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Italiadomani
PIANO NAZIONALE
DI RIPRESA E RESILIENZA



Cosmopolitan and local Italian beef cattle breeds uncover common patterns of heterozygosity related to fitness traits

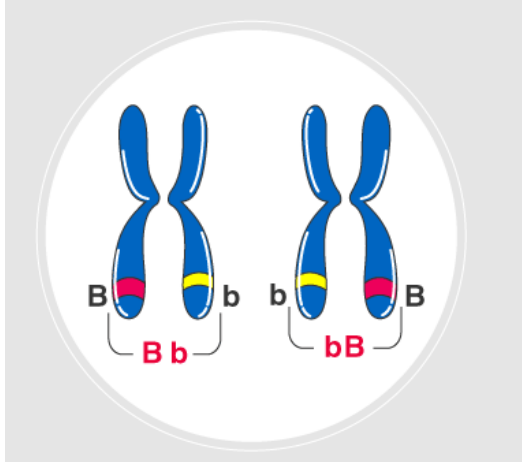
Maria Chiara Fabbri ^{1*}, Francesco Tiezzi ¹, Alessandro Crovetto ¹, Christian Maltecca ^{1, 2}, Riccardo Bozzi ¹

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Università degli Studi di Firenze, Piazzale delle Cascine 18, 50144 Florence, Italy;*

² *Department of Animal Science, North Carolina State University, 120 W Broughton Dr, Raleigh, NC 27607, USA;*



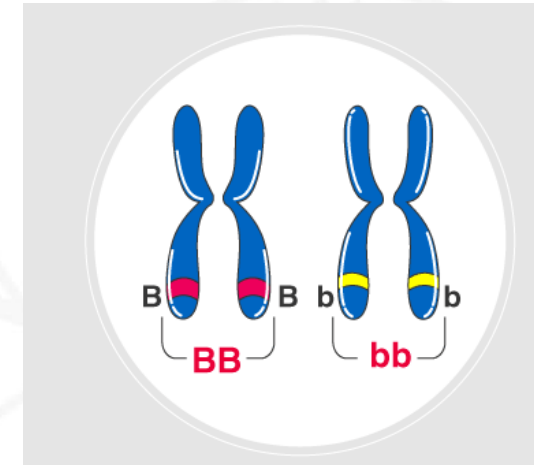
Introduction



Heterozygosity is the possession of two **different allelic forms**



Genetic Diversity

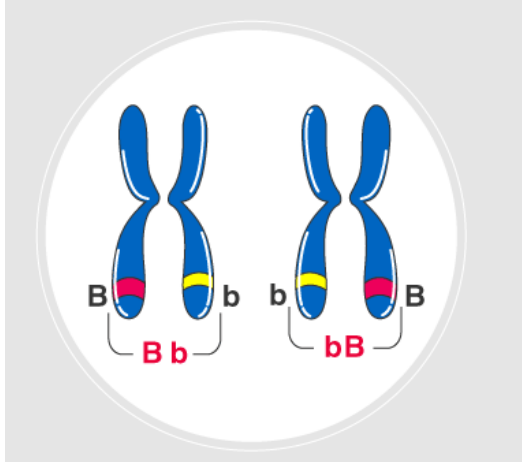


Homozygosity is the state of possessing two **identical allelic forms**

Fitness



Introduction



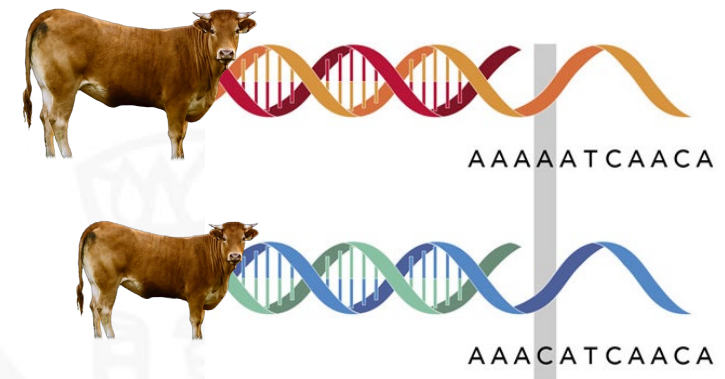
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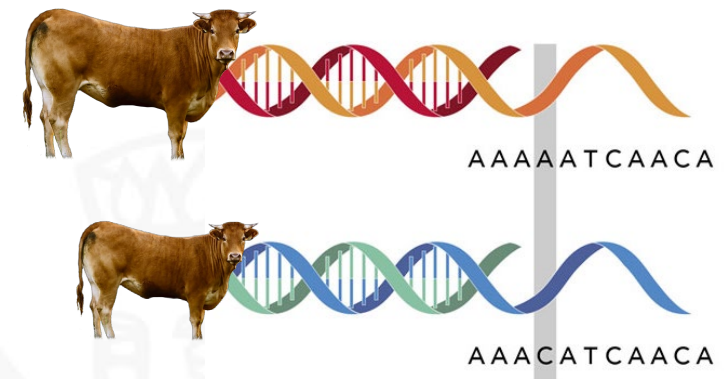
Introduction



- Heterozygous-Rich Regions (HRRs) = regions of consecutive heterozygous sites
- *“The analysis of HRR aims to identify genomic regions with high genetic variability, to provide information about the populations’ genetic diversity and evolutionary history⁵, as well as to identify specific segments in the genome where increased genetic diversity could be beneficial^{6,7}”*

Chessari, G., Criscione, A., Marletta, D. et al. Characterization of heterozygosity-rich regions in Italian and worldwide goat breeds. Sci Rep 14, 3 (2024).
<https://doi.org/10.1038/s41598-023-49125-x>

Introduction

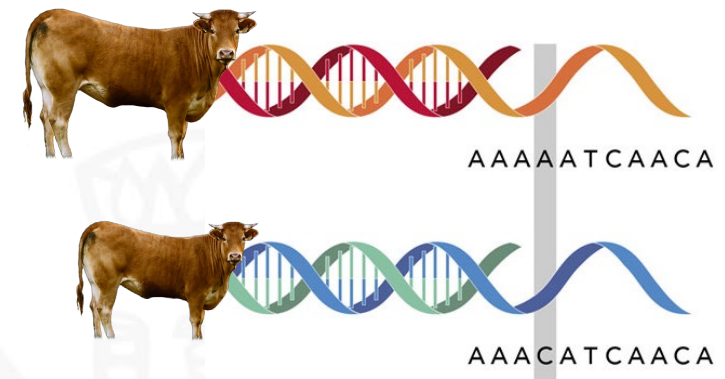


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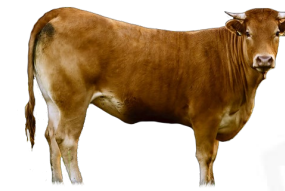


Evidence suggests that increased heterozygosity occurs in regions under **balancing selection** or with a high recombination rate, as low linkage disequilibrium leads to high region diversity.

Introduction

The increase in inbreeding is:

Unwanted



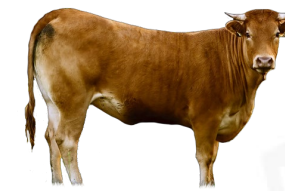
Introduction

The increase in inbreeding is:

Unwanted



Wanted



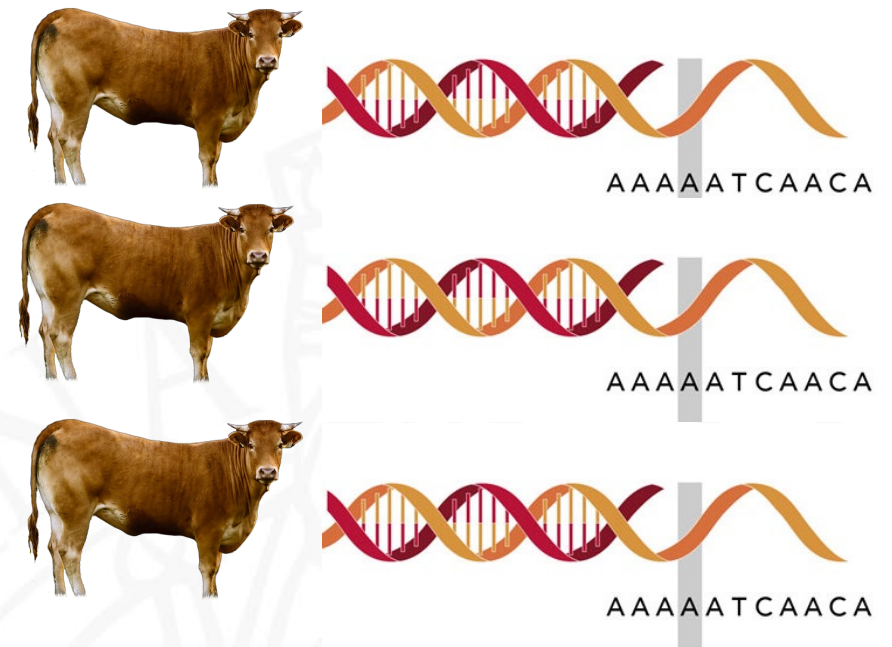
Introduction

The increase in inbreeding is:

Unwanted

Wanted

Consequently, fundamental to investigate regions which **should be** maintained **heterozygous**.

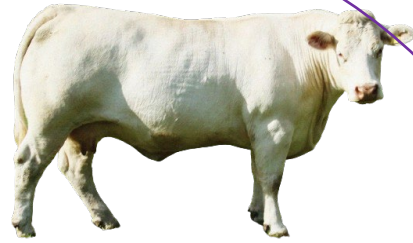


AIM:

To identify and to compare patterns of heterozygosity in five Italian beef breeds, with the purpose to elicit particular selection patterns present in the local breeds that might differentiate them from the cosmopolitan ones.



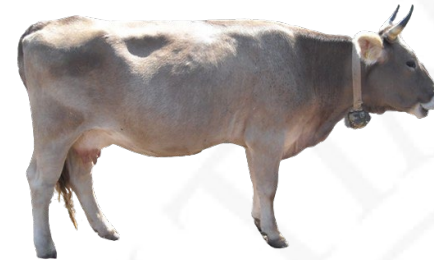
Limousine, LIM



Charolaise, CHA



Calvana, CAL



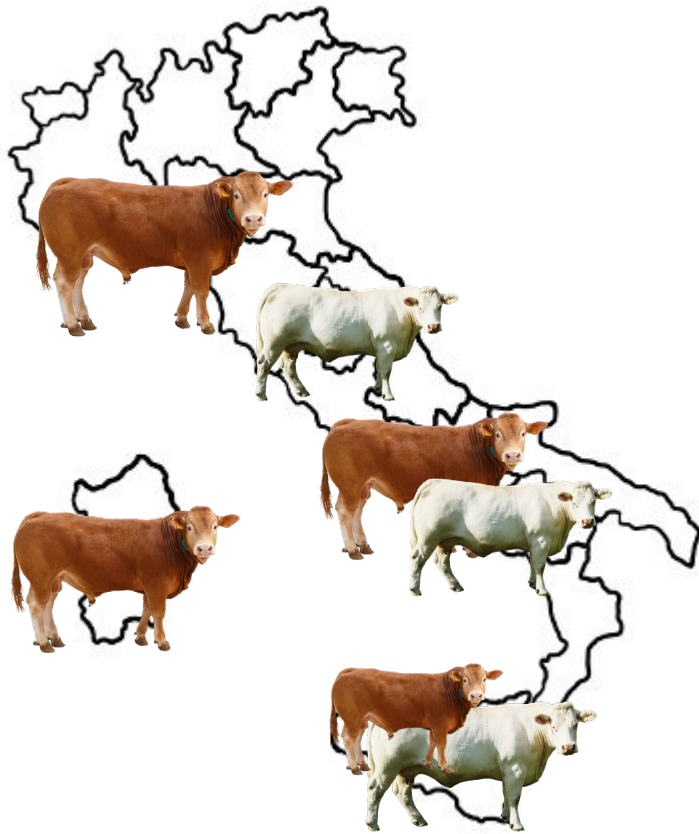
Sardo Bruna, SAB



Sarda, SAR

The breeds' **population size is high** but **different selective history**.

Material & Methods

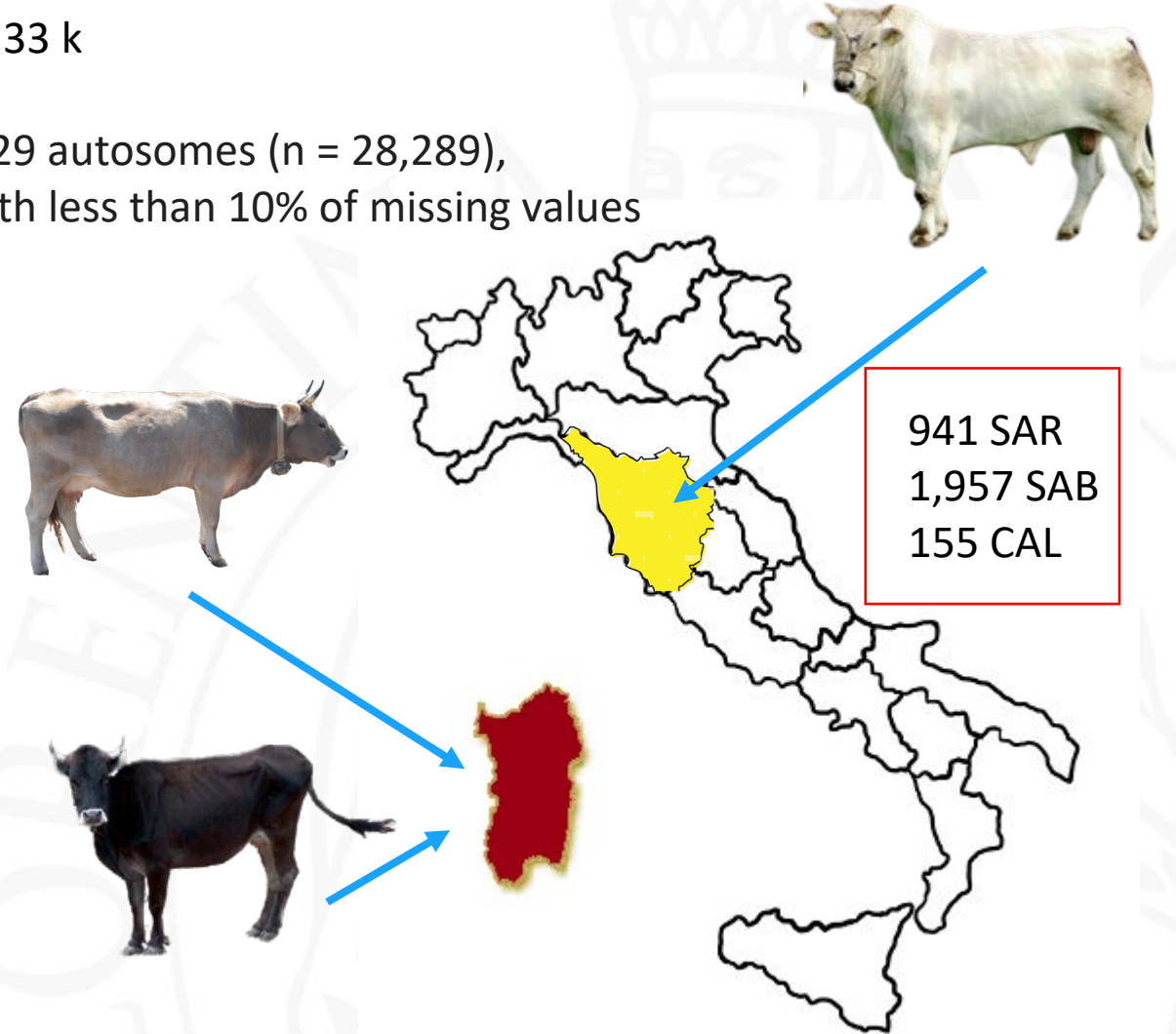
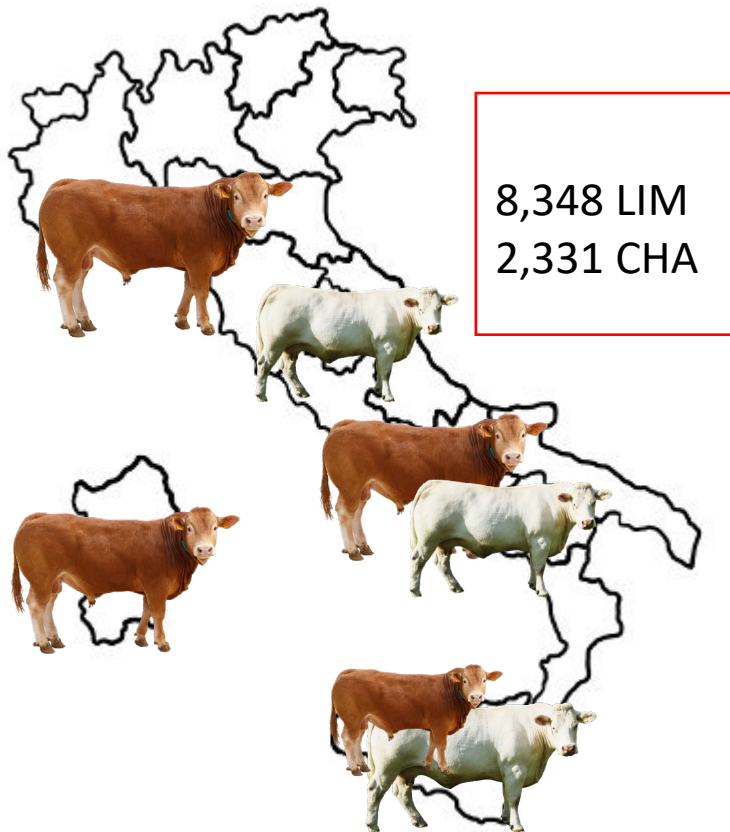


- 13,732 DNA samples

- GeneSeek GGP-LDv4 33 k

- SNPs located on the 29 autosomes ($n = 28,289$), individuals and SNPs with less than 10% of missing values

Material & Methods



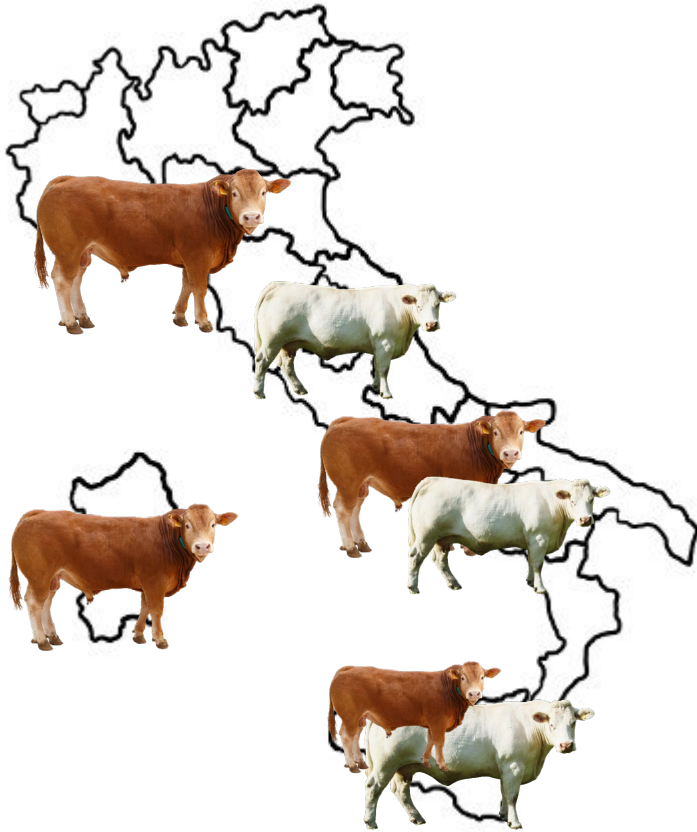
Material & Methods

1 – Genetic distances among breeds
Multidimensional Scaling and
ADMIXTURE Analyses

2 – Investigation of Heterozygous Rich
Regions through *detectRuns* R package

- N. Minimum SNPs: 15
 - Length: 10 kbp
 - Missing genotypes: 1
 - Opposite genotypes: 2
-
- Significant HRR: represented in more than **25%** of all individuals for each breed.

3 - Gene Enrichment Analysis



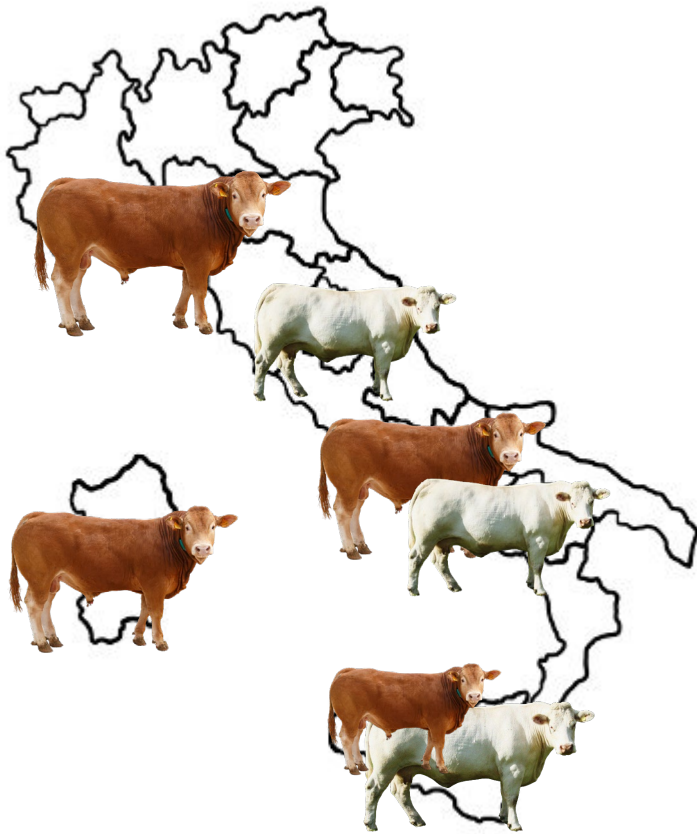
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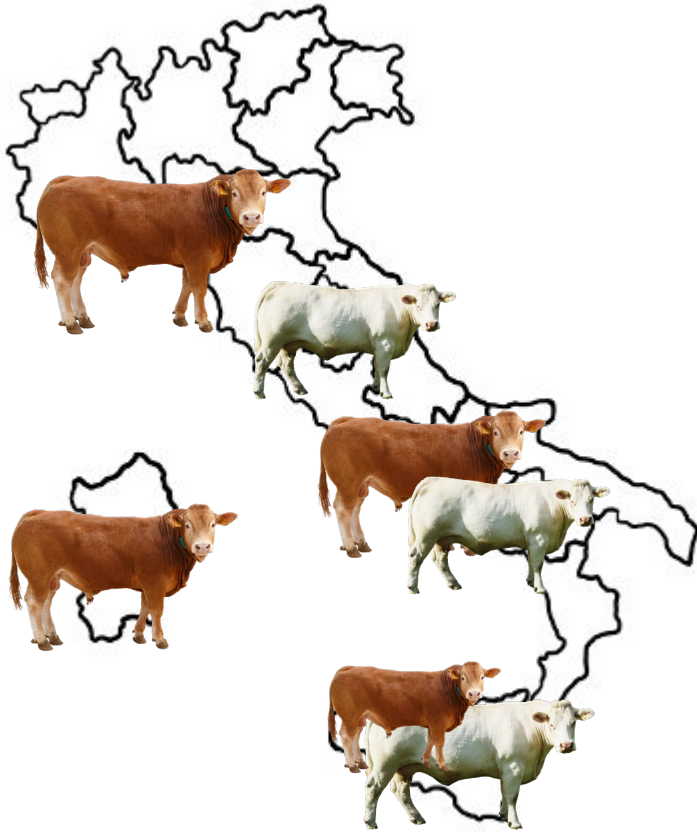
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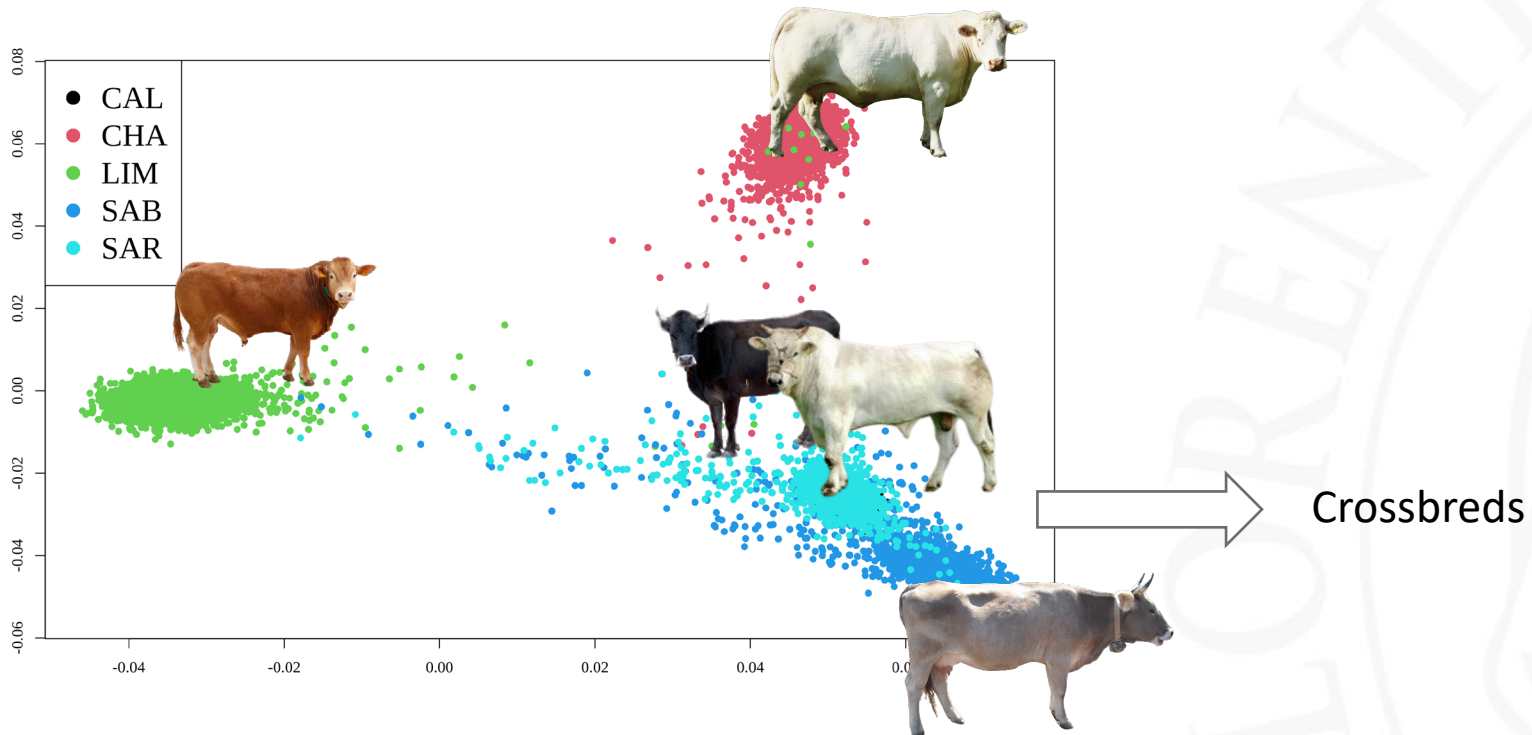
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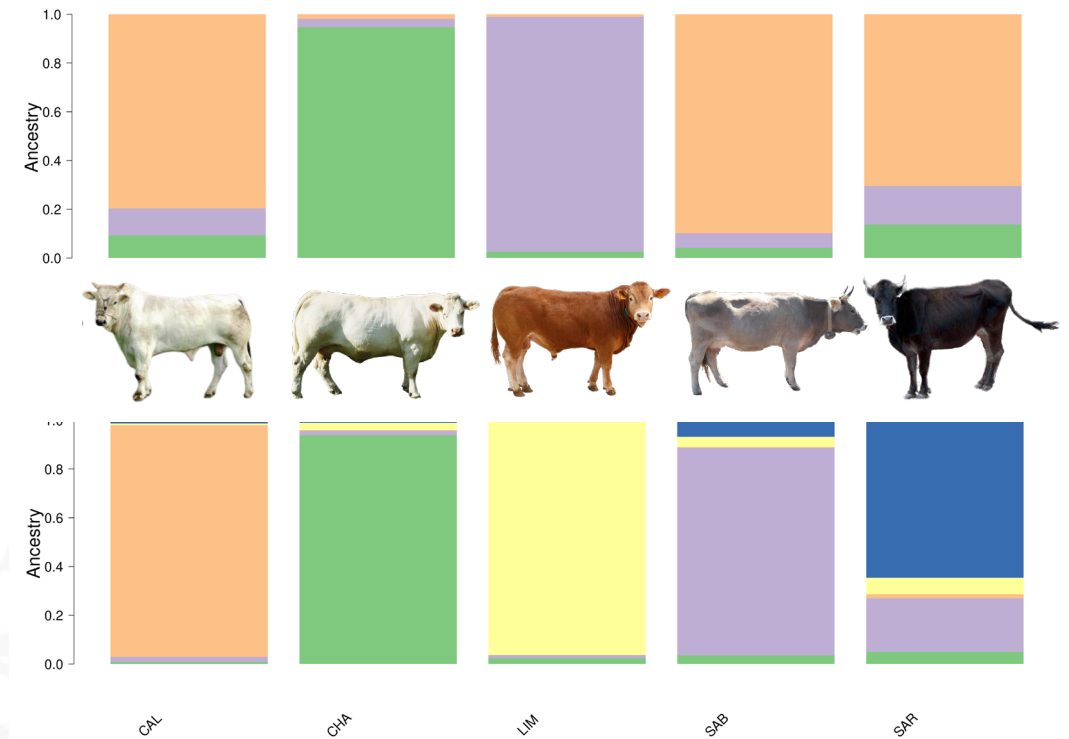
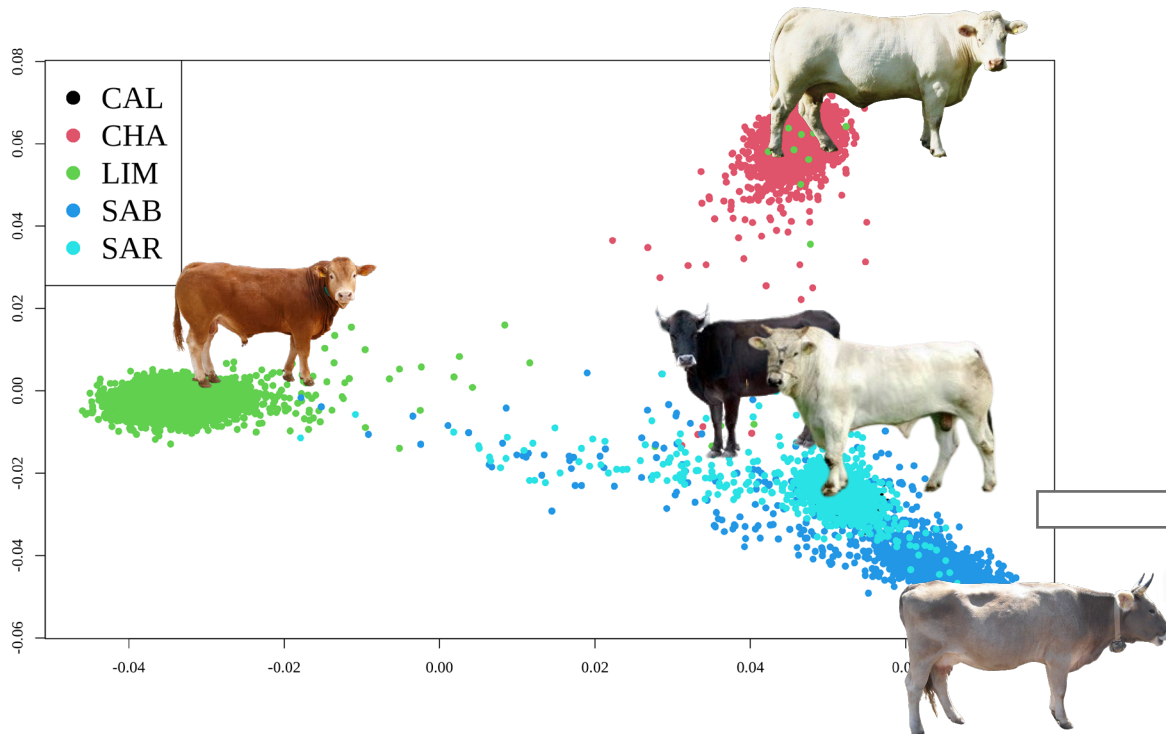
Results

Genetic Distances among the five Italian beef breeds
27,089 SNPs and 12,801 cattle



Results

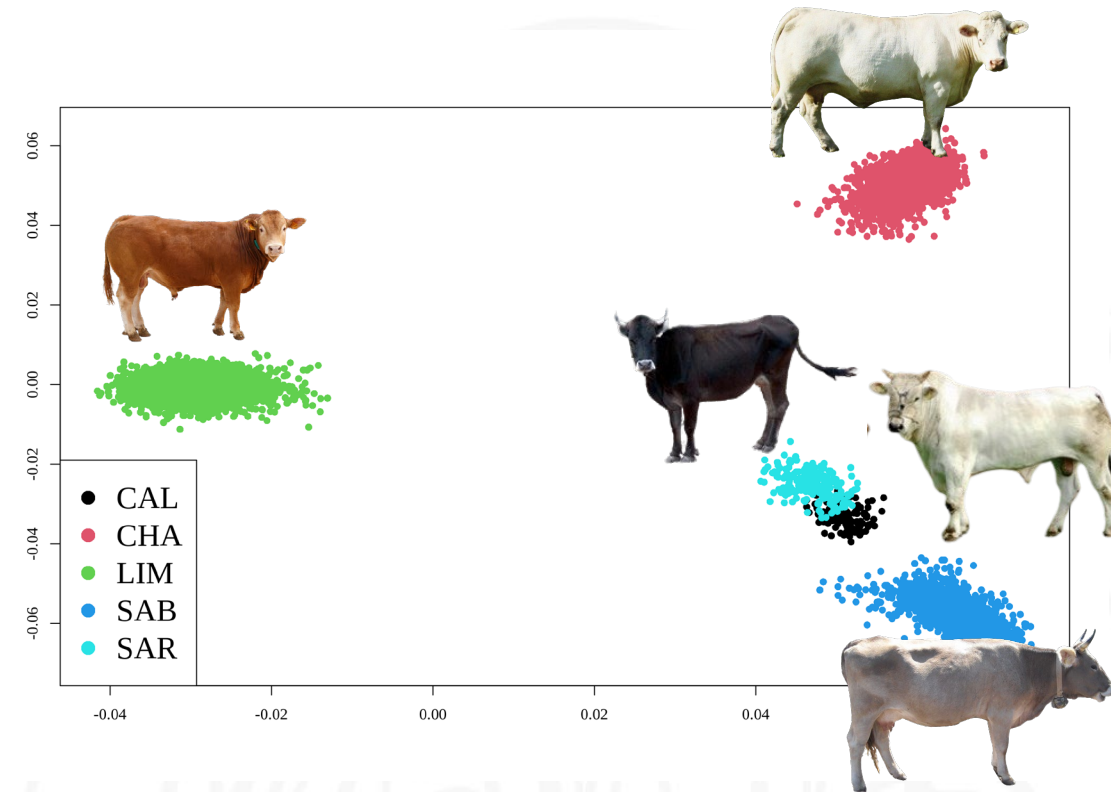
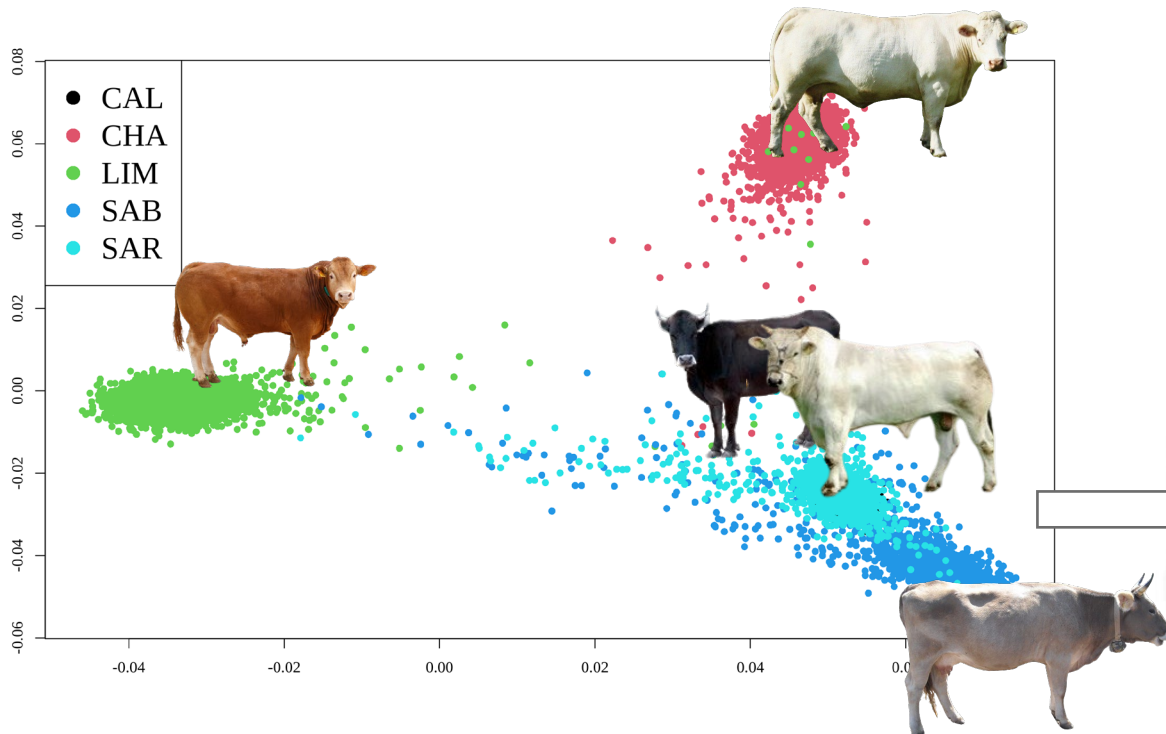
Genetic Distances among the five Italian beef breeds
27,089 SNPs and 12,801 cattle



Only animals with $Q \geq 80\%$ have been retained for HRR analysis

Results

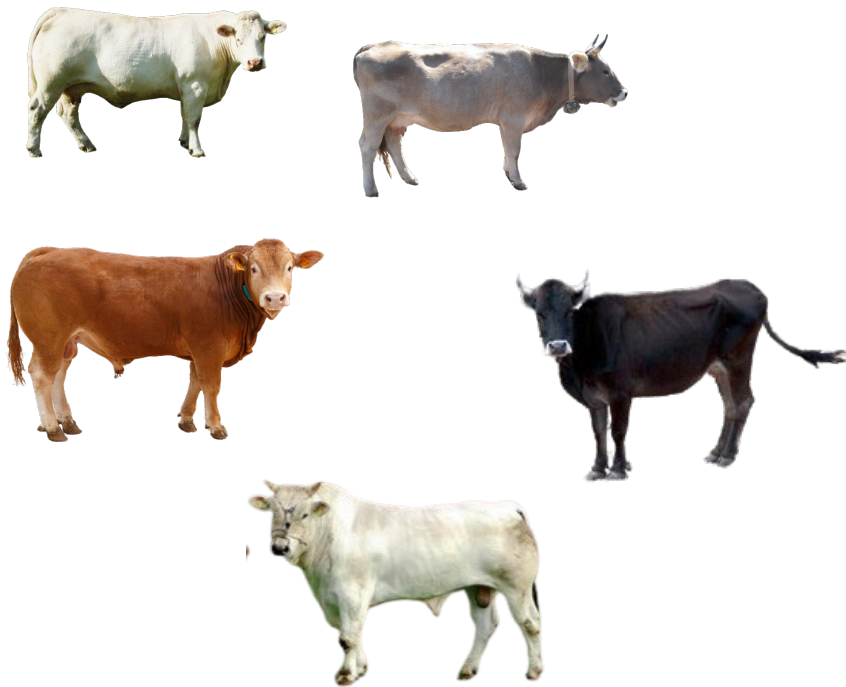
Genetic Distances among the five Italian beef breeds
27,089 SNPs and **11,374** cattle



~ 1,400 potential crossbreeds/classification errors removed

Results

Heterozygous Rich Regions



Breed	N.HRR	N.samples	Average per id
CAL	1233	148	8.3
CHA	18895	1989	9.5
LIM	78523	7733	10.1
SAB	14347	1482	9.7
SAR	1811	215	8.5

Results

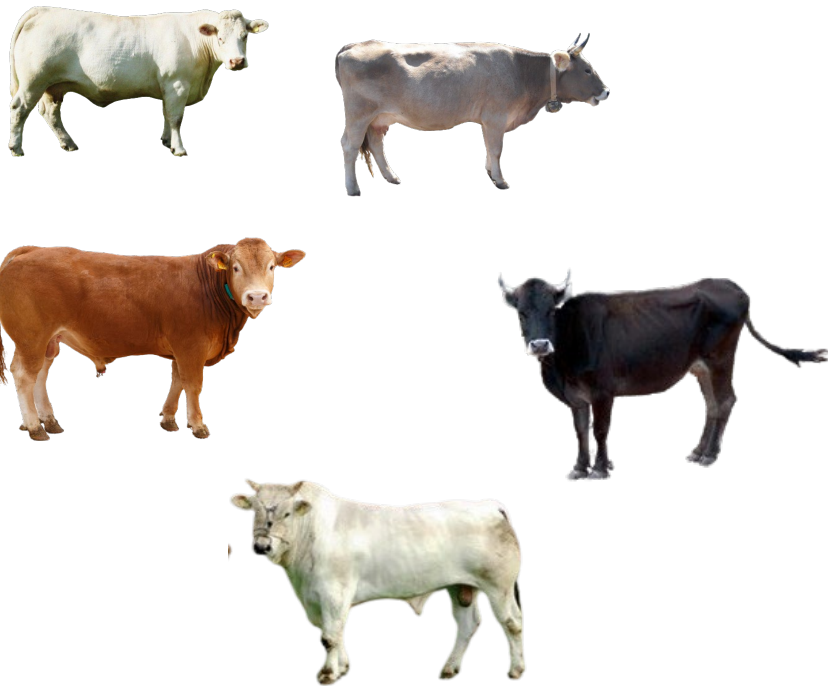
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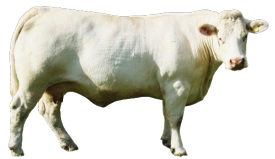


HRRs classes of length

Mbp	CAL	CHA	LIM	SAB	SAR
0 – 0.05	64.1 %	69.8 %	72.5 %	71.7 %	71.5 %
0.05 – 1	9.6 %	11.4 %	11.4 %	12 %	10.2 %
1 – 2	23.3 %	17.2 %	14.6 %	14.4 %	17 %
2 - 4	3 %	1.5 %	1.47 %	1.8 %	1.3 %

Results

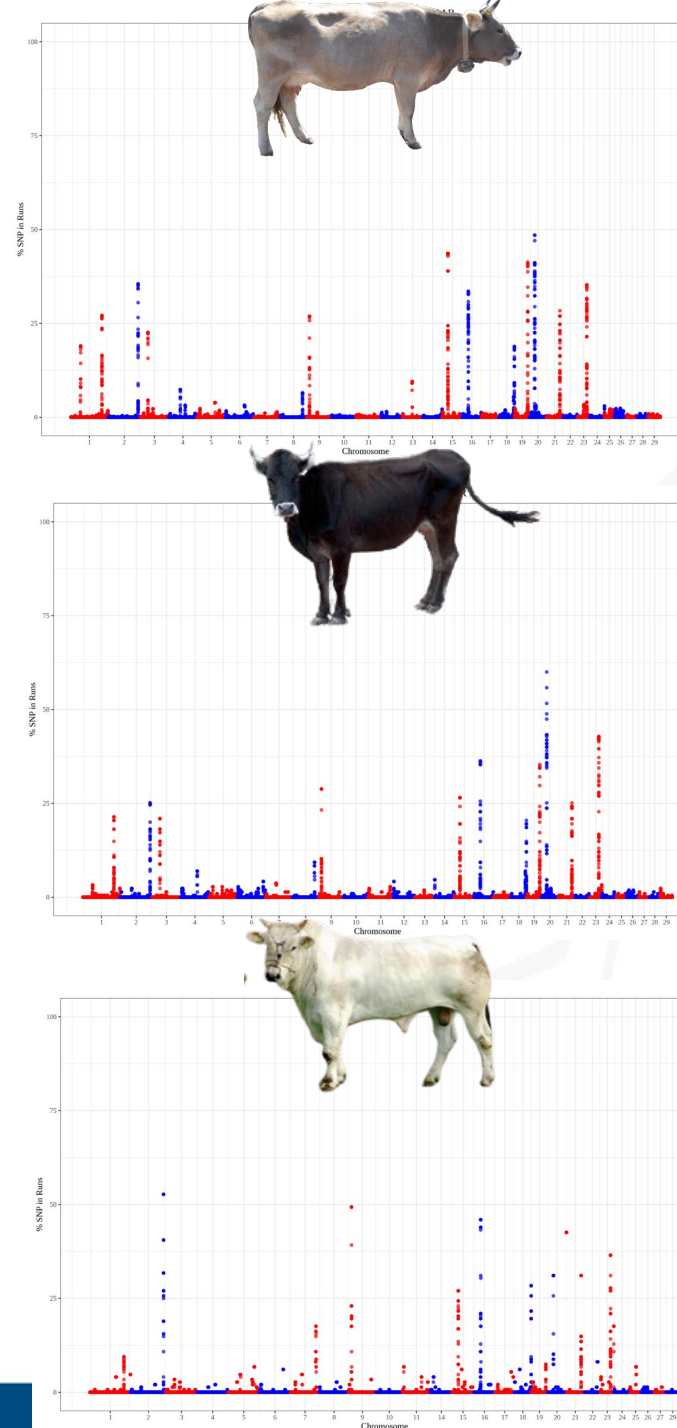
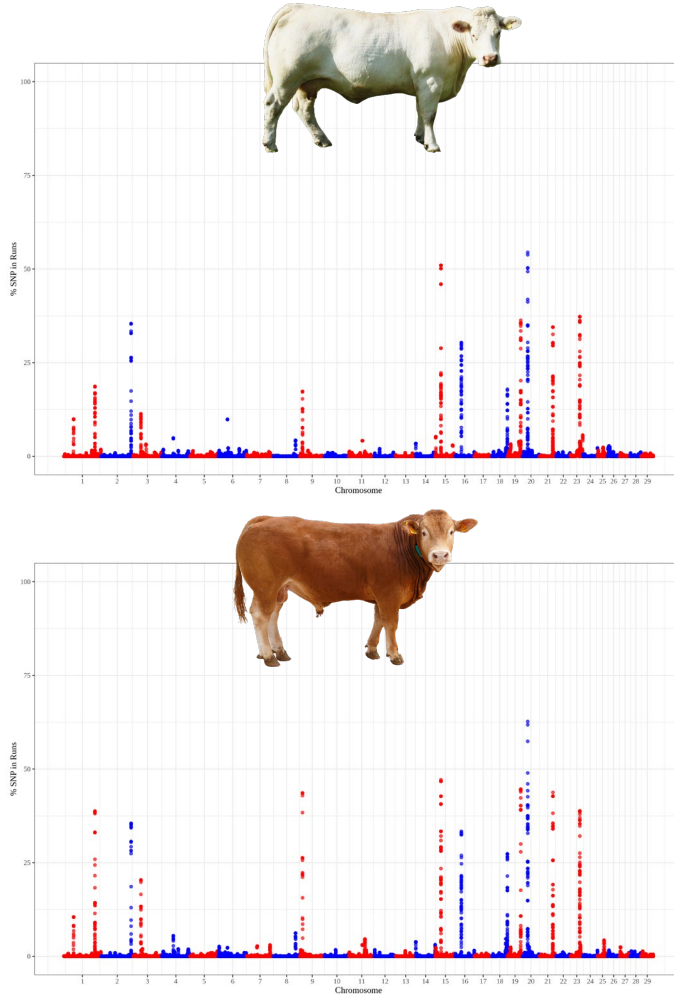
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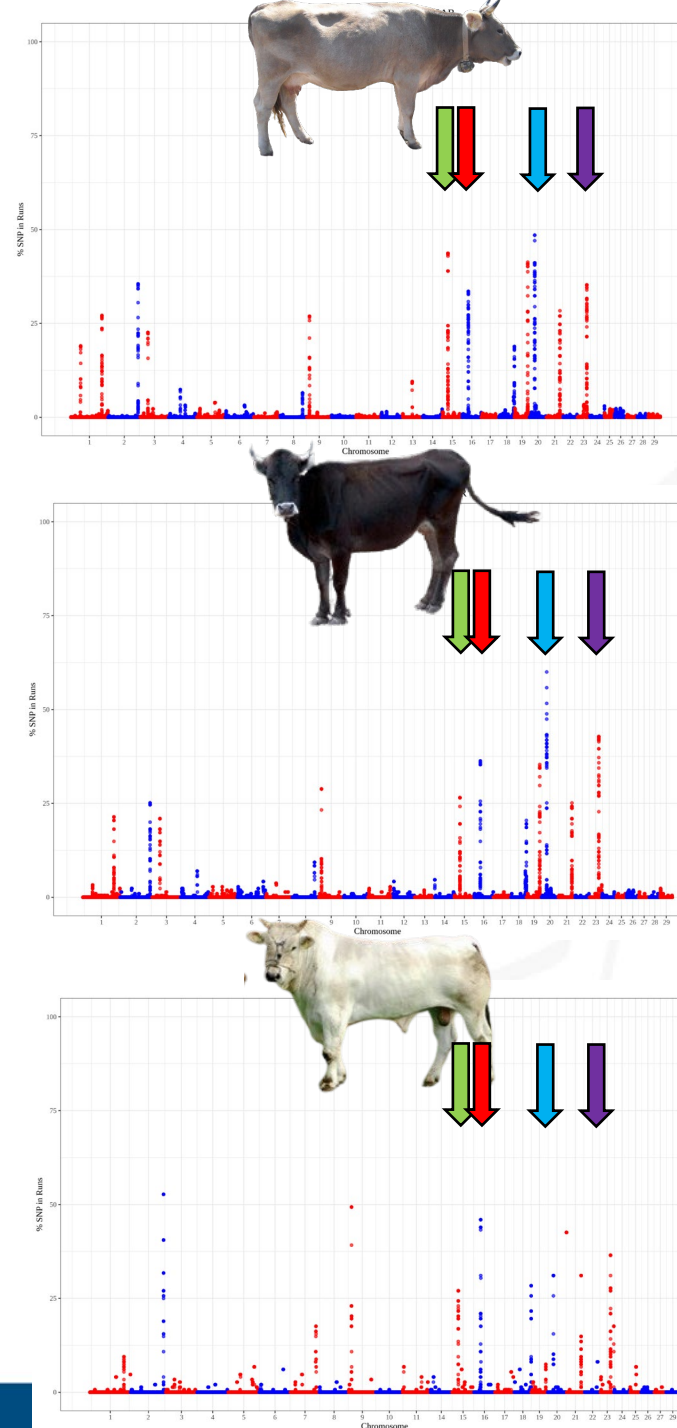
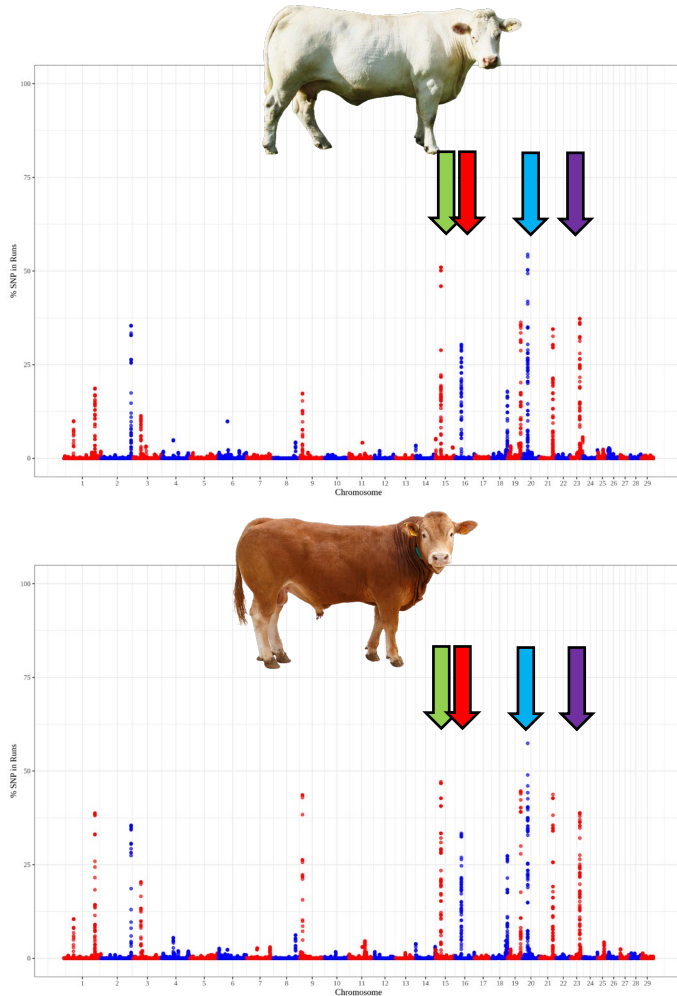
Heterozygous Rich Regions



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- Peak on BTA 1 was identified only in LIM and SAB.

Results

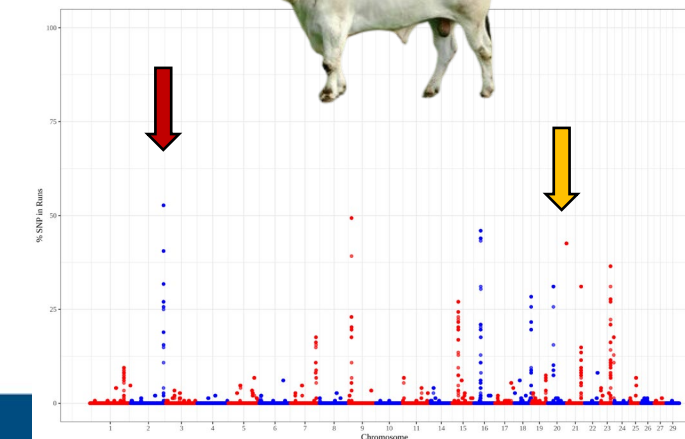
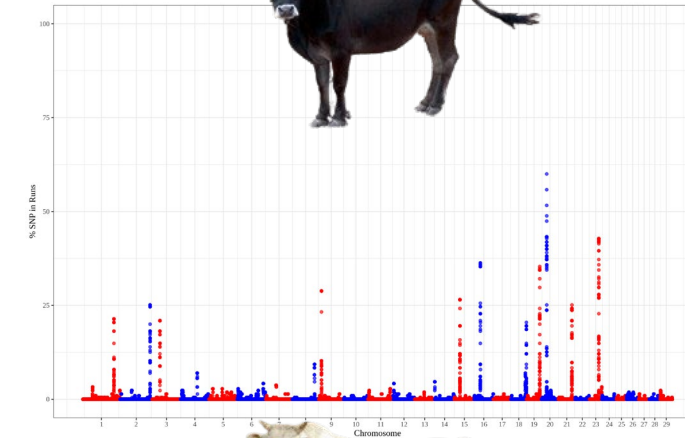
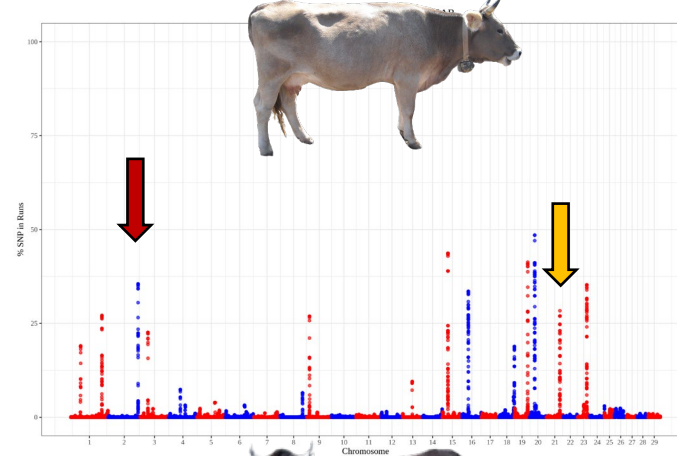
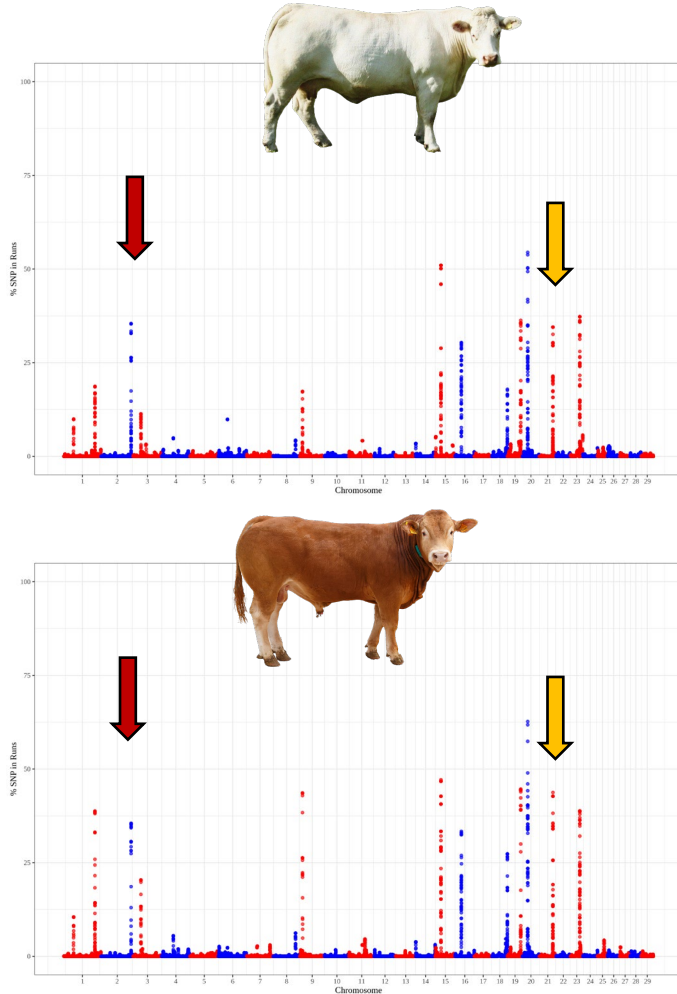
HRR



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- Peak on BTA 1 was identified only in LIM.

Results

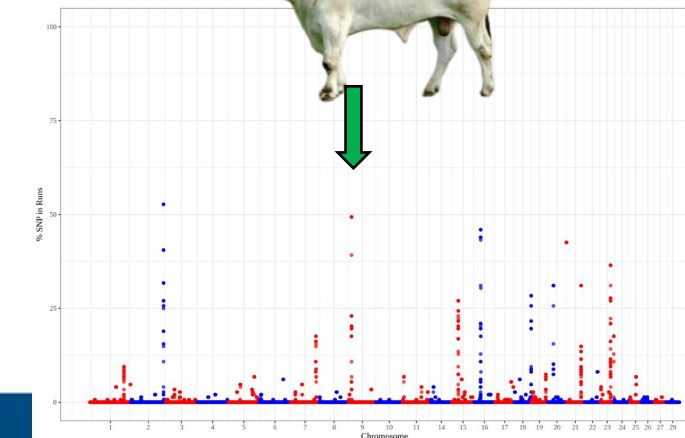
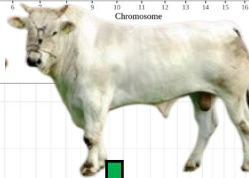
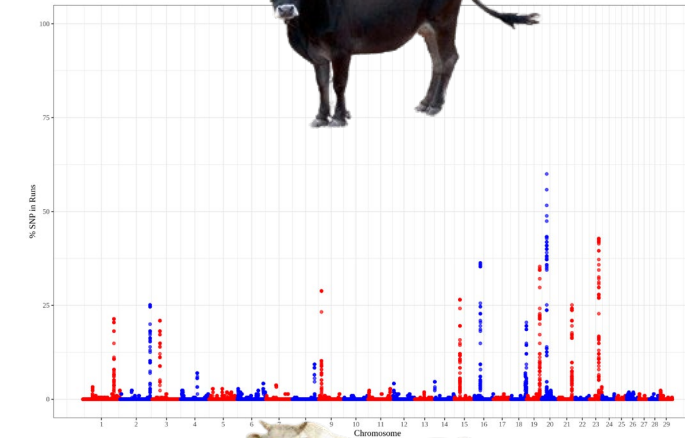
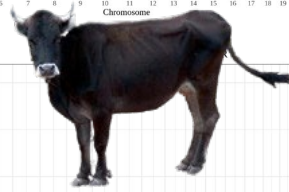
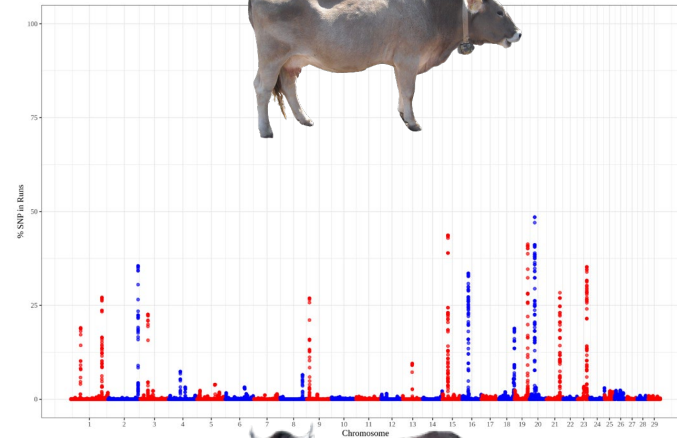
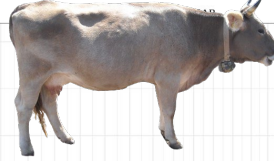
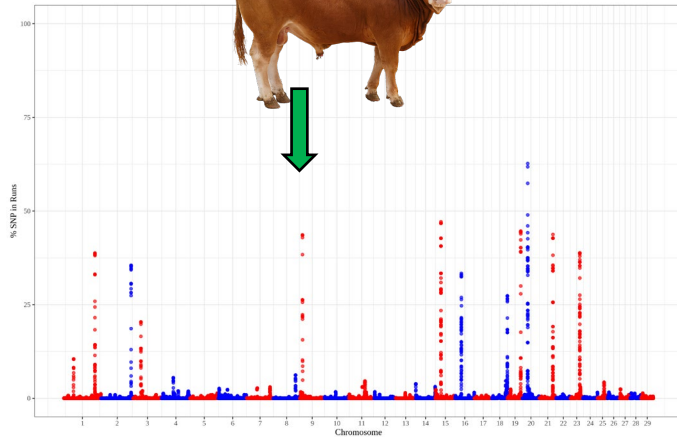
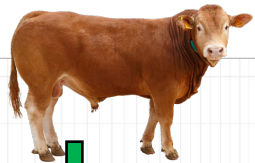
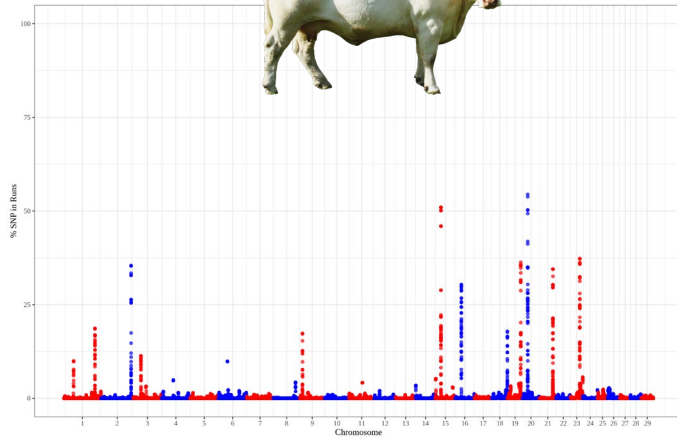
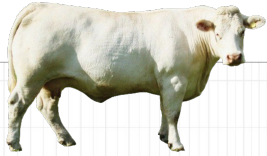
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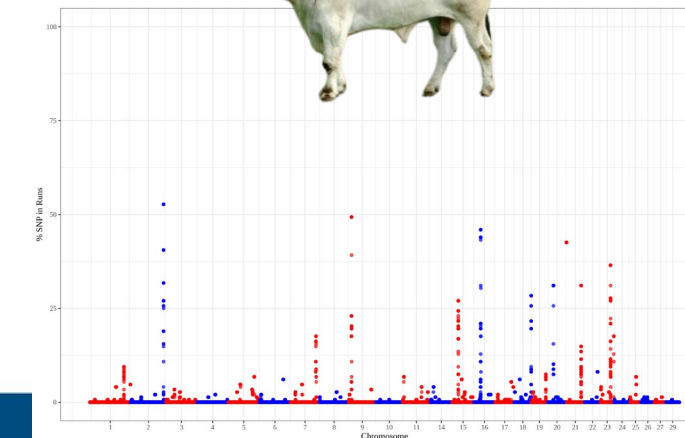
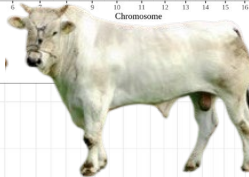
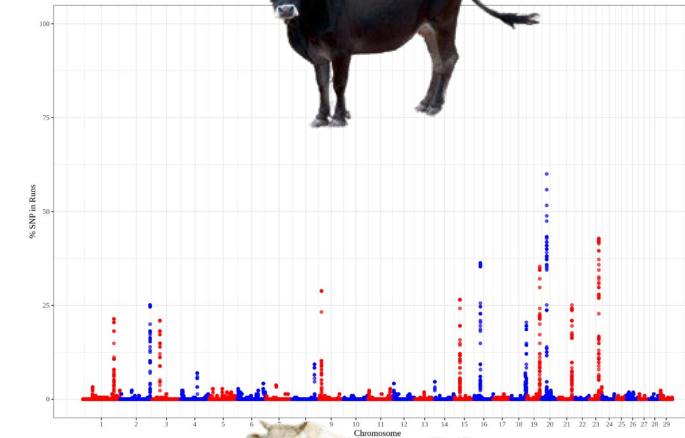
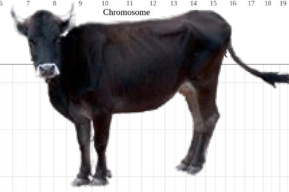
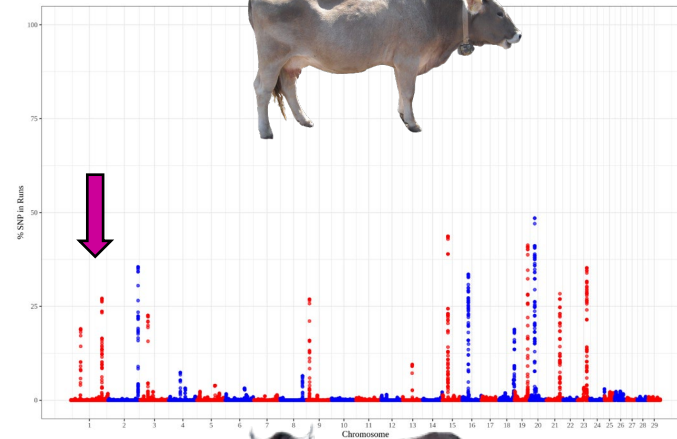
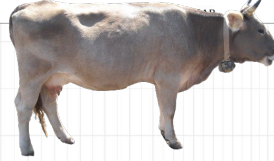
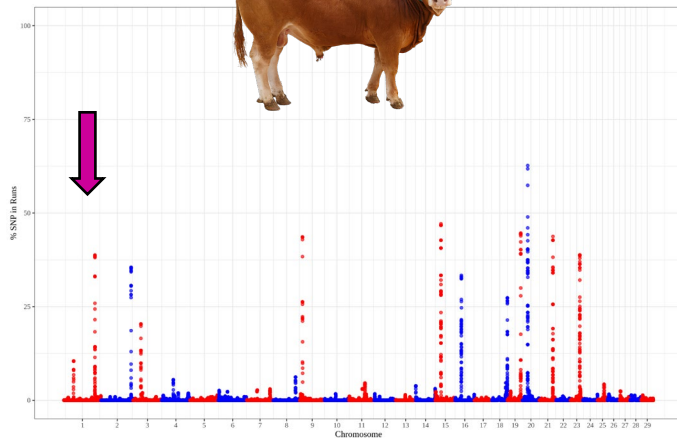
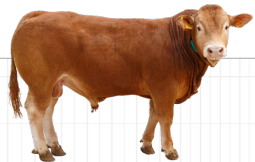
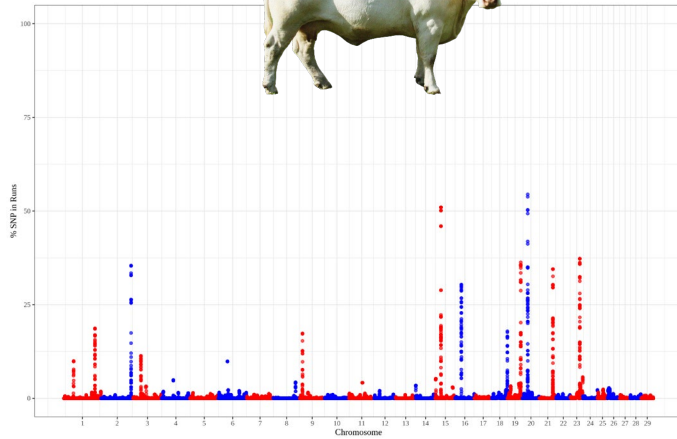
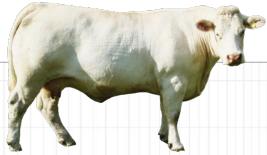
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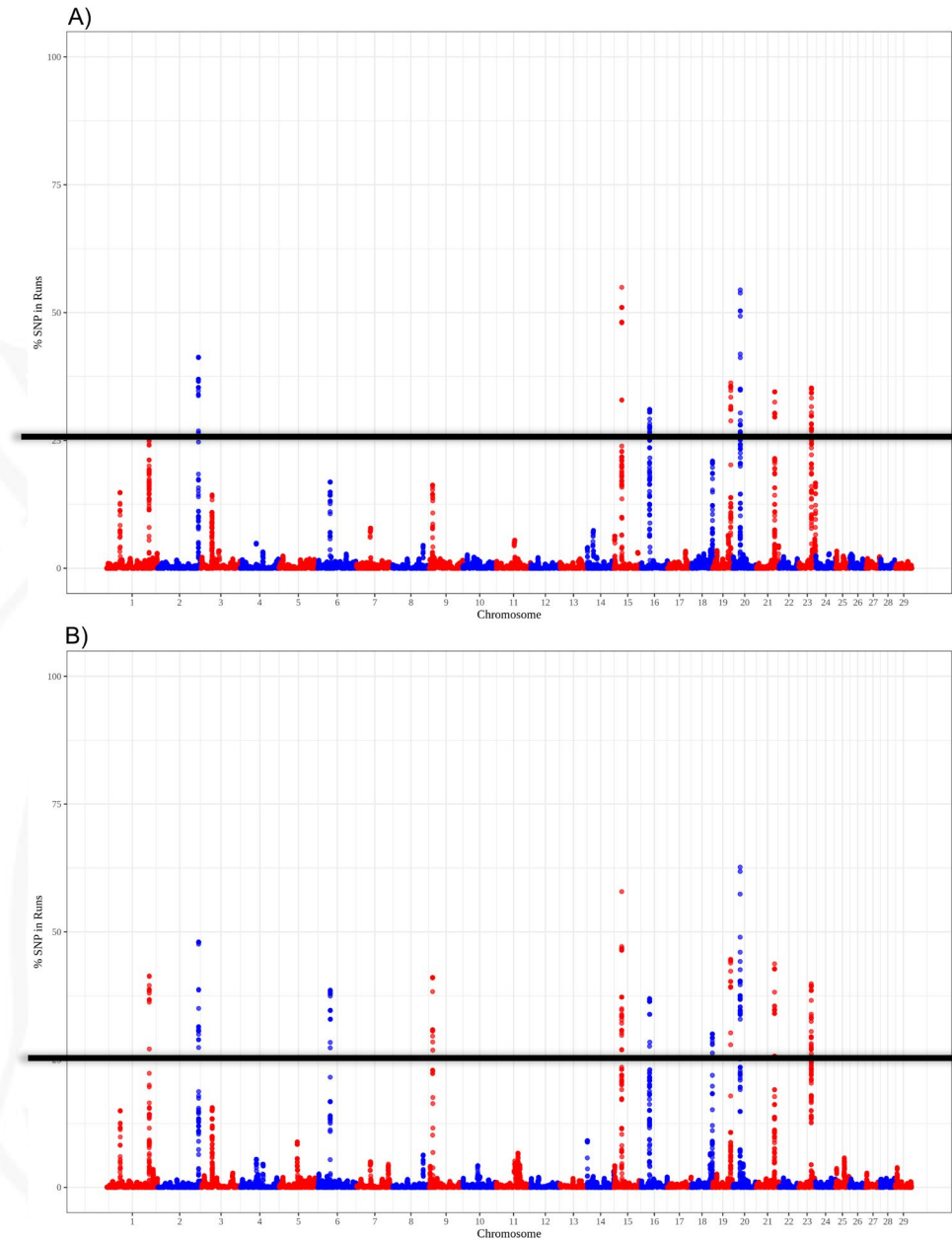
Genes within Significant HRR

Applying the threshold of 25%, **38** HRRs

=

11 LIM, 8 CHA, 9 CAL, 8 SAB and 2 SAR

ATCCCGTTATTACGGCGCATTAGGCA



Results

Genes within Significant HRR

- ❑ 8 overlapped HRRs among breeds
- ❑ Collectively contained **14 unique genes**.

BTA:START-END	Genes	CAL	CHA	LIM	SAB	SAR
2:127476802-127540073	CATSPER4 CNKSR1 ZNF593 FAM110D	X	X	X	X	
2:127644712-127680352	EXTL1 SLC30A2	X	X	X		
15:24209707-24238959	TTC12	X	X	X	X	
16:25915302-25954959	DUPS10	X	X	X	X	
19:56537361-56564441	SMIM6 SAP30BP RACQL5		X	X	X	
21:57719367-57750099	SLC24A4 MIR2284F	X	X	X		
20:22151938-22171796	Downstream MIER3	X	X	X	X	X
23:39285499-39337614		X	X	X	X	X

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Genes within Significant HRR

Chromosome	Start-End	Genes	CAI	CHA	LIM	SAB	SAR
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		CNKSR1	X	X	X	X	
		ZNF593					
		FAM110D					
2	127644712-127680352	EXTL1	X	X	X		
		SLC30A2					
15	24209707-24238959	TTC12	X	X	X	X	
		DUPS10	X	X	X	X	
19	56537361-56564441	SMIM6					
		SAP30BP		X	X	X	
		RACQL5					
21	57719367-57750099	SLC24A4					
		MIR2284F	X	X	X		
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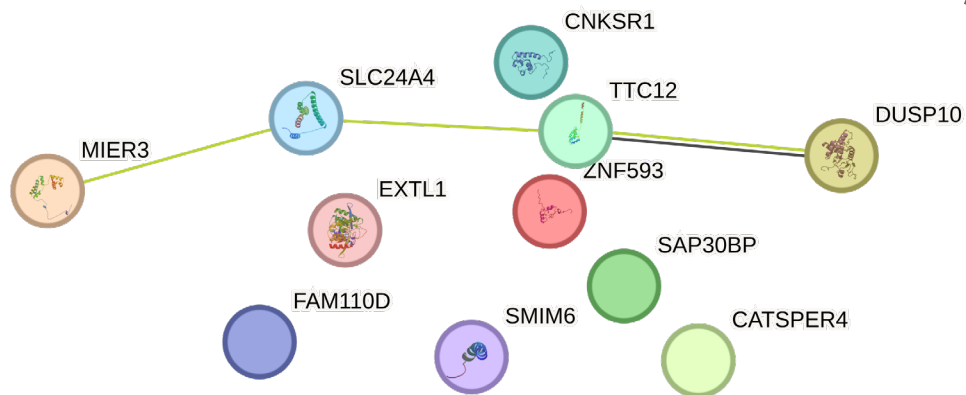
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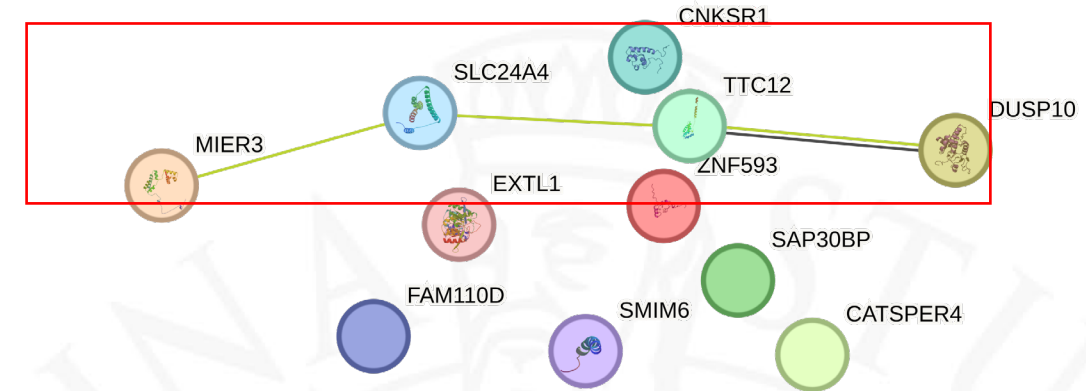
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	ZNF593					
	FAM110D					
2:127644712-127680352	EXTL1	X	X	X		
	SLC30A2					
15:24209707-24238959	TTC12	X	X	X	X	
16:25915302-25954959	DUPS10	X	X	X	X	
19:56537361-56564441	SMIM6					
	SAP30BP		X	X	X	
	RACOL5					
	SLC24A4	X	X	X		
21:57719367-57750099	MIR2284F					
20:22151938-22171796	Downstream MIR3	X	X	X	X	X
23:39285499-39337614		X	X	X	X	X



Results

Genes within Significant HRR



1. **TTC12** gene is particularly interesting due to its association with male fertility.
2. **DUSP10** can either increase or decrease inflammation in response to factors like infection, injury, disease, or certain treatments
3. **SLC24A4** is linked to body conformation (Yan et al., 2021) and calving interval traits in dairy cattle (Nayeri et al., 2016). Signatures of selection housing the SLC24A4 gene in dairy cows (Maiorano et al., 2018).
4. **MIER3** gene was found to be located in proximity to the most significant SNP associated with survival (Illa et al., 2021)

Results

Genes within Significant HRR

Other genes not in cluster: related to **male and female fertility**, and **lactation traits**

1. **ZNF593** (Zinc Finger Protein 593) and **FAM110D** (Family With Sequence Similarity 110 Member D) were identified in a genomic region associated with lactation persistency in Holstein cattle (Do et al., 2017)
2. **CATSPER4**, which belongs to the CatSper family, plays a crucial role in sperm motility and sodium ion transport, making it related to male infertility (Sivakumar et al., 2018).

Conclusion

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Conclusion

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 - Almost **identical** heterozygous genomic regions across all four breeds were found.



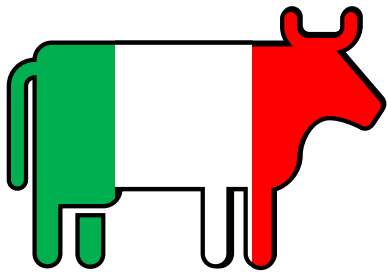
Genes associated with **fertility**, **survival**, **growth**, and **adaptation** traits.

Heterozygosity studies are fundamental both in **breeding programs** and in **conservation schemes**.



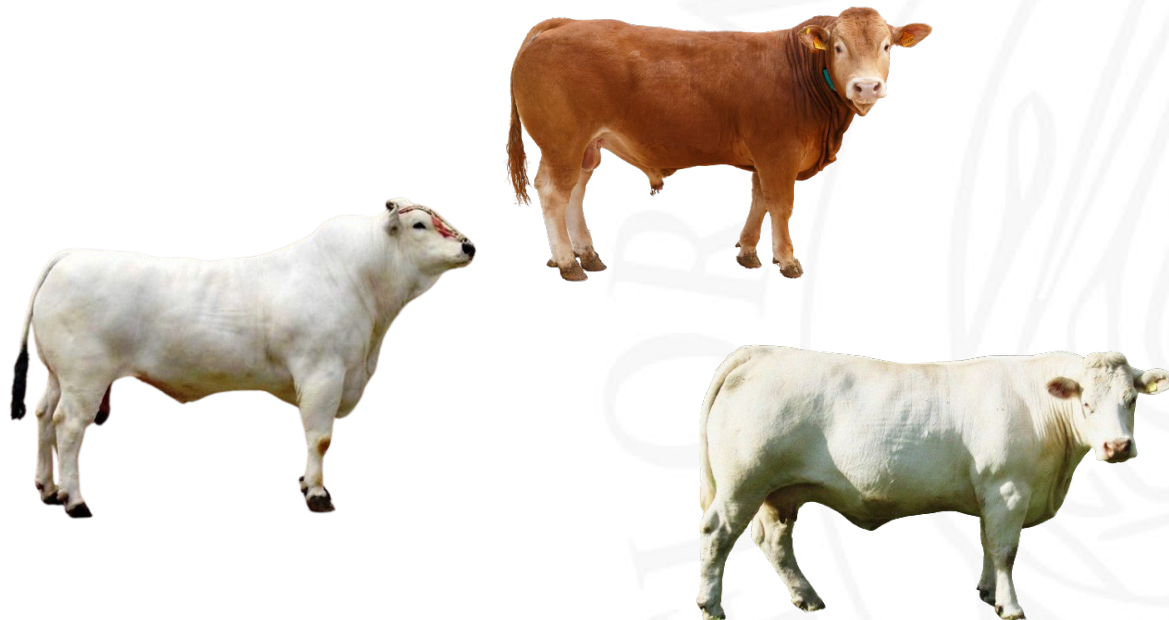
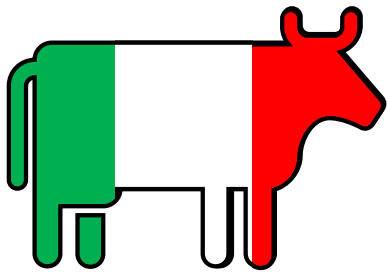
Further works

It could be interesting to extend this study to other cattle breeds to verify if these heterozygous regions are characteristic of **Italian** beef breeds.



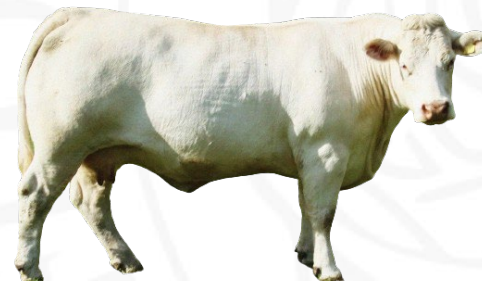
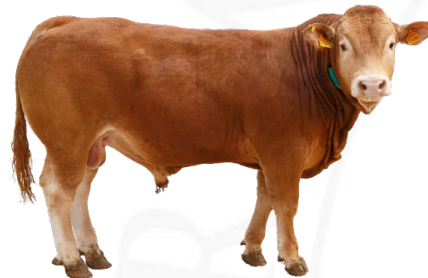
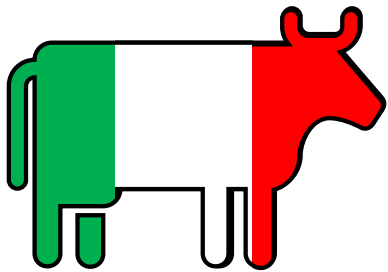
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It could be interesting to extend this study to other cattle breeds to verify if these heterozygous regions are characteristic of **Italian** beef breeds, or specific **beef** breeds, or in more general, in **cattle** population.





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Thank you for your attention

Any Questions?

Acknowledgement

Spoke 7

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“Nucleotide diversity values within regions that include HRR islands were compared with values from other genomic intervals (Fig. 6), resulting in significantly higher and more distinctly distributed π values within HRR regions”.