Expression quantitative trait loci in whole blood influence putative immune genes in sheep

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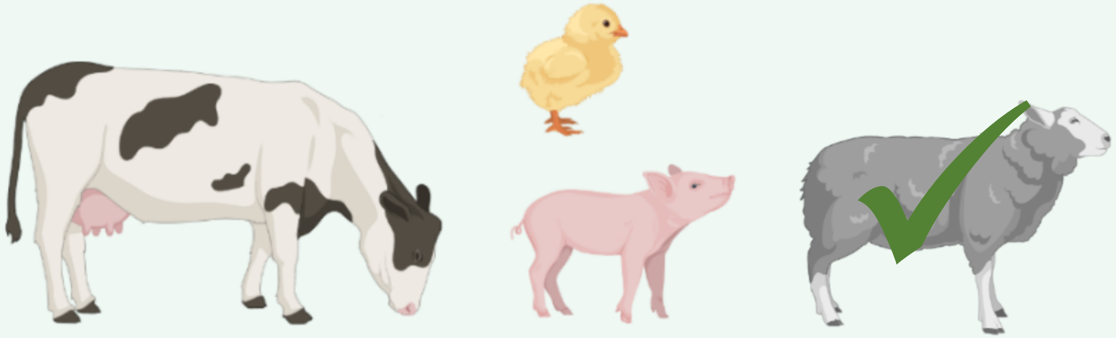
74th

Kate Dubarry
University of Edinburgh

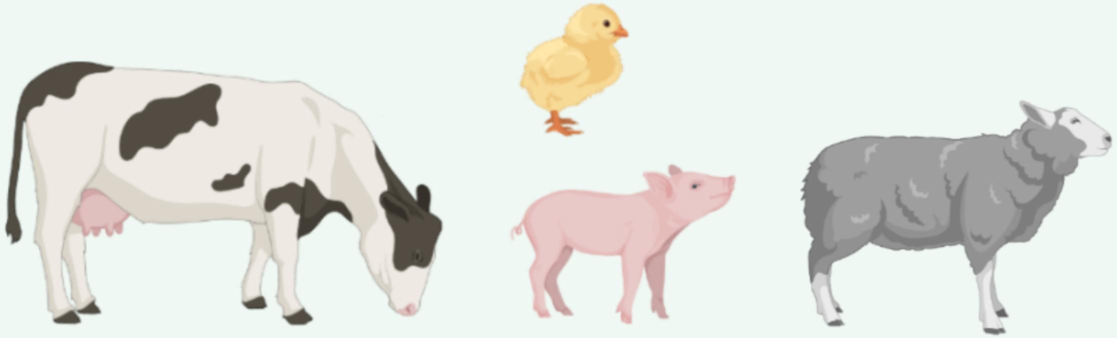
ROSLIN

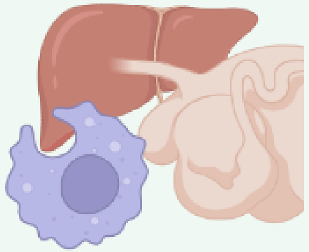
Context

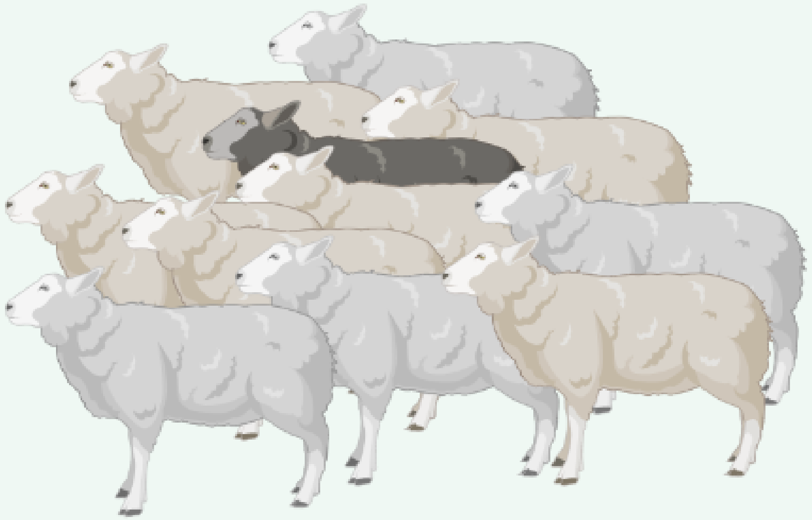


- Genomic Selection = improved genetic gain
- Some traits are difficult to influence
- Gene expression can help unpick difficult phenotypes e.g. immune traits
- Can focus on immune relevant tissues and cell types
- Identify genomic regions controlling traits of interest
- SNPs can be incorporated into GS algorithms

Context & aims







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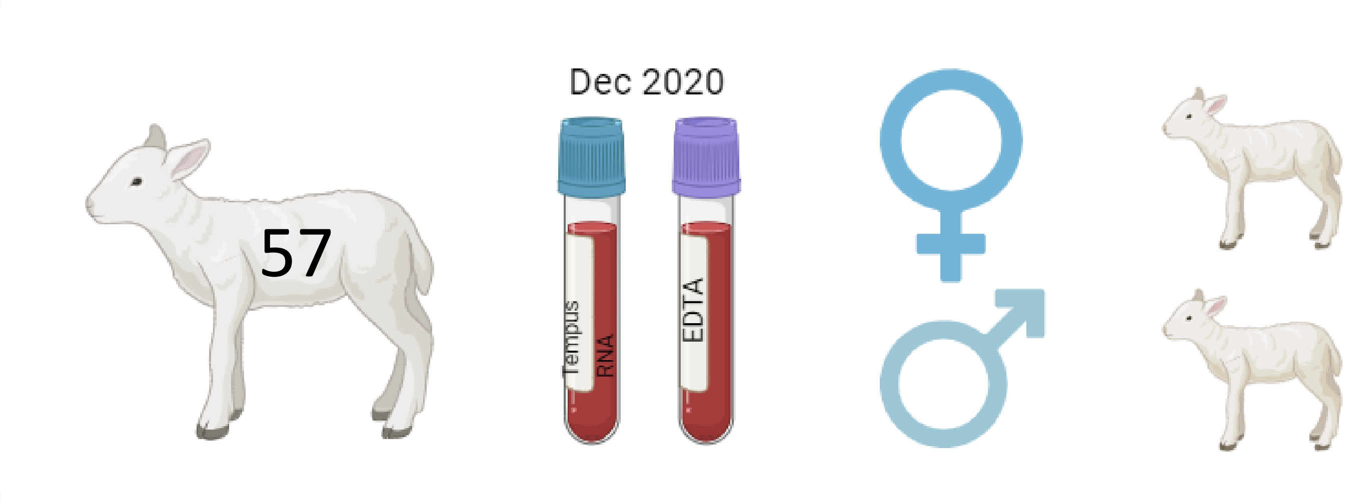
Study populations

- 1 group of animals
- Lambs ~9 months old
- Blood samples
  - RNA-sequencing
  - Matched genotypes



Methods

Wet Lab:

- RNA-sequencing of whole blood
  - White blood cells
- SNP genotyping
  - Illumina Ovine 50k chip

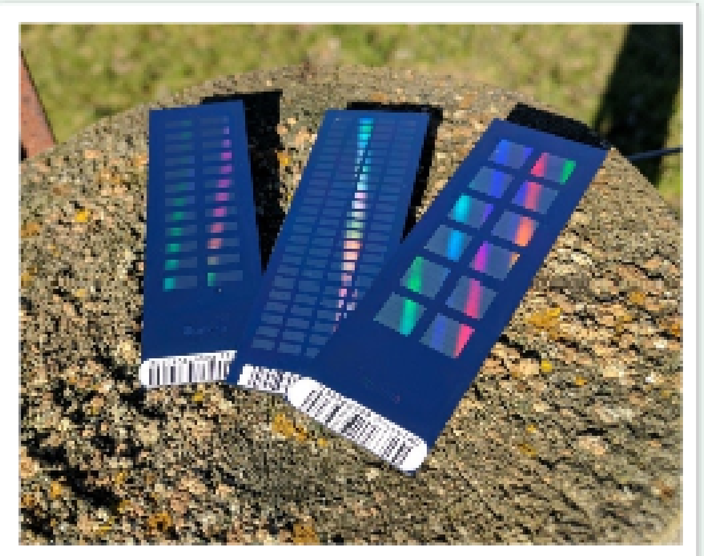
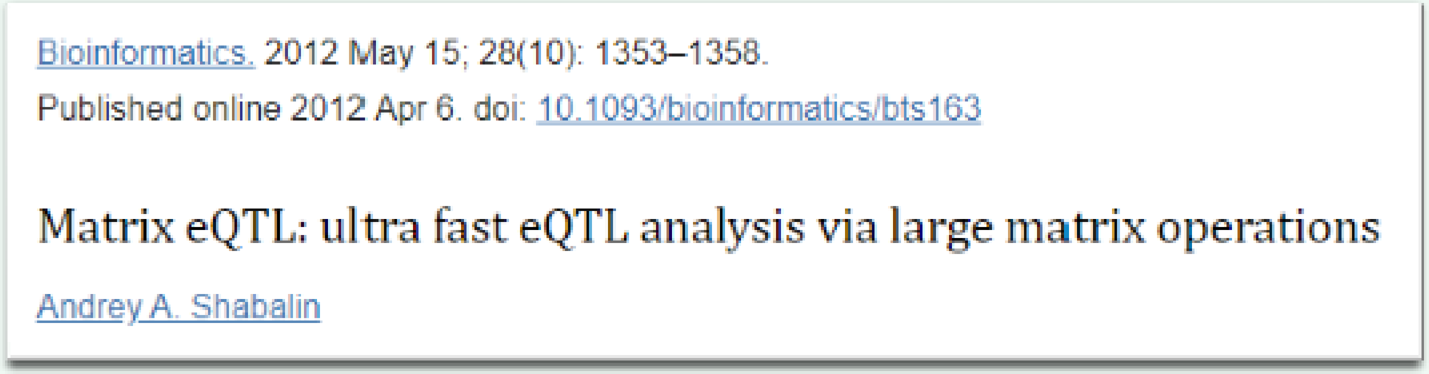


Image courtesy of ISGC - sheephapmap.org

Computational:

- Transcript quantification (Kallisto)
  - Count matrix for downstream analysis
- Gene Ontology (EnrichR)
  - Detection of functional pathways
- eQTL analysis (MatrixQTL)



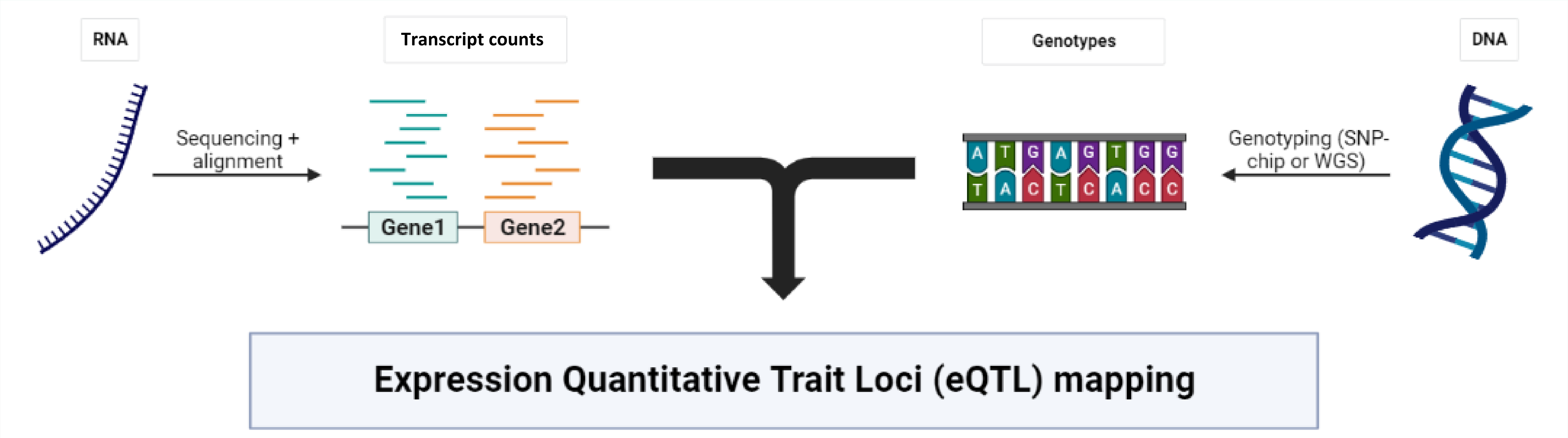
Bioinformatics. 2012 May 15; 28(10): 1353–1358.

Published online 2012 Apr 6. doi: 10.1093/bioinformatics/bts163

Matrix eQTL: ultra fast eQTL analysis via large matrix operations

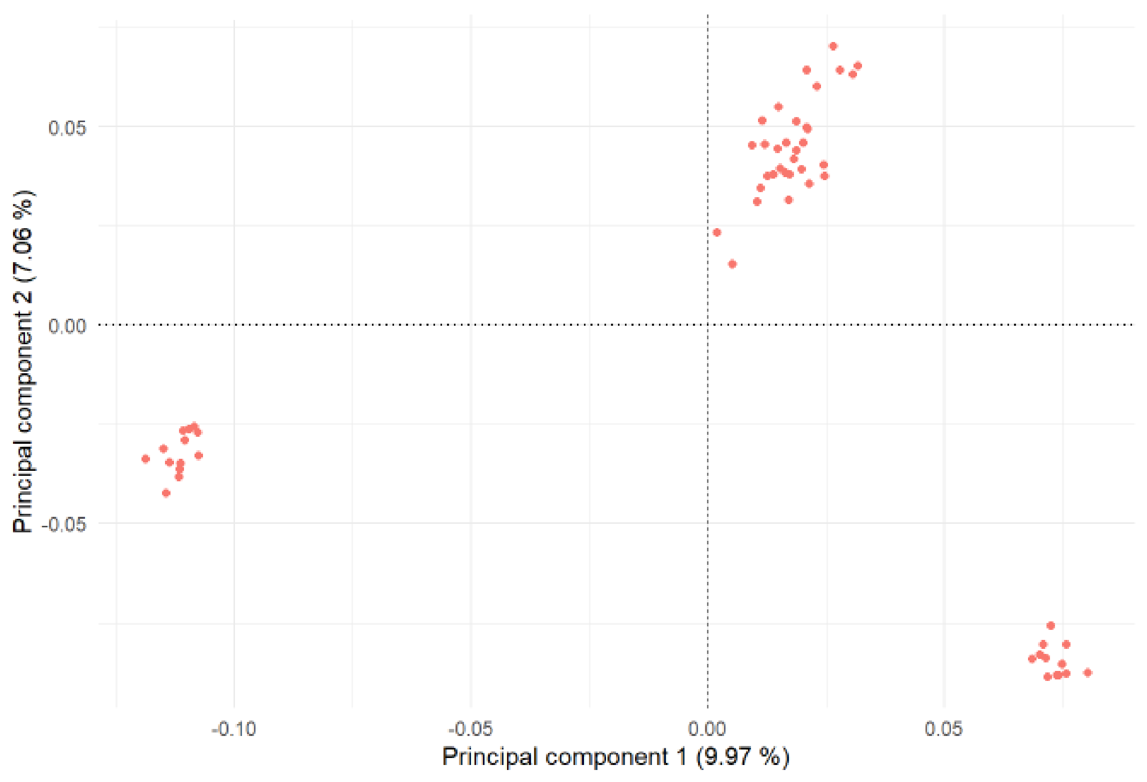
Andrey A. Shabalin

eQTL analysis

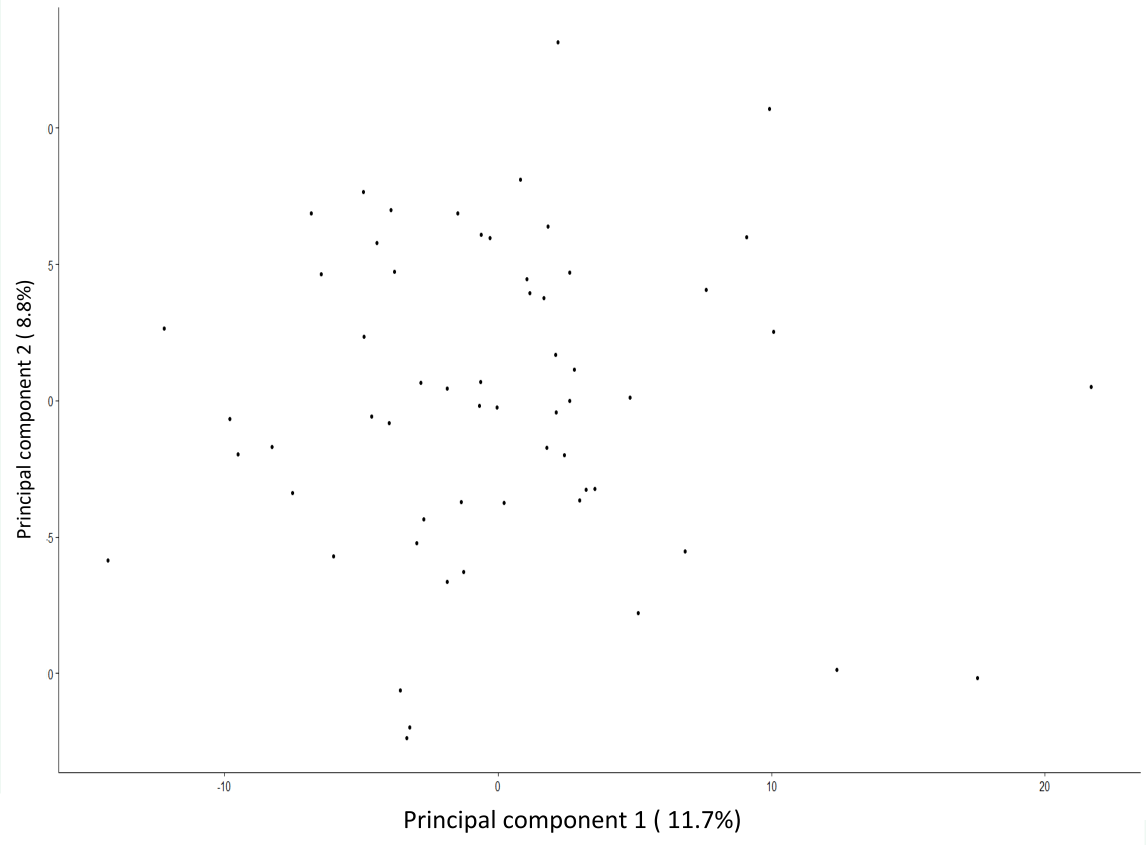


eQTL analysis - covariates

PCA of study population genotypes

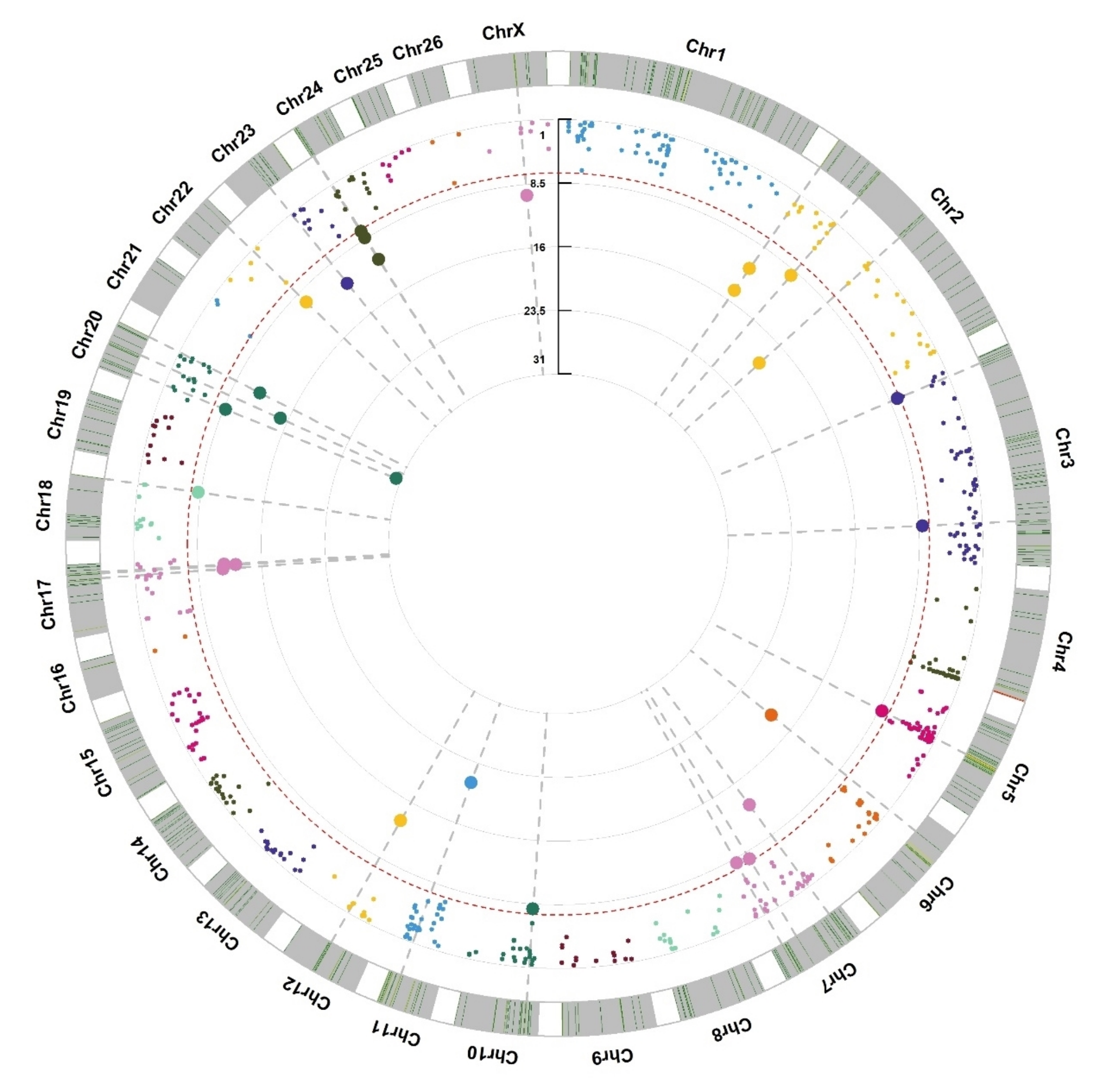


PCA of study population gene expression



eQTL analysis finds significant associations

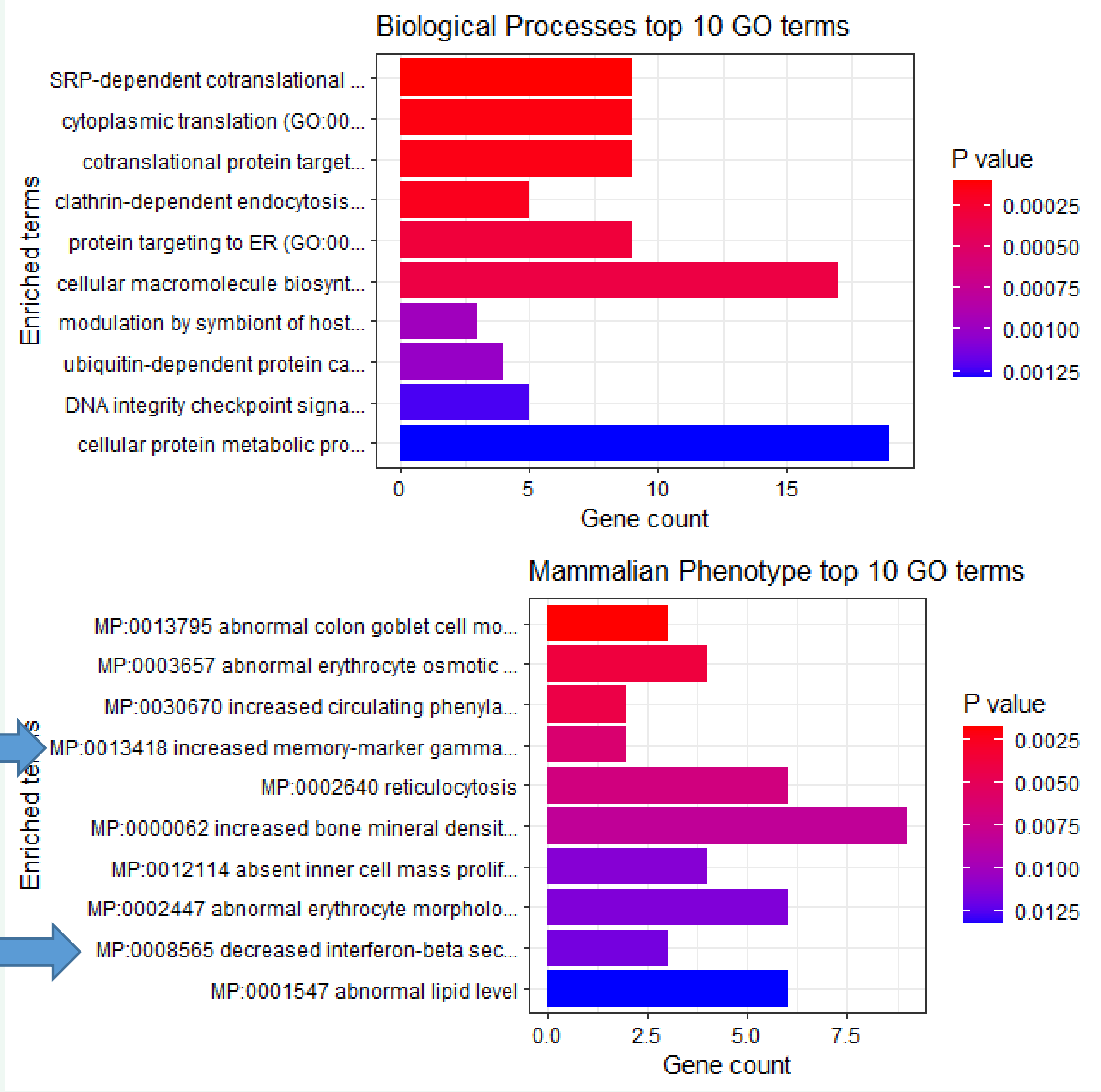
- 611 eQTL found (FDR <0.05)
- Distributed across the genome



Gene ontology pathways

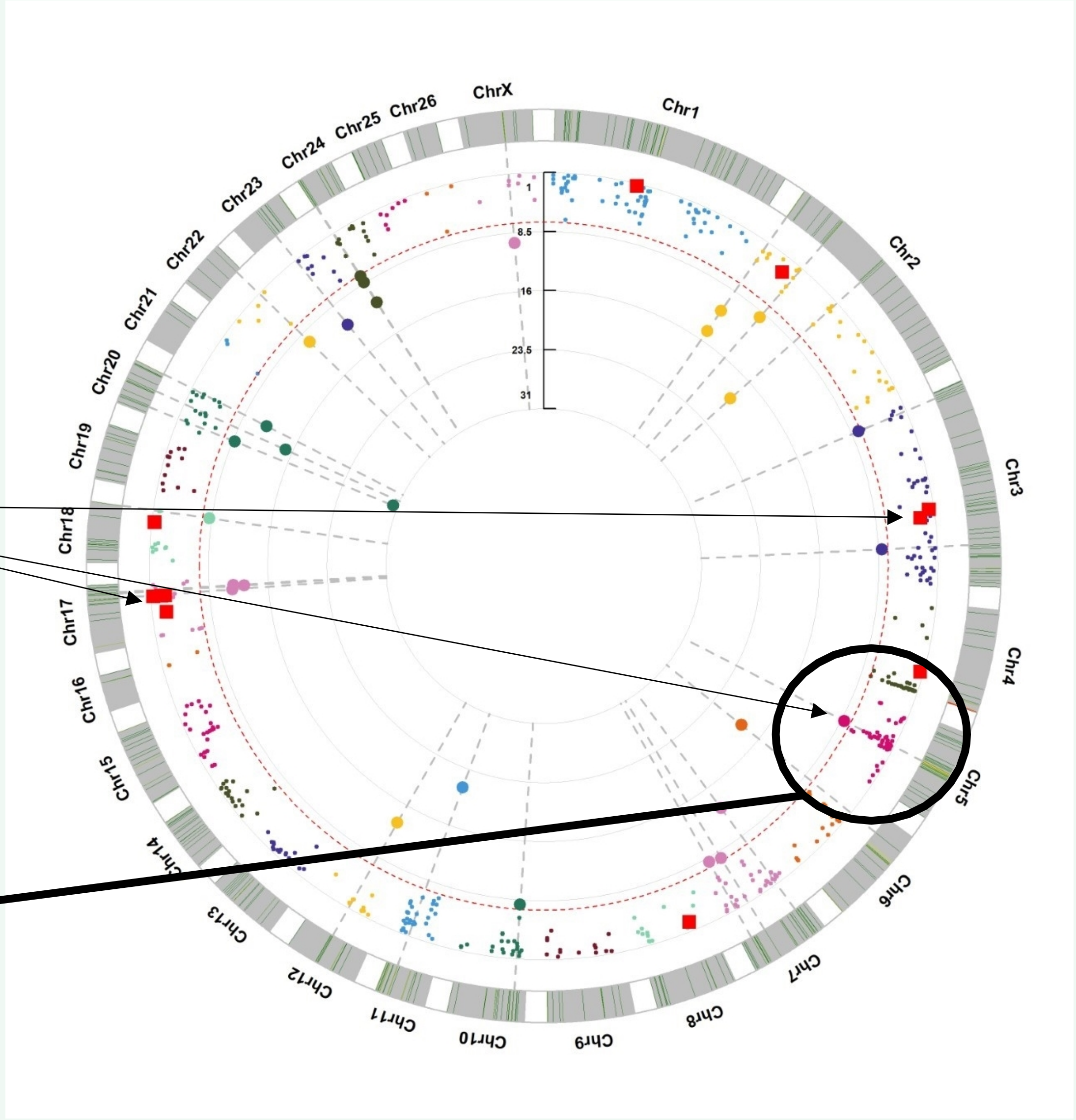
- ‘Housekeeping’ pathways were abundant

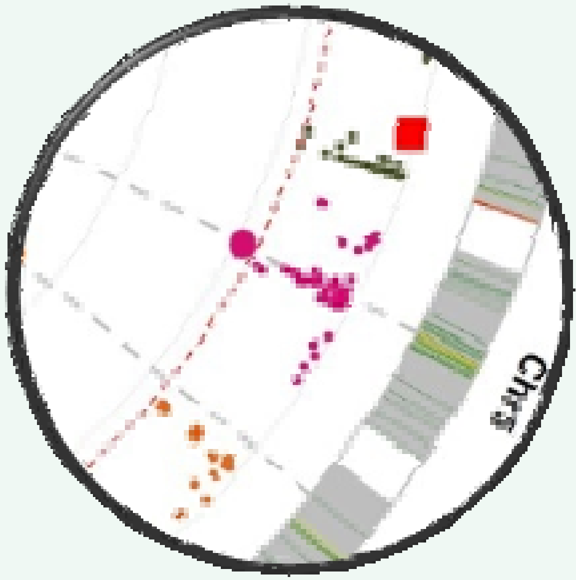
- Pathways related to immune functions



Annotated eQTLS

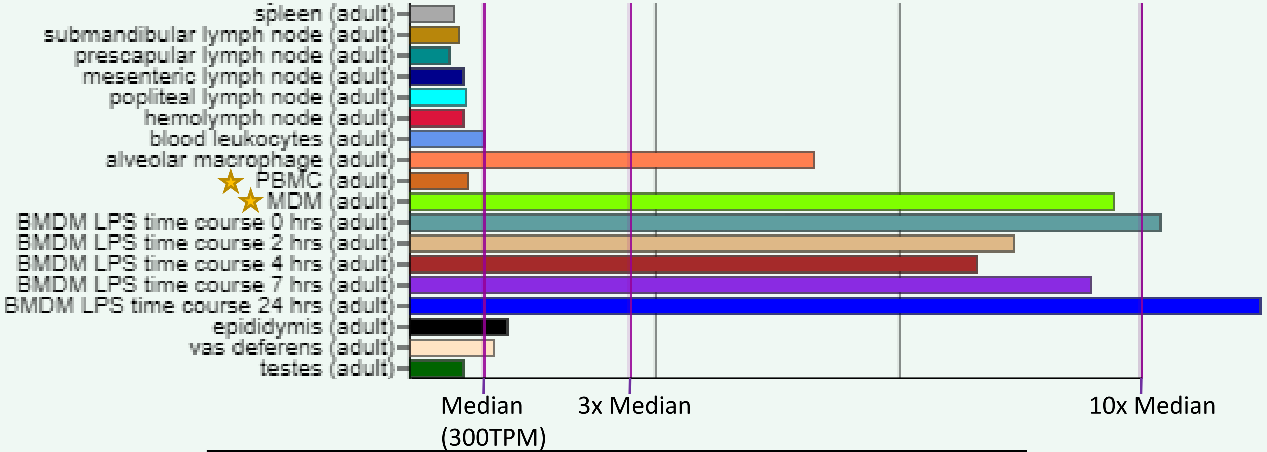
- eQTL related to genes in immune pathways
- Clusters on chromosomes 3, 5, 17



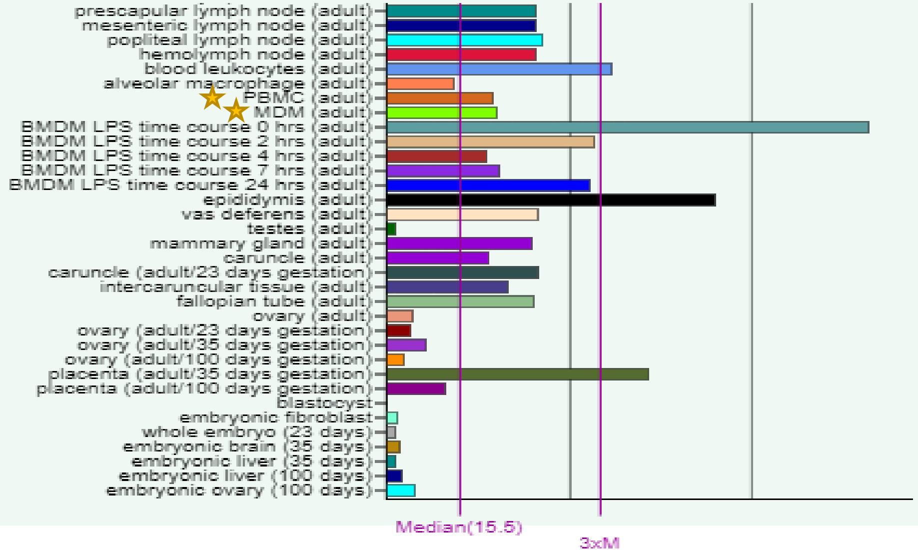


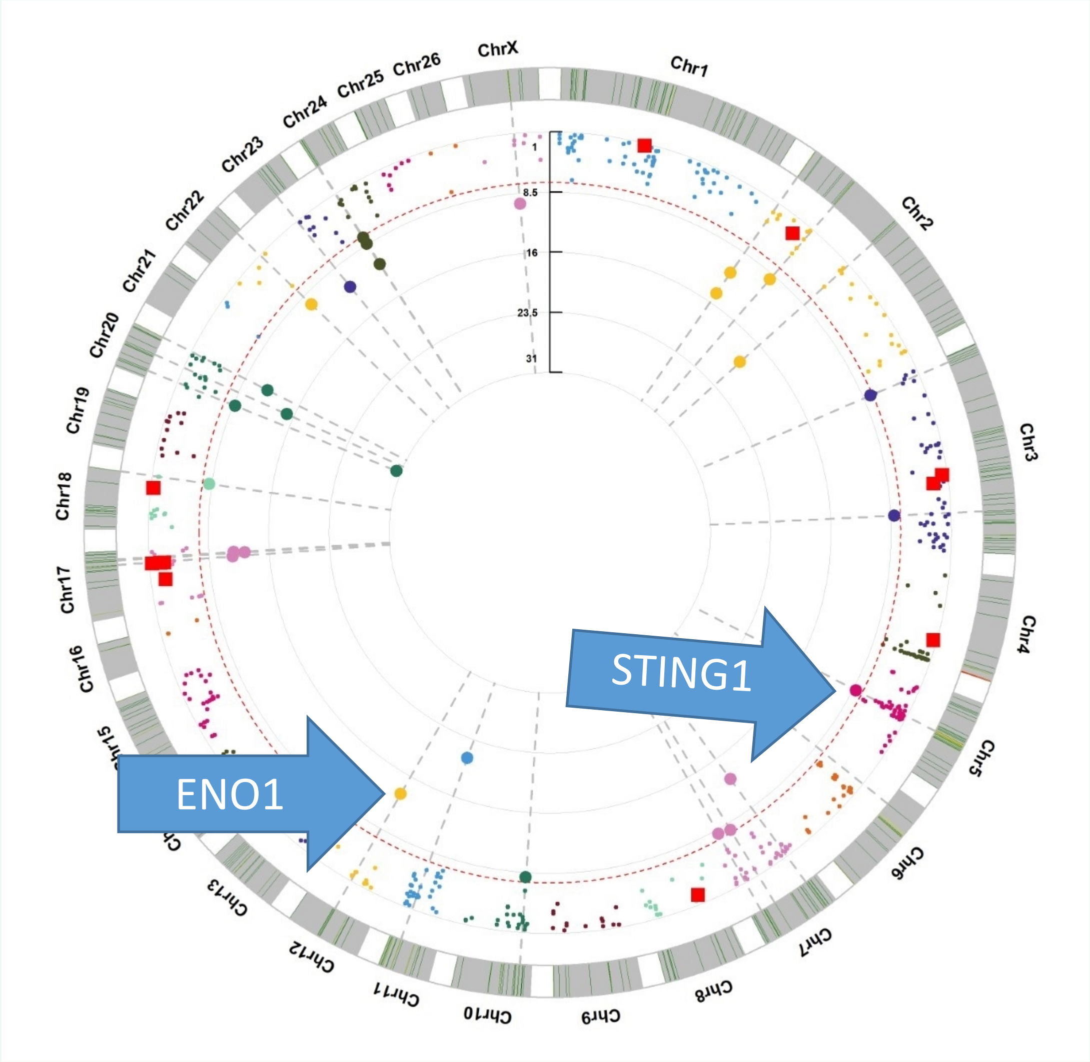
Potential regions of interest

ENO1 in Sheep Gene Expression Atlas



STING1 in Sheep Gene Expression Atlas





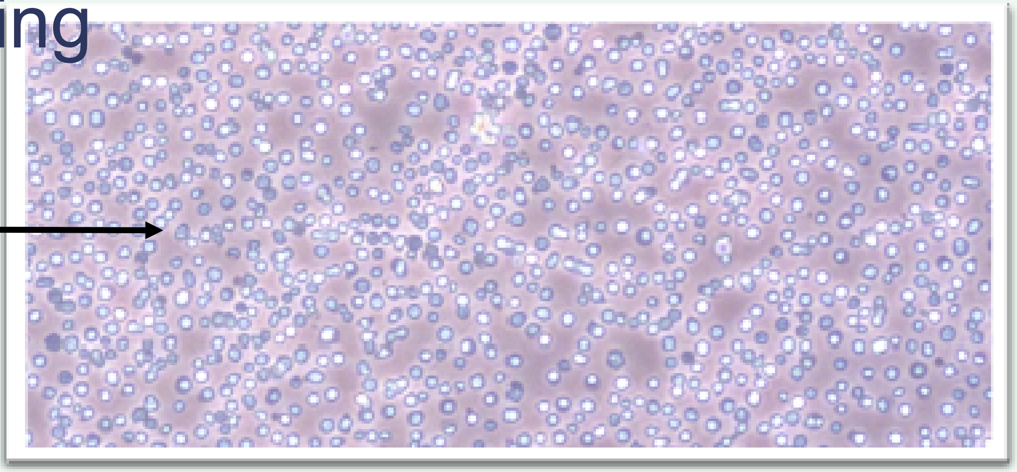
Conclusions

Expression quantitative trait loci in sheep liver and muscle contribute to variations in meat traits

Zehu Yuan, Bolormaa Sunduimijid, Ruidong Xiang, Ralph Behrendt, Matthew I. Knight, Brett A. Mason, Coralie M. Reich, Claire Prowse-Wilkins, Christy J. Vander Jagt, Amanda J. Chamberlain, Iona M. MacLeod, Fadi Li, Xiangpeng Yue ✉ & Hans D. Daetwyler ✉

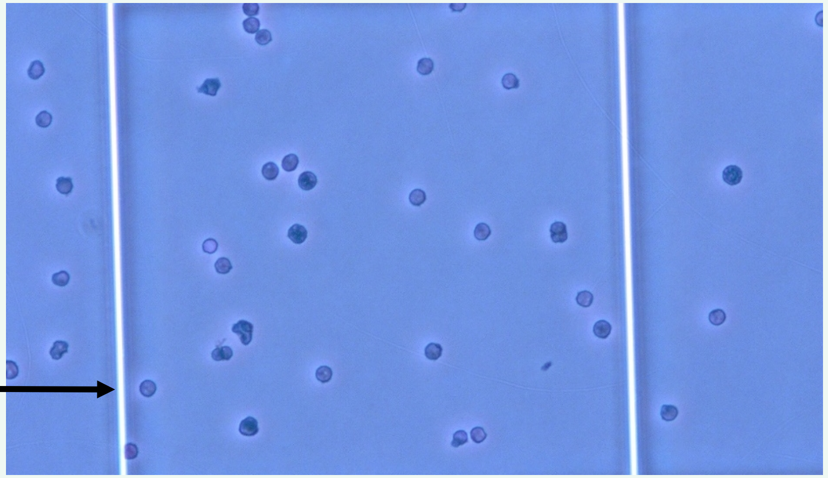
- One of the first eQTL studies in sheep
- Immune traits are complex, eQTL can help
- Further investigation of these markers to validate role in immune function
    - Integration with GWAS datasets to determine genomic regions underlying phenotypes
- Potential use in genomic selection in the future

Next steps - Single-nuclei RNA-sequencing



Ovine PBMCs isolated from whole blood (x20 magnification)

- 3 adult sheep
- Ficoll sorting of whole blood
- Nuclei fixation
- Parse Evercode assay
- Multiplexing barcode protocol
- RNA-sequencing (Nextseq)

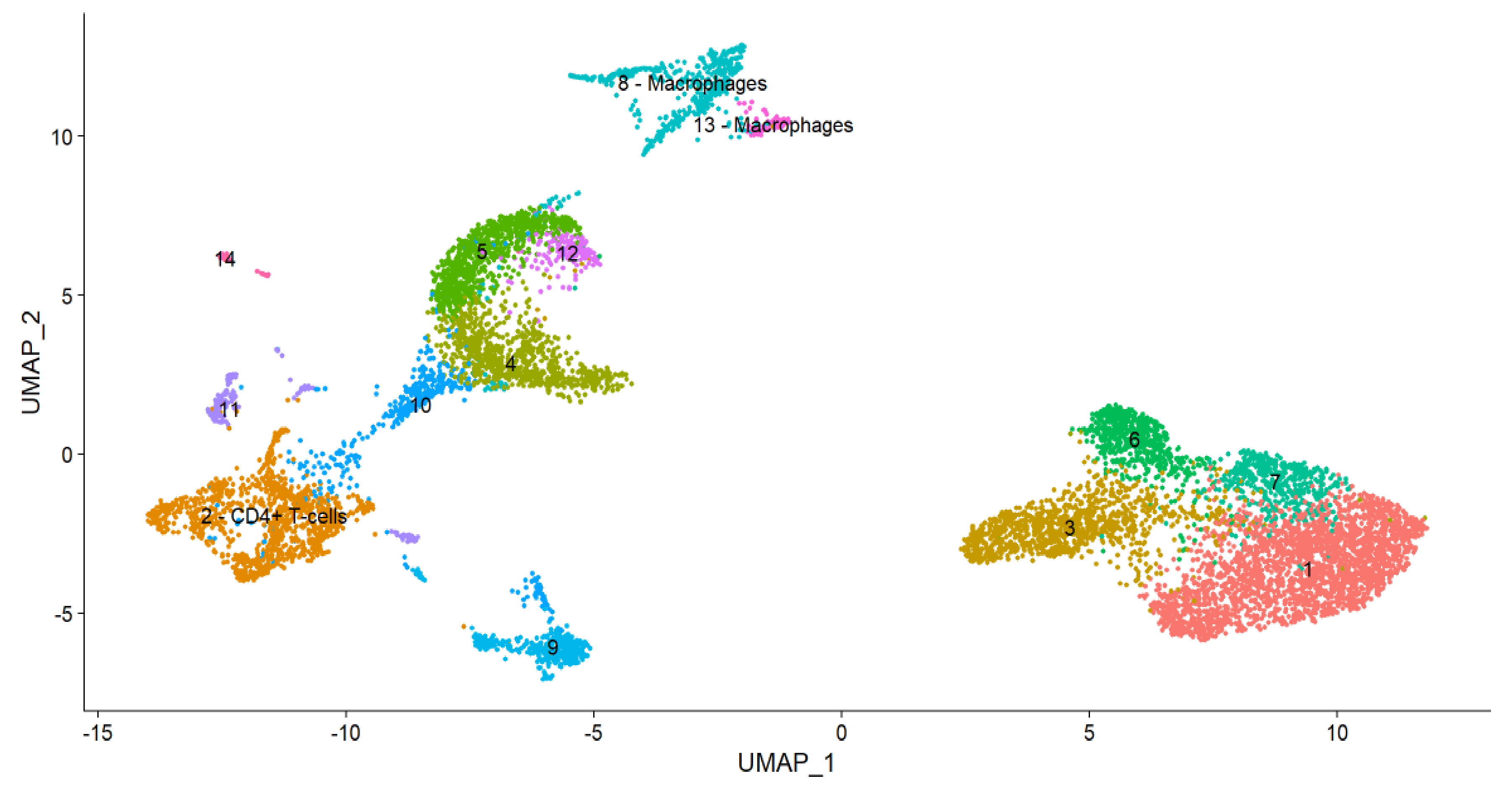


Fixed nuclei

Parse BIOSCIENCES

Single-nuclei RNA-sequencing

- Demultiplexing
- Analysis using Seurat
- Cluster identification



Thank you!

Kdubarry.com

Dr Emily Clark
Prof Mike Coffey

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