

Molecular Mechanisms associated with Mycobacterium Avium Subspecies Paratuberculosis Infection in Dairy Cattle

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Introduction

- The California dairy industry is valued over 7.6 billion dollars.
- Johne's disease (JD) is one of many cow diseases causing a loss of 1.5 billion dollars/year in the U.S. agriculture economy due to the mandatory culling of dairy cows.
- JD is a contagious chronic intestinal inflammatory disease caused by Mycobacterium avium subspecies paratuberculosis (MAP) found mostly in cattle.
- JD is a huge concern as 68% of dairy herds have at least 1 to 100% positive cows.



Figure 1: Bos Taurus with Johne's disease

Objective

- Identify genes, single nucleotide pairs (SNPs), and biological pathways, with the use of genome-wide association study (GWAS), that may contribute to the development of Johne's disease in dairy cows.
- To understand the molecular mechanisms behind these associations

Material and Methods

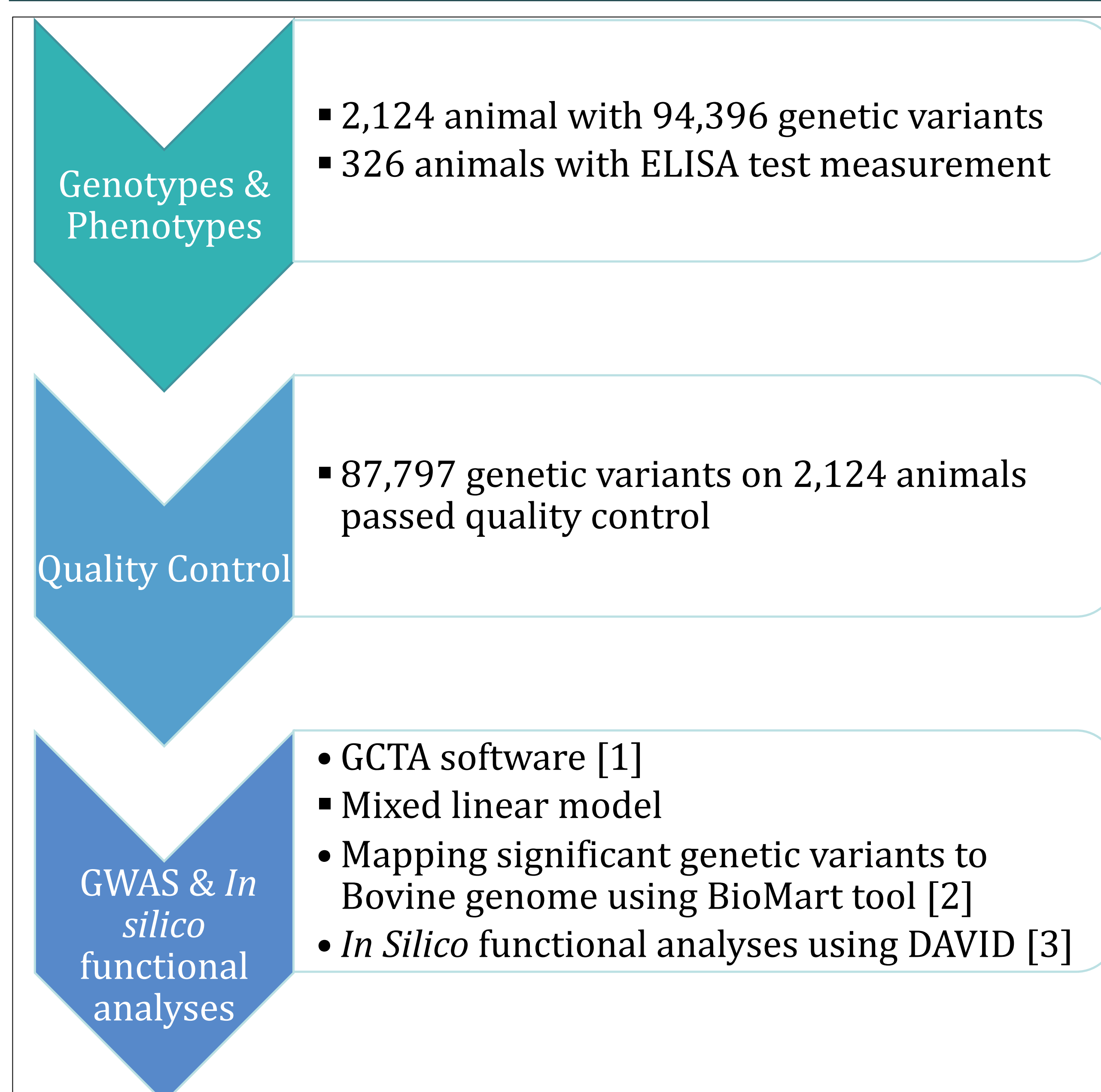


Figure 2: Following processes to obtain genotypes associated with JD

Results & Discussion

- Manhattan plot showing significant chromosomes involved with JD (**Figure 3**)
- Most important potential biological processes and KEGG pathways were identified from DAVID enrichment analyses (**Figure 4, Figure 5**)
 - Involving top 20 genes derived from 10 most significant SNP positions identified by Ensembl BioMart tool and GWAS, respectively

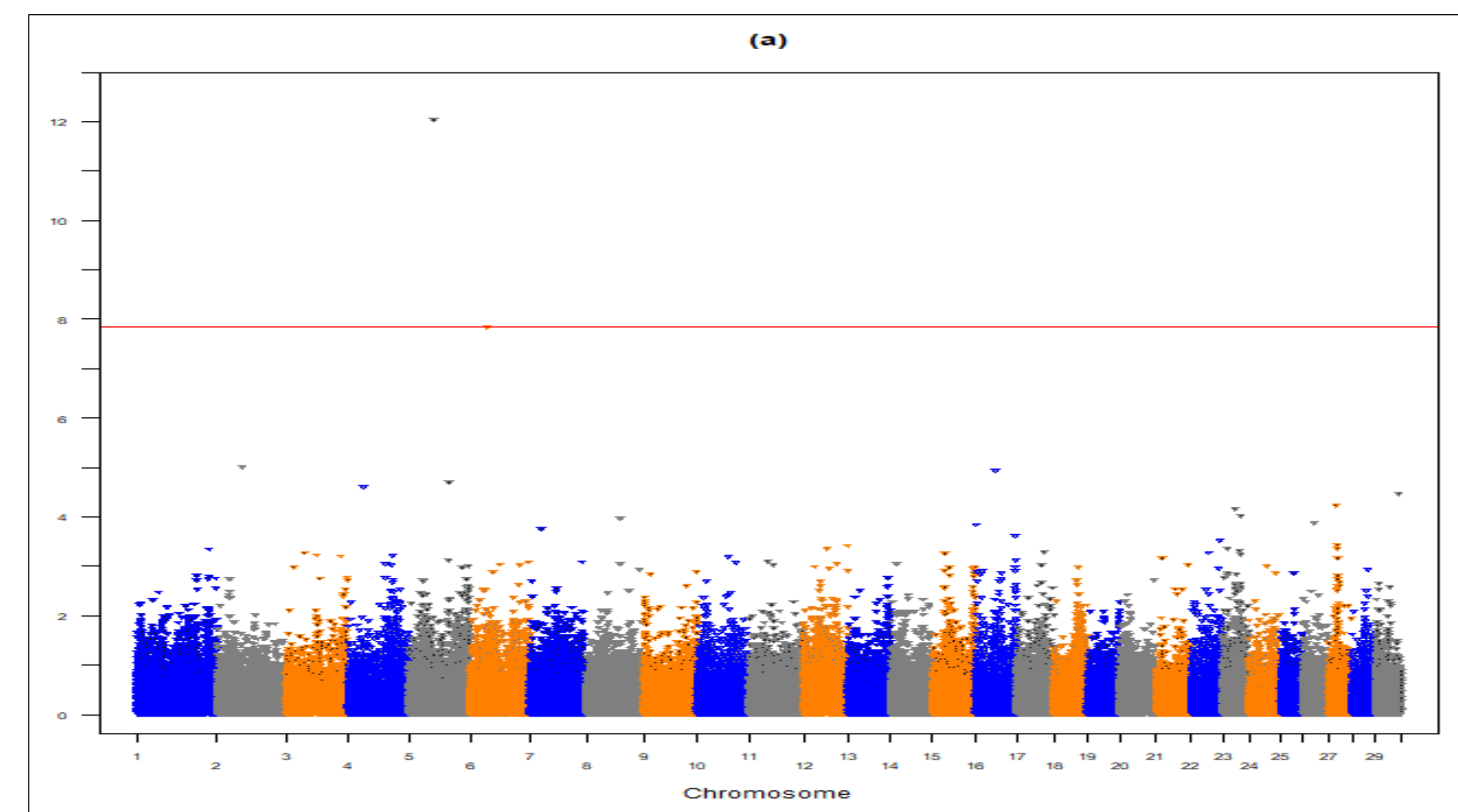


Figure 3: Most significant chromosomes with the ELISA results without breed effect

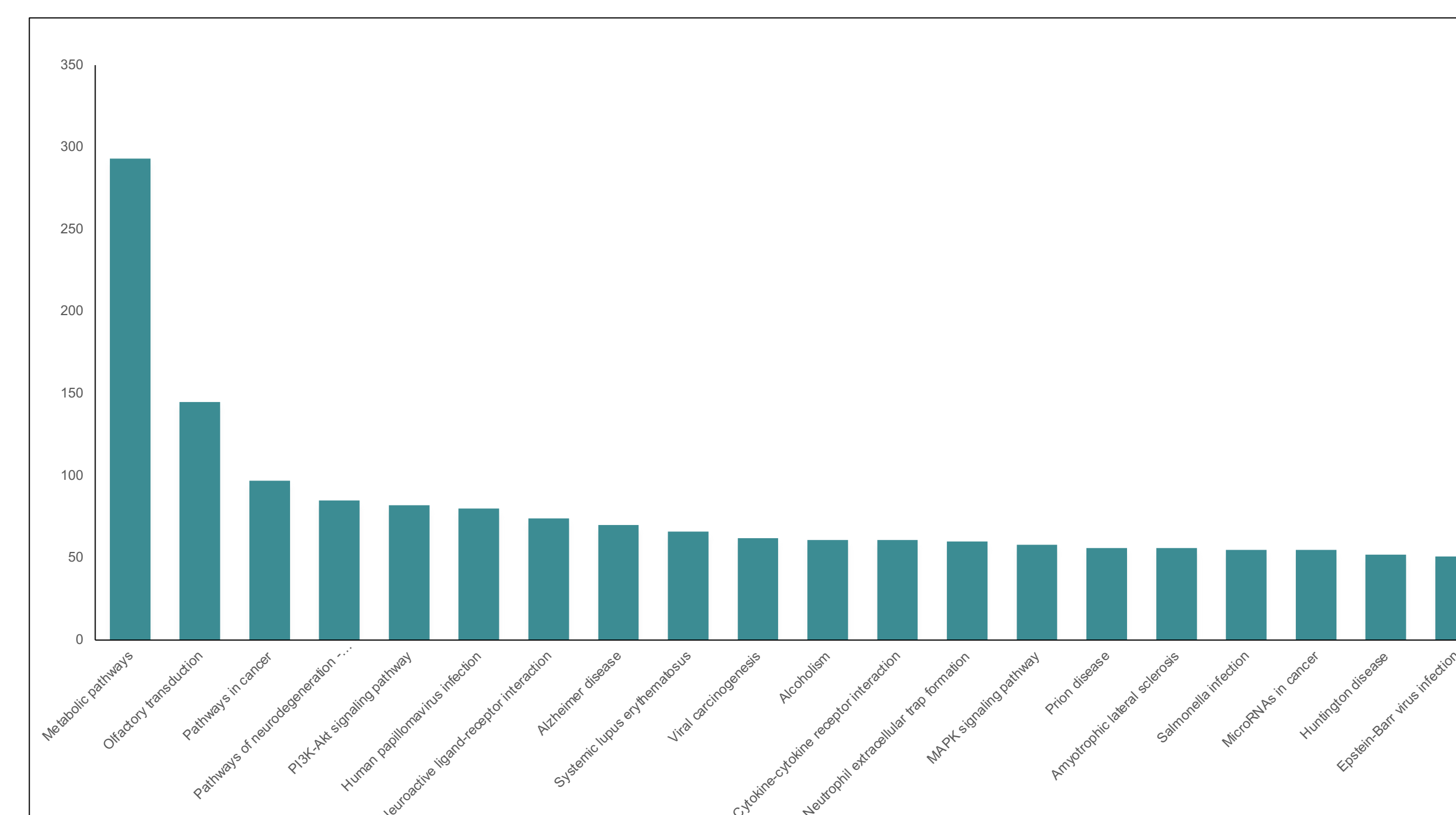


Figure 4: Potential KEGG pathways found significant to the genes involved in JD

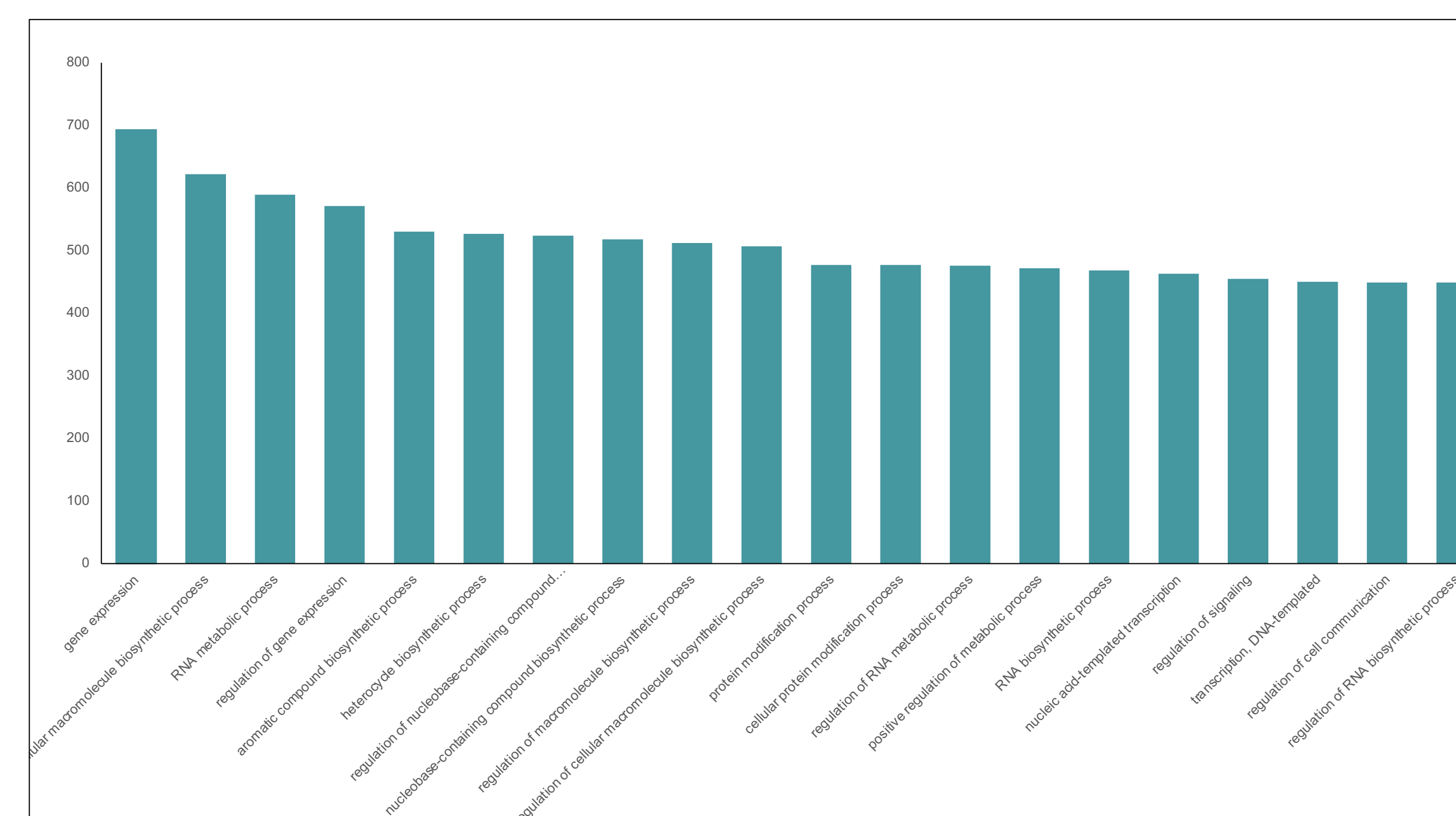


Figure 5: Potential biological pathways found significant to the genes involved in JD

Results & Discussion cont.

- Manhattan plot describing Elisa results without breed effect identified many significant genetic variants on several cow autosomes using a false discovery rate of 5%.
- Out of the top 20 genes, 345 KEGG pathways were found to be involved with genes associated with Johne's
- KEGG pathway candidates include prion disease, neuroactive ligand receptor interaction, and MAPK signaling pathway.
- Numerous biological pathways found in connection to Johne's include RNA metabolic process, protein modification process, and regulation of macromolecule biosynthetic process.
- Our results validated a previous study which found pyruvate metabolism, lipid metabolism, biotin metabolism, and cytochrome P450 pathways to be associated with JD or MAP infection [4].

Conclusion

- The study shows that there is a correlation between multiple bos taurus autosomes and in the development of Johne's disease and MAP infection.
- Further mutations need to be validated in across other dairy farms before the consideration of the use of genomic evaluation in Johne's disease development.

References

- [1] Yang et al. 2011. Am J Hum Genet, 88: 76-82
- [2] <http://useast.ensembl.org/biomart/martview>
- [3] Huang et al. 2009. Nature Protoc., 4: 44-57.
- [4] Ariel O et al. (2021). BMC genomics vol.22.:

Acknowledgements

