

Cross-Species Analysis of Highly Heterozygous Regions

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Introduction

- Diverse gene pool allow livestock to adapt to changing environmental conditions and ensure long-term productivity and sustainability of livestock populations
- Does genetic diversity hold the same level of importance across the entire genome?

Introduction

- Existence of balancing selection
- The presence of *ZNF* genes in HRRIs of various species has been confirmed (Halvoník et al., 2025; Mulim et al., 2024; Ruan et al., 2022)
- Cross-species diversity of major histocompatibility complex (MHC)

- Ruan, Donglin, et al. "Assessment of heterozygosity and genome-wide analysis of heterozygosity regions in two Duroc pig populations." *Frontiers in Genetics* 12 (2022): 812456.
- Mulim, Henrique A., et al. "Detection and evaluation of parameters influencing the identification of heterozygous-enriched regions in Holstein cattle based on SNP chip or whole-genome sequence data." *BMC genomics* 25.1 (2024): 726.
- Halvoník, Adrián, et al. "Heterozygosity-Rich Regions in Canine Genome: Can They Serve as Indicators of Balancing Selection?." *Animals* 15.4 (2025): 612.

Aim of study

- This study aimed to determine whether any genes remain heterozygous across diverse species and whether these genes reveal common patterns related to survivability, health, and fitness

Materials and methods



- 510 individuals
- 4 breeds
- 718607 autosomal SNPs
- Zinovieva et al. (2020) and Hussain et al. (2018)



- 78 individuals
- 2 breeds
- 522958 autosomal SNPs
- Jenkins et al. (2021)

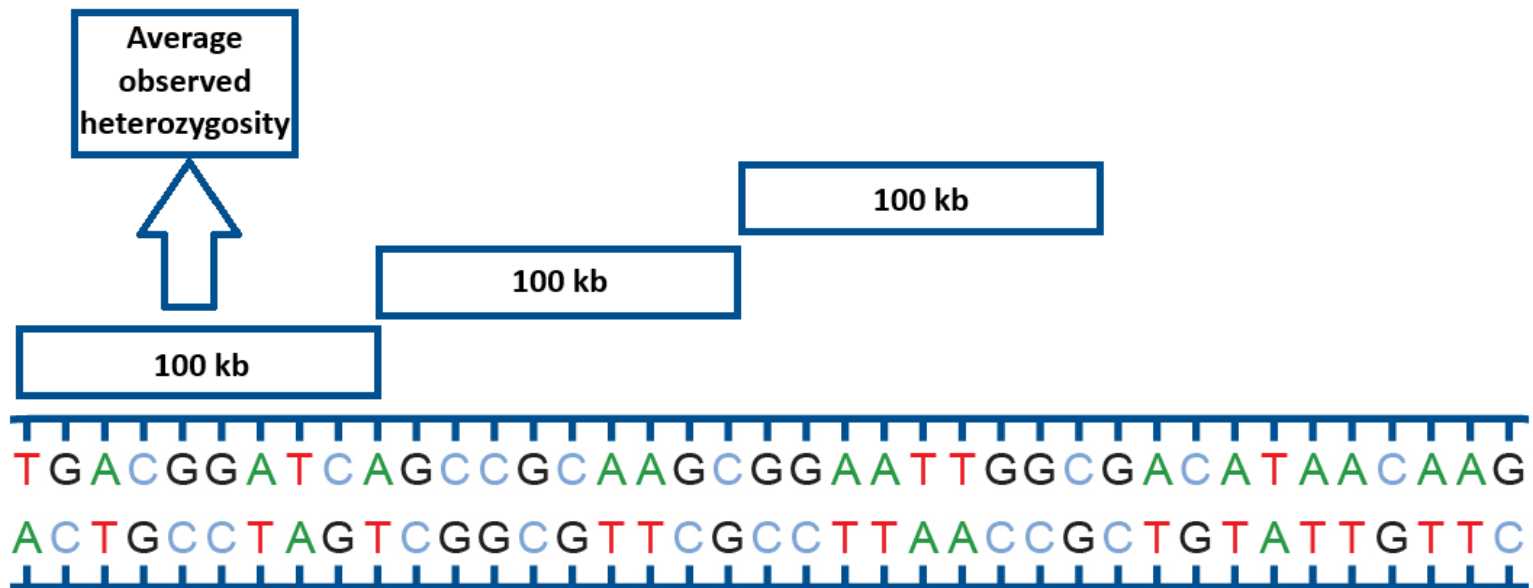


- 101 individuals
- 12 breeds
- 320863 autosomal SNPs
- Sadeghi et al. (2019)

- Sadeghi, Raheleh, et al. "Genetic diversity of Persian Arabian horses and their relationship to other native Iranian horse breeds." Journal of Heredity 110.2 (2019): 173-182.
- Jenkins, Christopher A., et al. "Improving the resolution of canine genome-wide association studies using genotype imputation : A study of two breeds." Animal genetics 52.5 (2021): 703-713.
- Bahbahani, Hussain, et al. "Signatures of selection for environmental adaptation and zebu x taurine hybrid fitness in East African Shorthorn Zebu." Frontiers in genetics 8 (2017): 68.
- Zinovieva, Natalia Anatolievna, et al. "Selection signatures in two oldest Russian native cattle breeds revealed using high-density single nucleotide polymorphism analysis." PLoS One 15.11 (2020): e0242200.

Materials and methods

- Observed heterozygosity was calculated for each SNP
- Average heterozygosity per 100 kb non-overlapping window



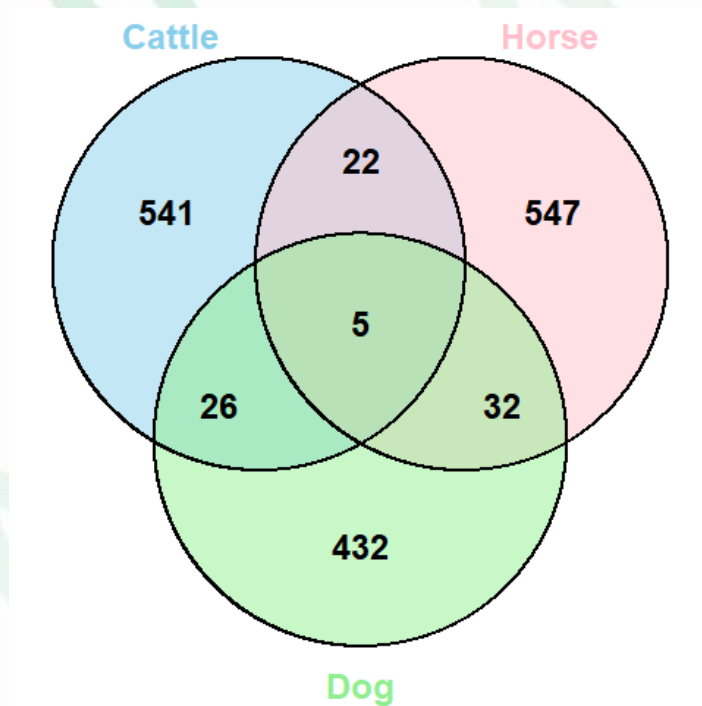
Materials and methods

- The top 2.5% of genomic windows with the highest heterozygosity were selected
- Genes located within the selected windows were identified (BioMart)
- Functional annotation of the identified genes was performed (DAVID)
- Overlaps were identified

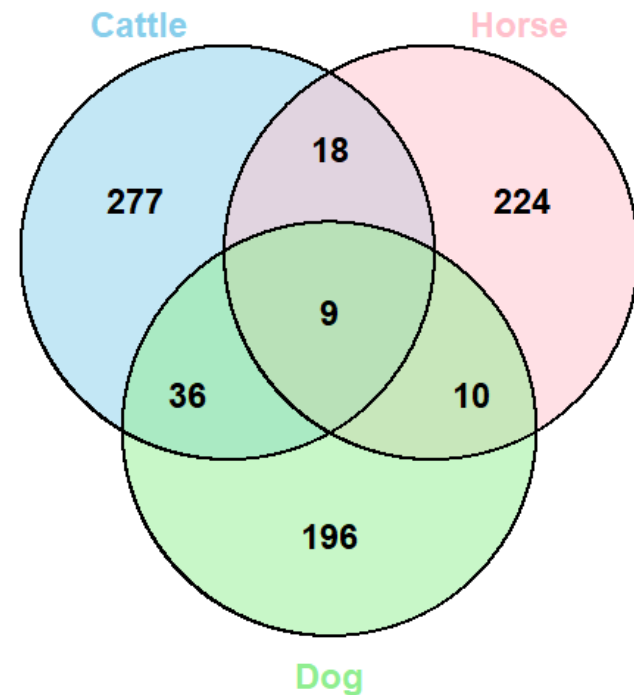
Results

Species	Number of selected windows	Average observed of all windows (95% CI)	Average observed heterozygosity of selected windows (95% CI)	Average number of SNPs in window selected windows (95% CI)
Cattle	628	0.26 (0.25 – 0.27)	0.39 (0.38 – 0.39)	31.39 (30.43 – 32.35)
Horse	562	0.31 (0.31 – 0.33)	0.46 (0.45 – 0.46)	10.28 (9.21 – 10.01)
Dog	552	0.22 (0.22 – 0.23)	0.38 (0.37 – 0.38)	17.51 (16.87 – 18.17)

Results



Venn diagram of detected genes



Venn diagram of functional annotation terms

Results

U6

- **Function:** Components of the spliceosome, essential for pre-mRNA splicing

RBFOX1

- **Function:** RNA-binding protein
- **Phenotypic connection:** neurodevelopmental disorders, skeletal and cardiac muscle structure and function

Results

GRID2

- **Function:** Encodes a subunit of ionotropic glutamate receptors, primarily expressed in cerebellar Purkinje cells
- **Phenotypic connection:** Neurodevelopmental disorders - cerebellar atrophy, movement abnormalities, coordination deficits and cerebellar ataxia

Results

PDE4D

- **Function:** Regulates cAMP signaling, which is a critical second messenger
- **Phenotypic connection:** immune response, endocrine signaling, neural activity and heat stress responses

Results

Neurological disorders

- GO:0098839 – Postsynaptic Density Membrane
- KW-0770 – Synapse
- KW-0677 – Repeat
- COMPBIAS: Polar Residues
- GO:0050804 – Modulation of Chemical Synaptic Transmission
- KW-0406 – Ion Transport

Cancer

- COMPBIAS: Polar Residues
- GO:0098609 – Cell-Cell Adhesion
- GO:0005515 – Protein Binding

Immune system

- GO:0005515 – Protein Binding
- KW-0407 – Ion Channel

Conclusion

- This study pointed out common patterns of genes showing high heterozygosity across multiple species, which may help identify specific genes that favorably affect phenotype in the heterozygous state
- However, a more robust and statistically unbiased approach, supported by a larger dataset, is necessary to validate these findings

Thank you for your attention

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