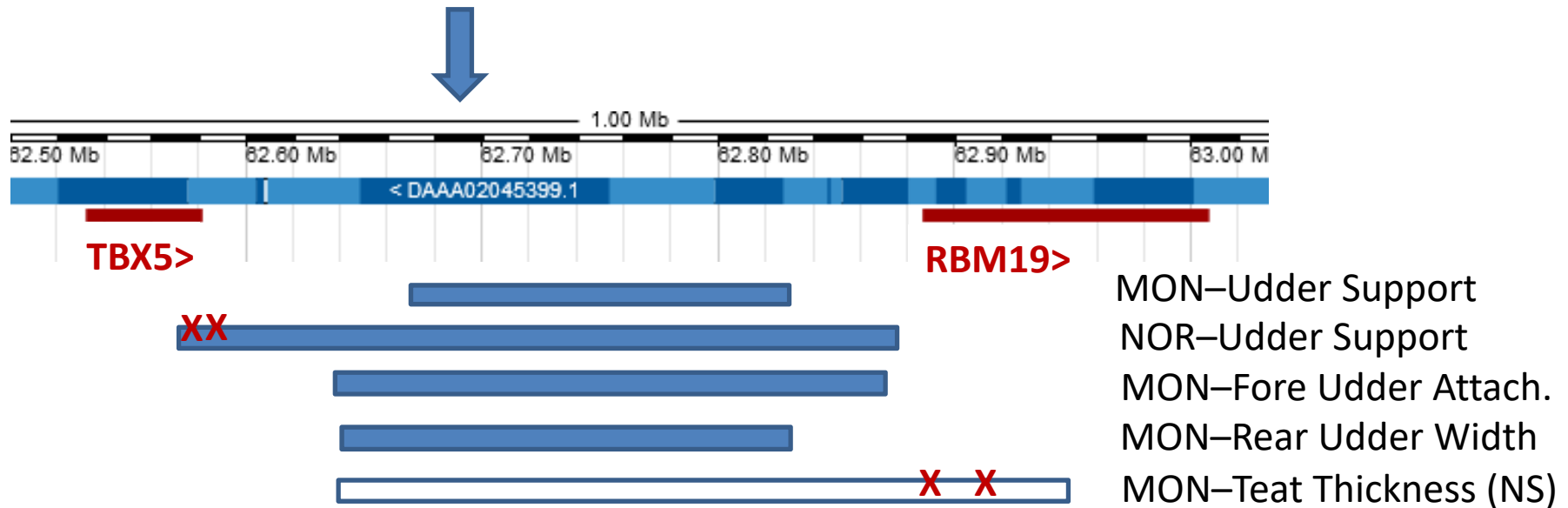
# Results: QTL *bta17* ~62.70 Mb

breed	Trait	Top variant (bp)	$-\log_{10}(P_{\text{value}})$ max
MON	Udder Support	62,714,882	12.32 < 1‰
NOR	Udder Support	62,694,032	10.00 < 1‰
MON	Fore Udder Attach.	62,679,331	13.09 < 1‰
MON	Rear Udder Width	62,714,882	11.00 < 1‰
MON	Teat Thickness	62,885,659	6.96 (NS)



## Results: QTL *bta17* ~62.70 Mb

Pausch et al (2016) : QTL for Teat Thickness, Fore Udder Length & Central Ligament at 62.69Mb in Flekvieh breed (TBX5, RBM19)



Among SNP with the lowest P-value in confidence intervals:

- MON-US, MON-FUA, MON-RUW: lowest  $P_{\text{values}}$  : **only intergenic SNP ...**
- NOR-US: **downstream region and introns of TBX5 gene**
- MON-TT: upstream region and introns of **RBM19 gene (but NS)**



# Aknowledgements

To the **1000 bull genomes** project partners

To **Apigene** and **ANR** for their financial support to sequencing



**Thank you for your attention**