

Boolean networks reveal opposing roles of SLC22A5 and SLC22A15 in inflammatory bowel disease

Rohan Subramanian¹, Sanjay Nigam², Debashis Sahoo^{2,3}

¹Harvey Mudd College, ²UC San Diego Health, Pediatrics, ³UC San Diego, Computer Science and Engineering

Background

- Inflammatory bowel disease (IBD) is a chronic autoimmune condition affecting the normal function of the gut [1].
- Boolean implication (“if-then”) relationships reveal asymmetric patterns in gene expression missed by standard correlation metrics [2].

Methods

Binarizing gene expression with StepMiner

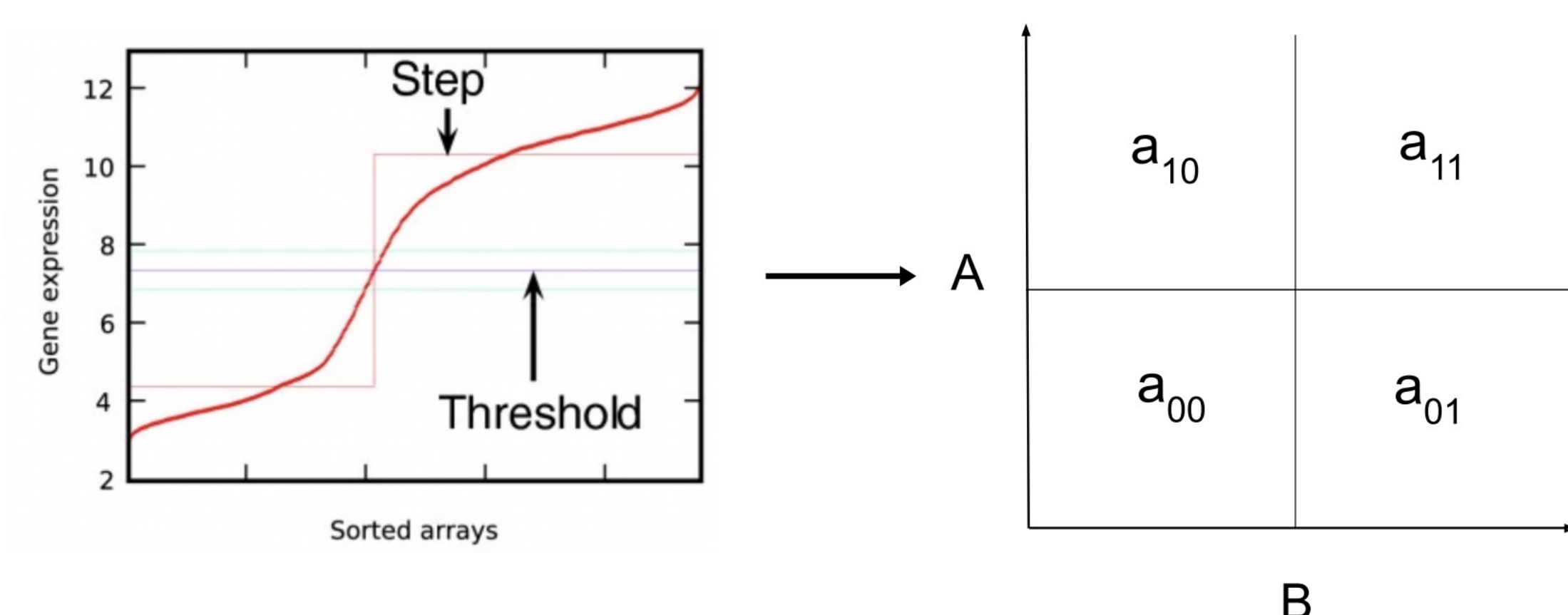


Figure 1. Fitting a step function to binarize gene expression values.

Boolean implication relationships

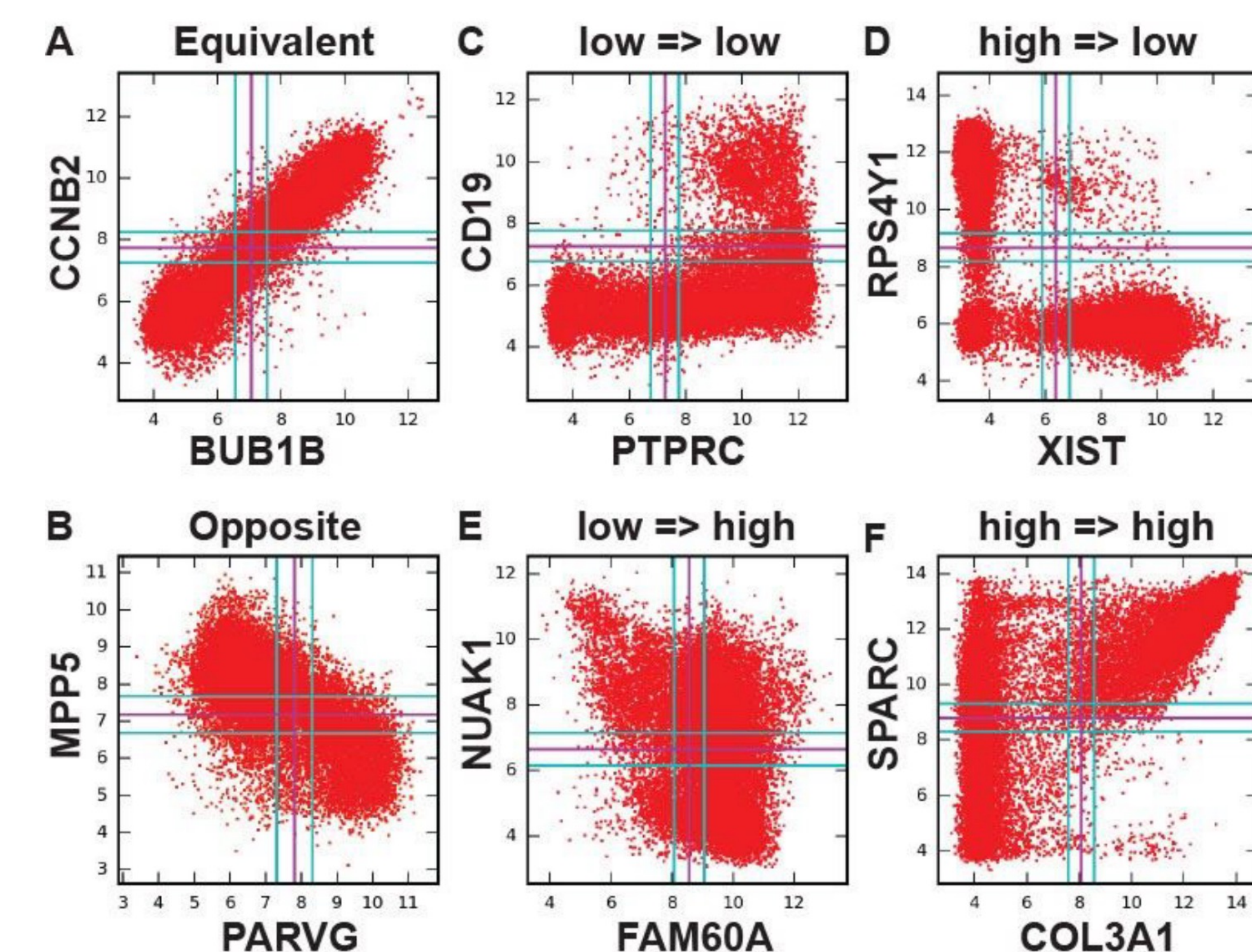


Figure 2. Six types of relationships.

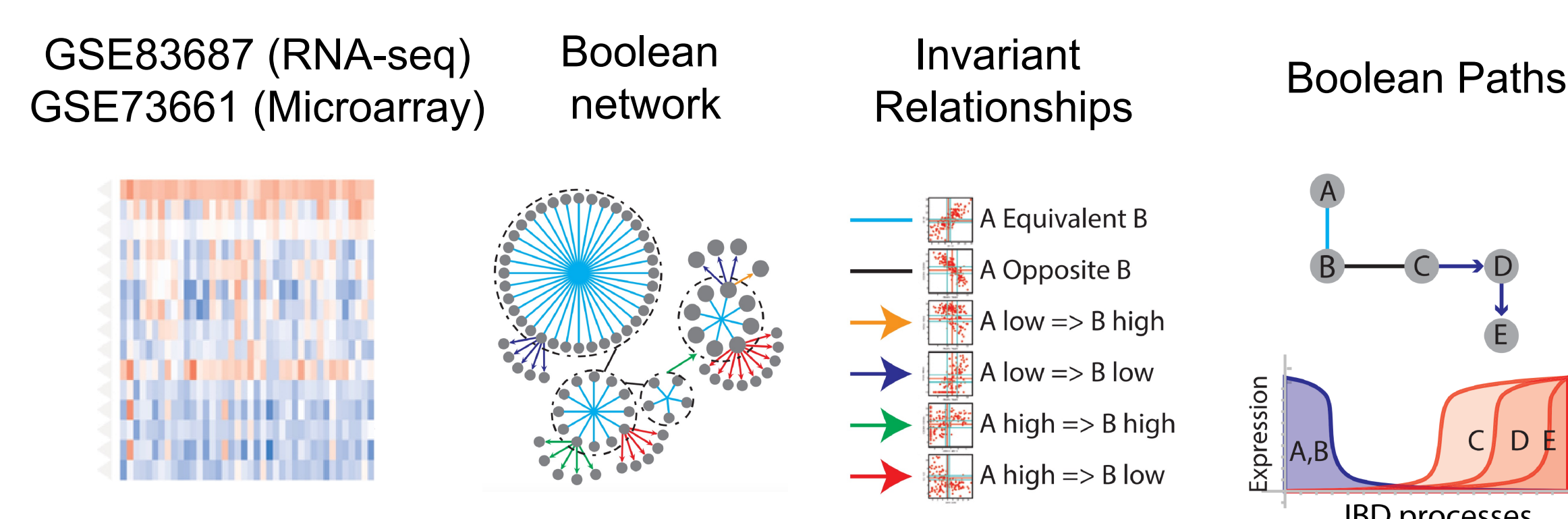


Figure 3. Boolean Network Explorer (BoNE).

Results

Constructing a clustered Boolean network of IBD

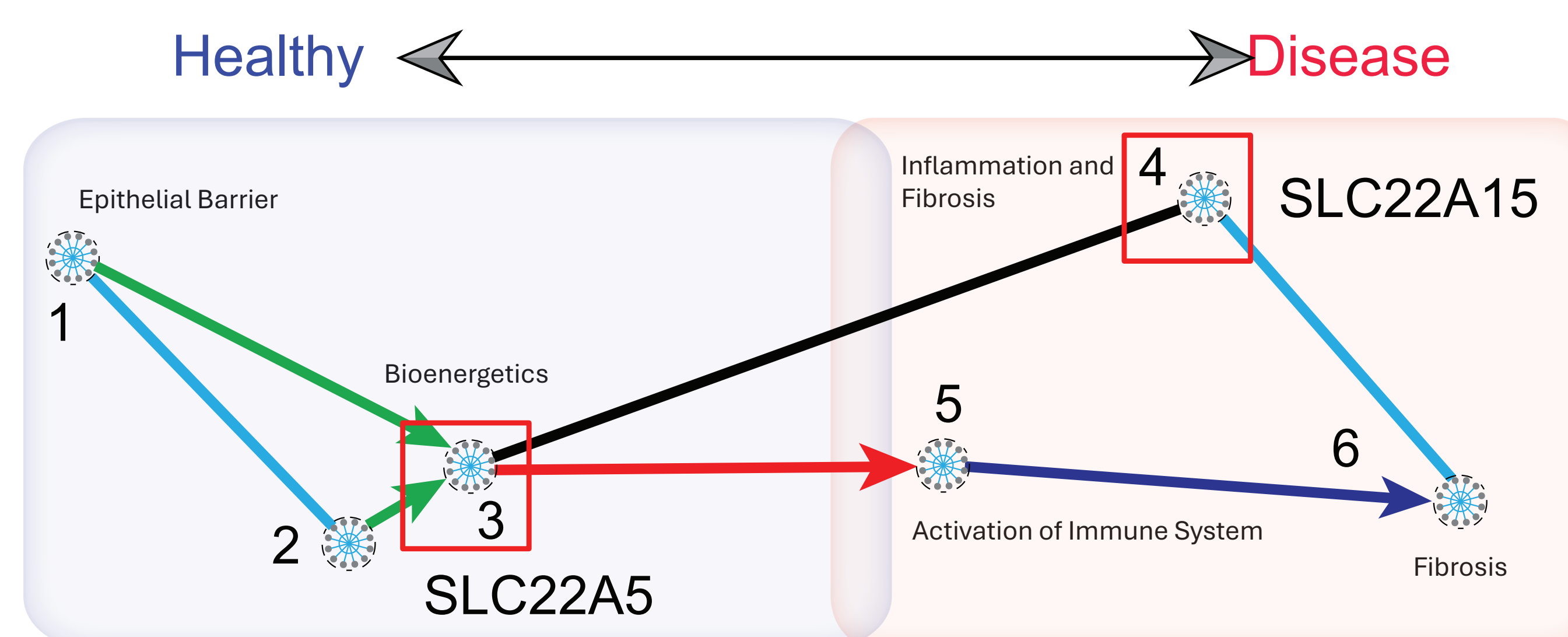


Figure 3. SLC22A5 is Cluster 3 and SLC22A15 is in Cluster 4, connected by a Boolean opposite relationship.

SLC22A5 and SLC22A15 are expressed on opposite sides of the IBD spectrum

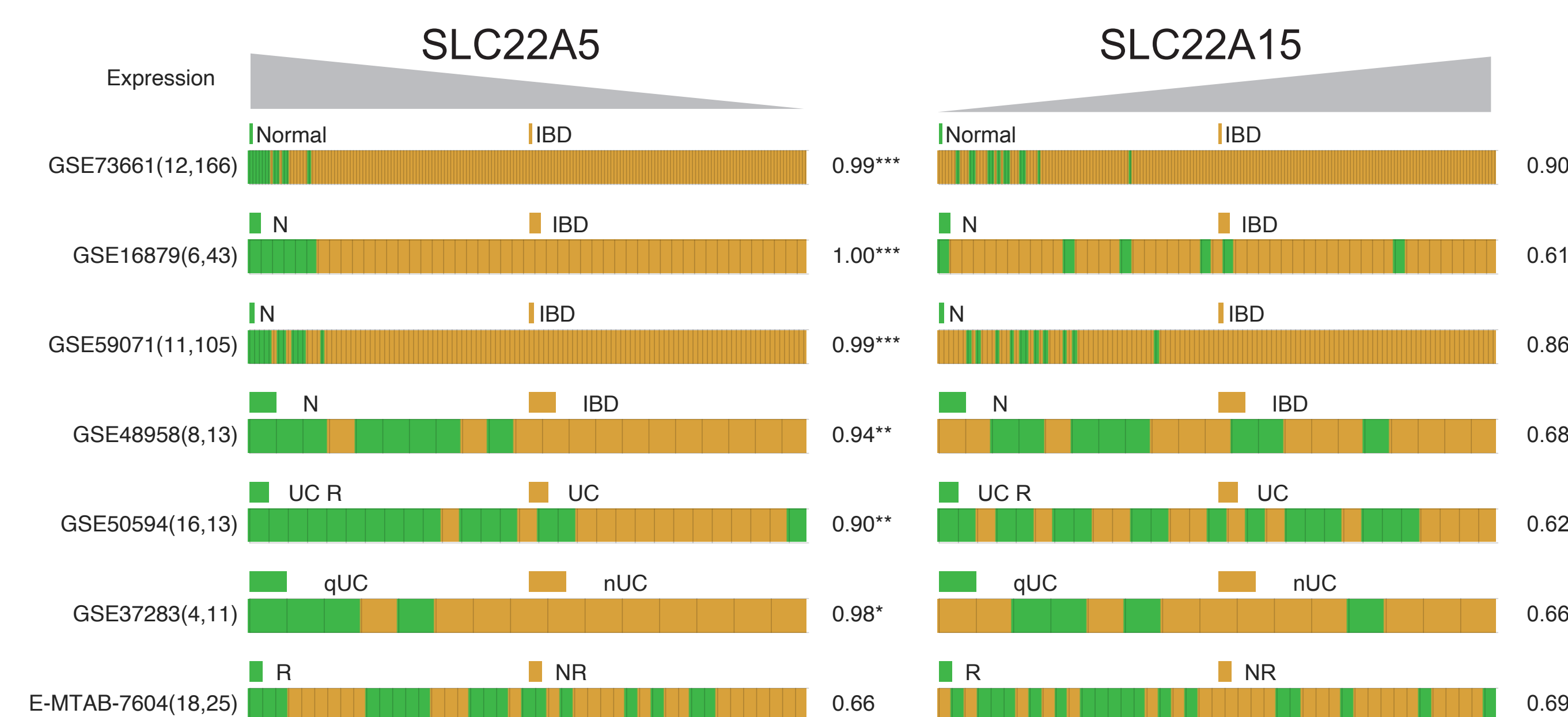


Figure 4. ROC-AUC scores for classification by gene expression in multiple independent IBD datasets.

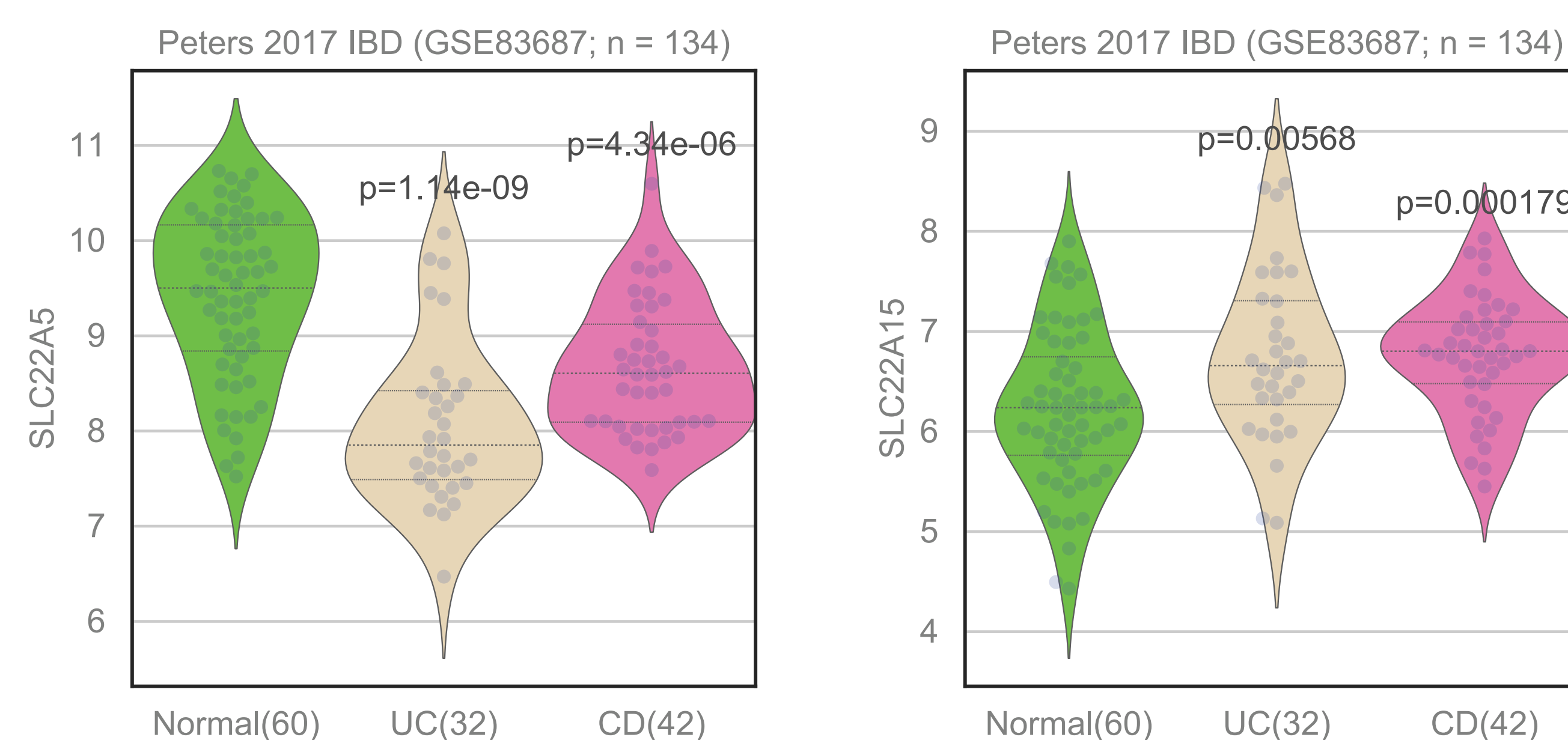


Figure 5. Comparison of SLC22A5 and A15 expression in healthy, ulcerative colitis, and Crohn's disease samples.

Relationship with known IBD biomarkers

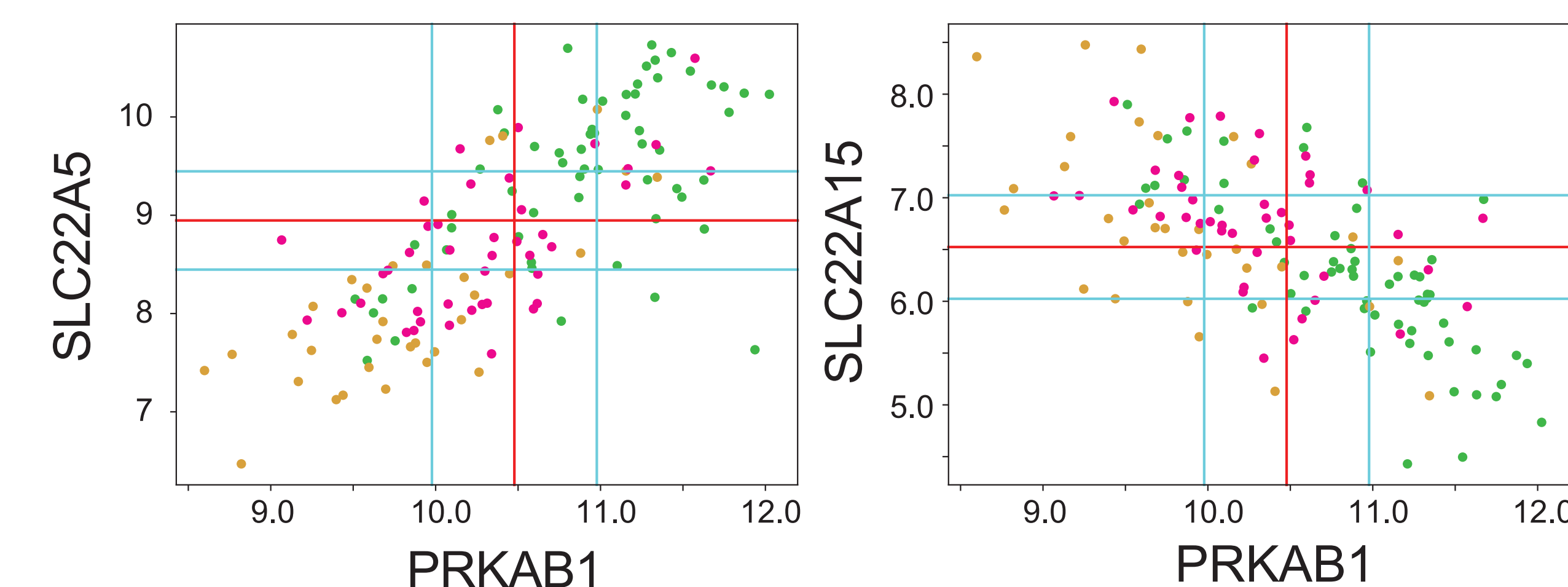


Figure 6. Scatterplot showing inverse relationship of SLC22A5 and A15 with PRKAB1.

Cell type-specific expression patterns

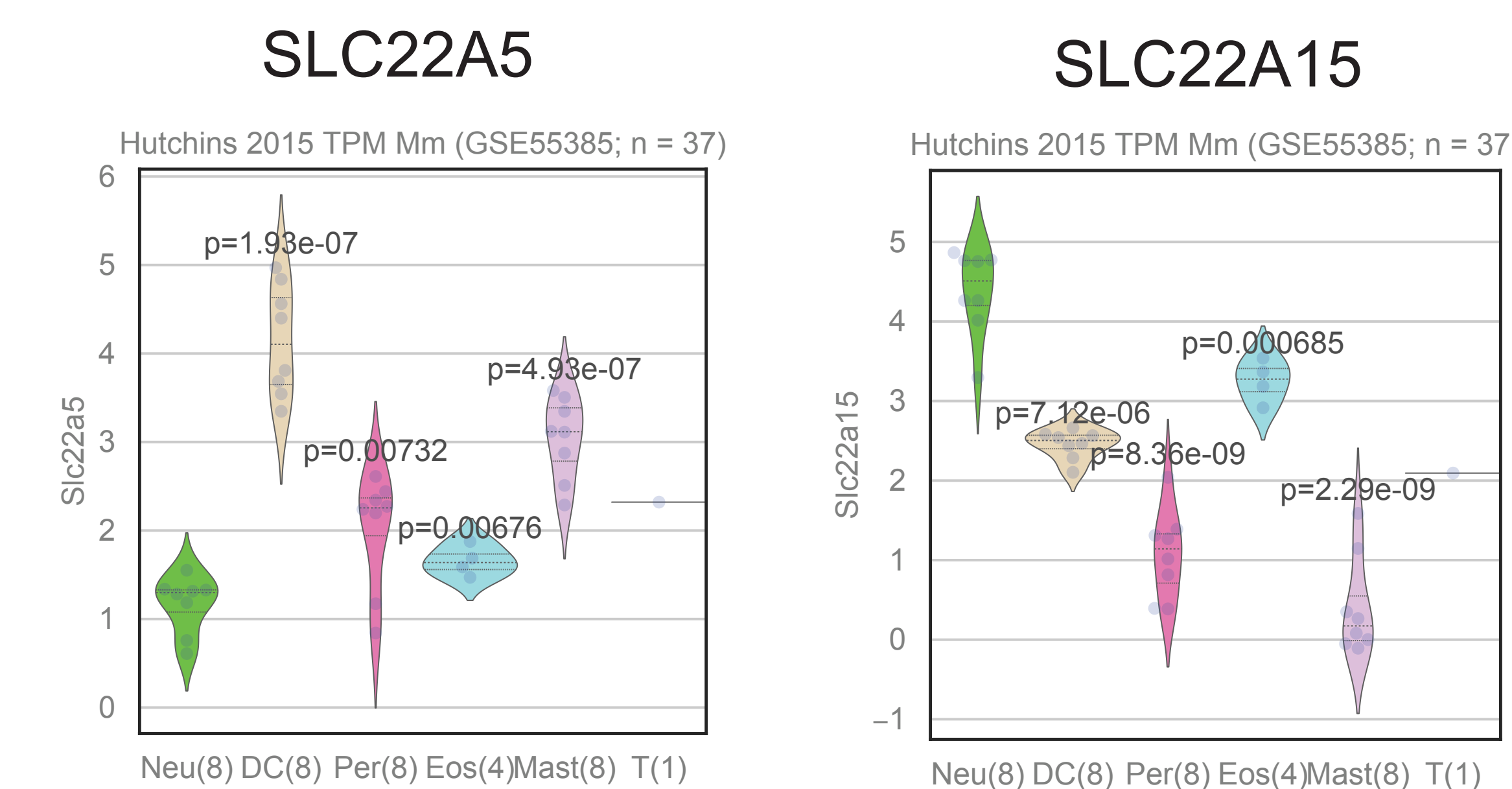


Figure 7. Immune cell type-specific expression of SLC22A5 (dendritic cells) and A15 (neutrophils).

Conclusions

- SLC22A5 is downregulated in IBD and associated with healthy states, while SLC22A15 is upregulated in IBD.
- Opposing roles suggest cell type-specific expression patterns and highlight opportunities for drug targeting.
- Ongoing experimental validation in knockout mice may reveal the role of solute carriers in IBD.

References

- Sahoo, Ghosh et al. Artificial intelligence guided discovery of a barrier-protective therapy in inflammatory bowel disease. Nat Commun. 2021
- Sahoo et al. Boolean implication networks derived from large scale, whole genome microarray datasets. Genome Biol. 2008.

Acknowledgments

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