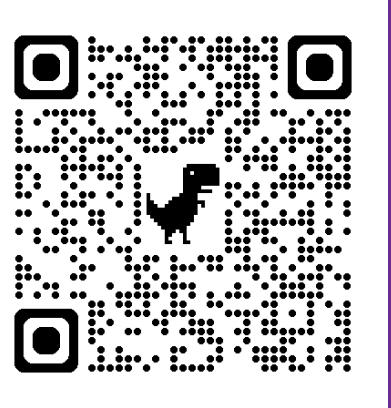
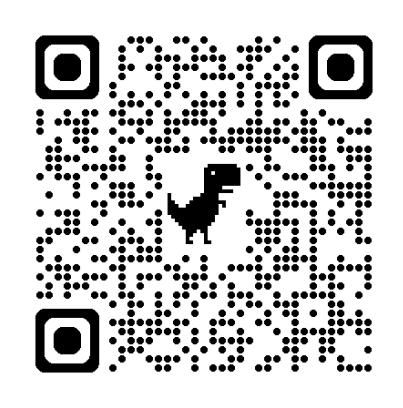


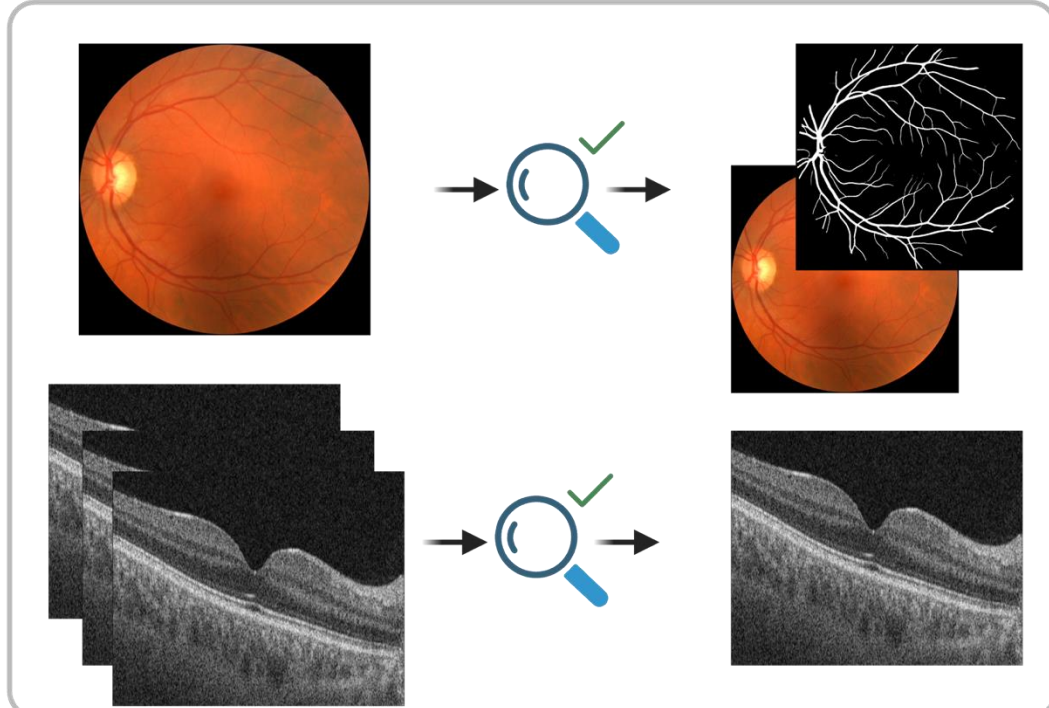


Ophthalmic imaging as a measure of cardiovascular and neurological health: a multi-omic analysis of deep-learning derived phenotypes

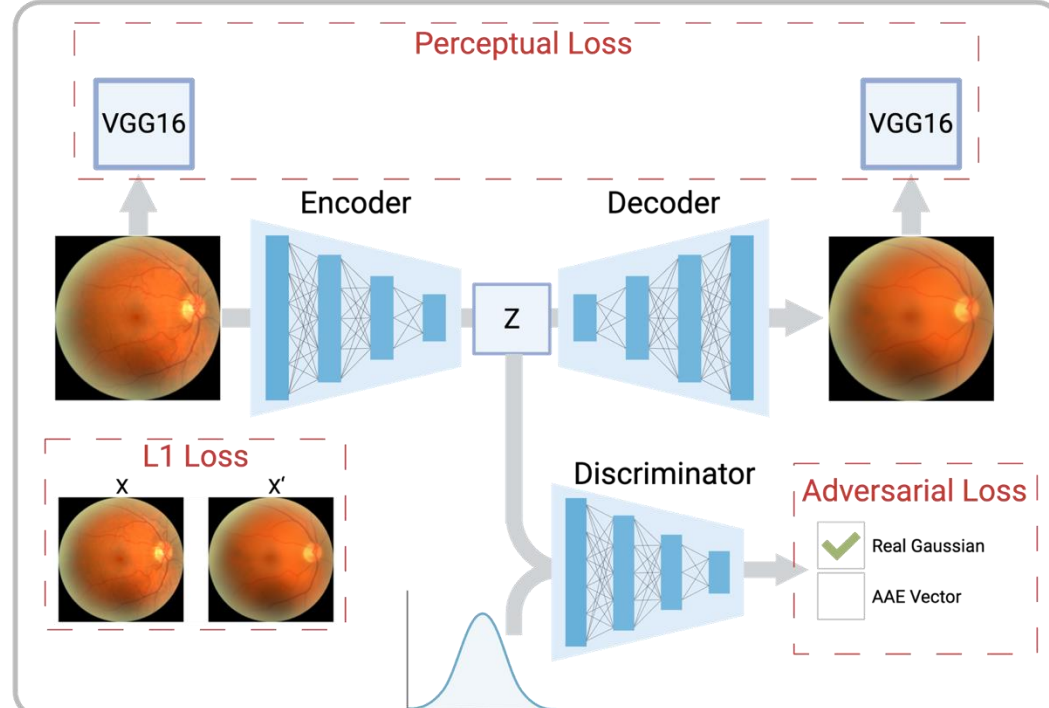
Thomas H Julian, Haoran Dou, Jinming Duan, Jinghan Huang, Esther Yoo, David J Green, Andrew Strange, Elham Alhathli, UK Biobank Eye and Vision Consortium, Matthew Sperrin, Pearse A Keane, Emily Y Chew, Bernard Keavney, Tomas W Fitzgerald, Johnathan Cooper-Knock, Ewan Biney, Alejandro F Frangi, Panagiotis I Sergouniotis

Graphical Overview

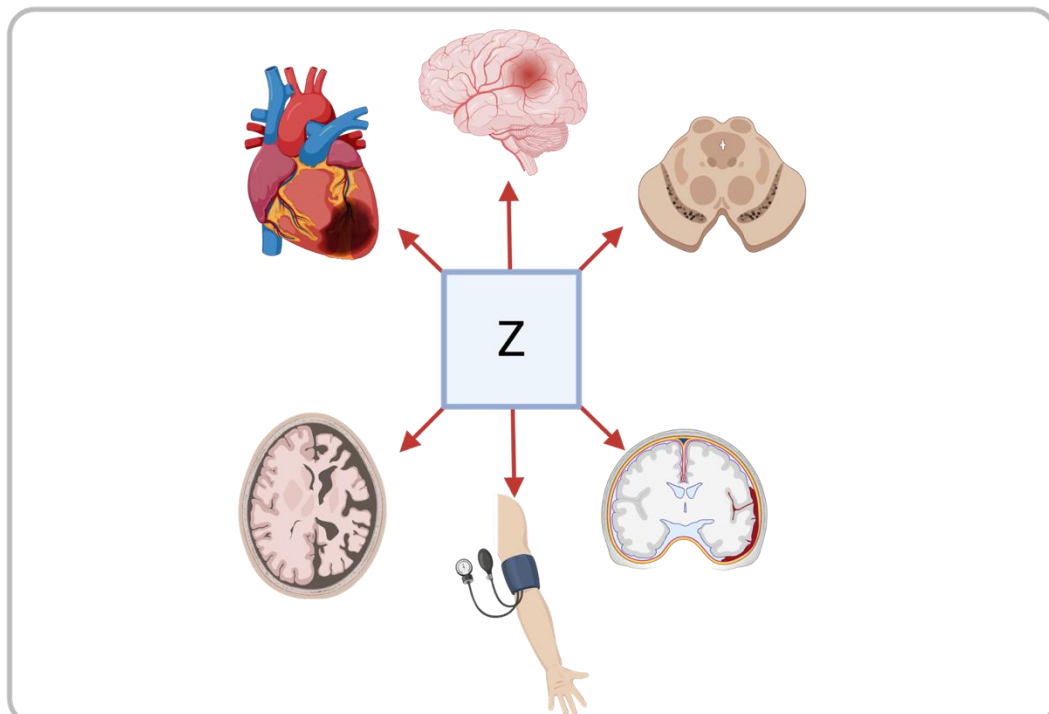
① QC and Pre-Processing



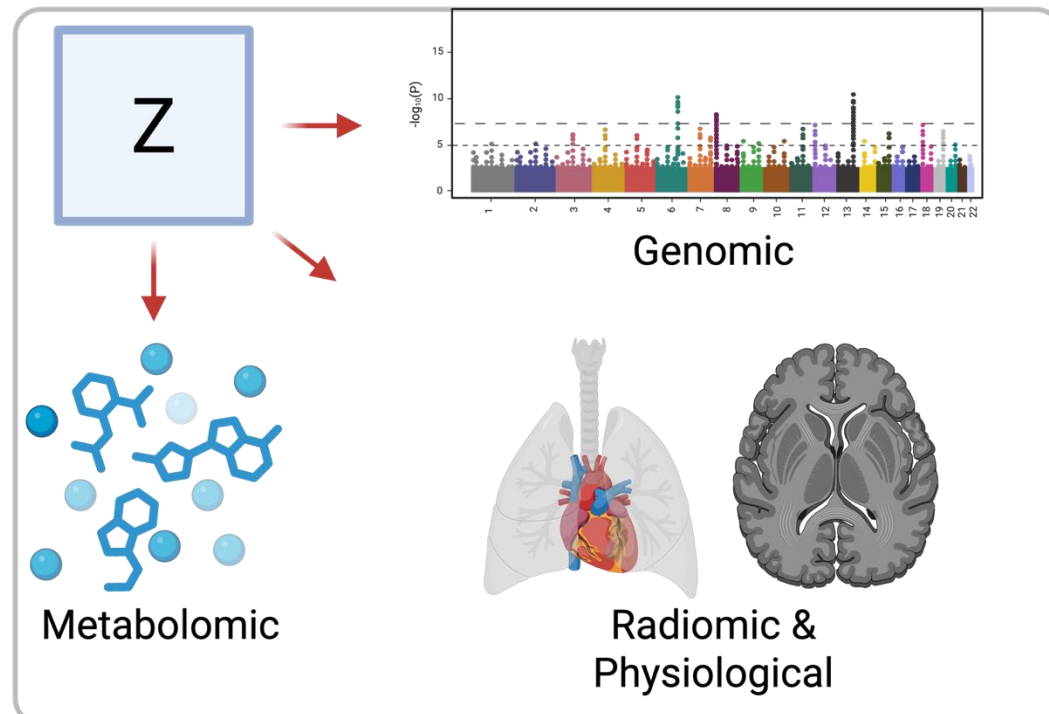
② Train Adversarial Autoencoder



③ Explore Disease Associations



④ Multi-Omic Analyses



Introduction

The eye is uniquely positioned among human organs in that it permits direct, non-invasive visualisation of both the vasculature and the central nervous system.

Given this property, ophthalmic structures have long been recognised as potential indicators of systemic health, particularly in relation to neurodegenerative and cardiovascular disease.

Here, we characterise the breadth of eye-disease associations using colour fundus photographs (CFP) and optical coherence tomography (OCT) images and identify biological axes that may mediate these associations.

Methods

Using UK Biobank data, we developed a multi-omic analysis pipeline integrating physiological, radiomic, metabolomic, and genomic information.

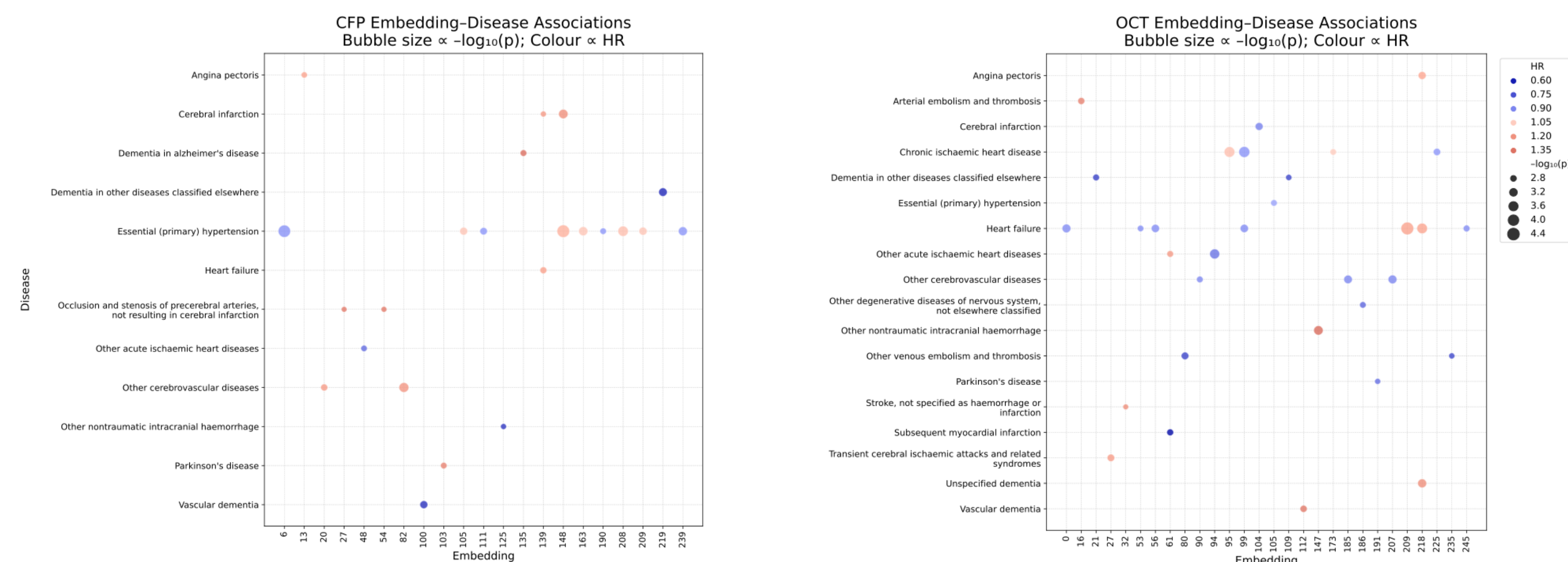
We trained adversarial autoencoders ('Ret-AAE') to represent OCTs (88,972 scans) and CFPs (63,946 scans) as 256-dimensional vectors.

Each dimension (z_i) was examined individually for multi-system associations. A total of 42,001 subjects were eligible for inclusion in downstream CFP analyses, and 68,942 in our OCT analyses.

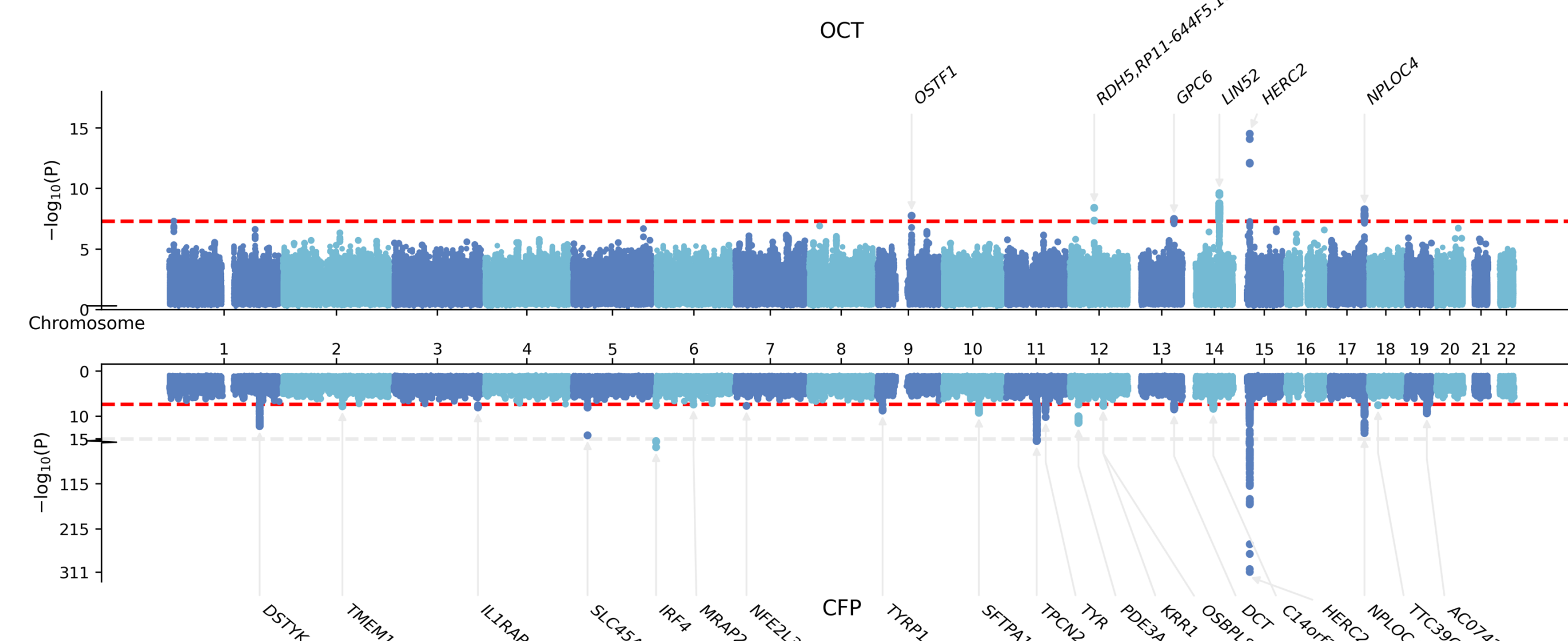
After training Ret-AAE, we explored the relationship between each embedding and:

- Future disease risk (Cox proportional hazards)
- Genetic variants (REGENIE)
- Gene sets (MAGMA) and genetic correlation with disease (LD score regression)
- Metabolomics (Canonical correlation analysis and sparse partial least squares)
- Radiomic and physiological traits (Pearson correlation)

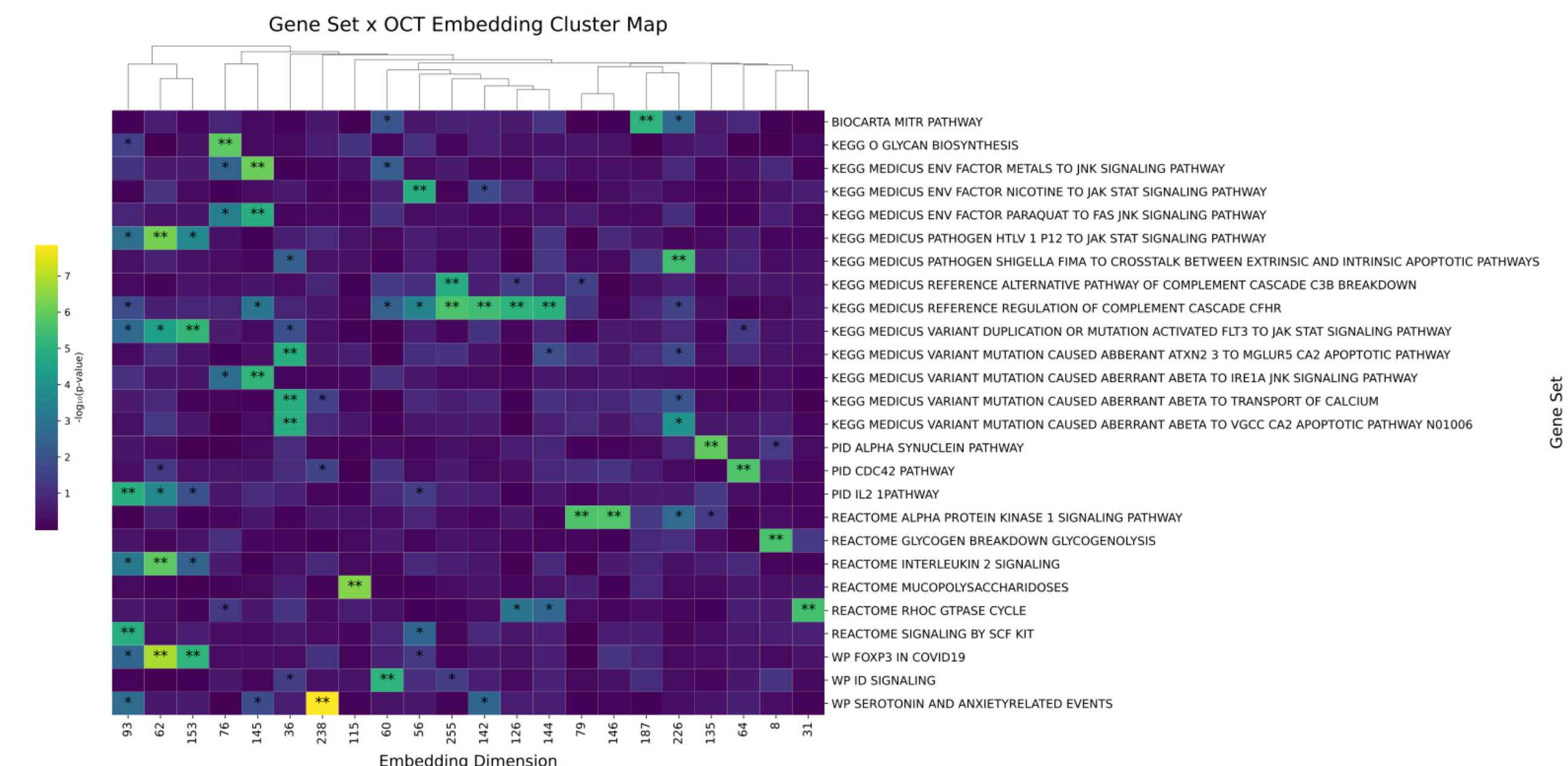
Results



Cox proportional hazards illustrated that CFP (left) and OCT (right) features are associated with future risk of a range of neurodegenerative and cardiovascular diseases.

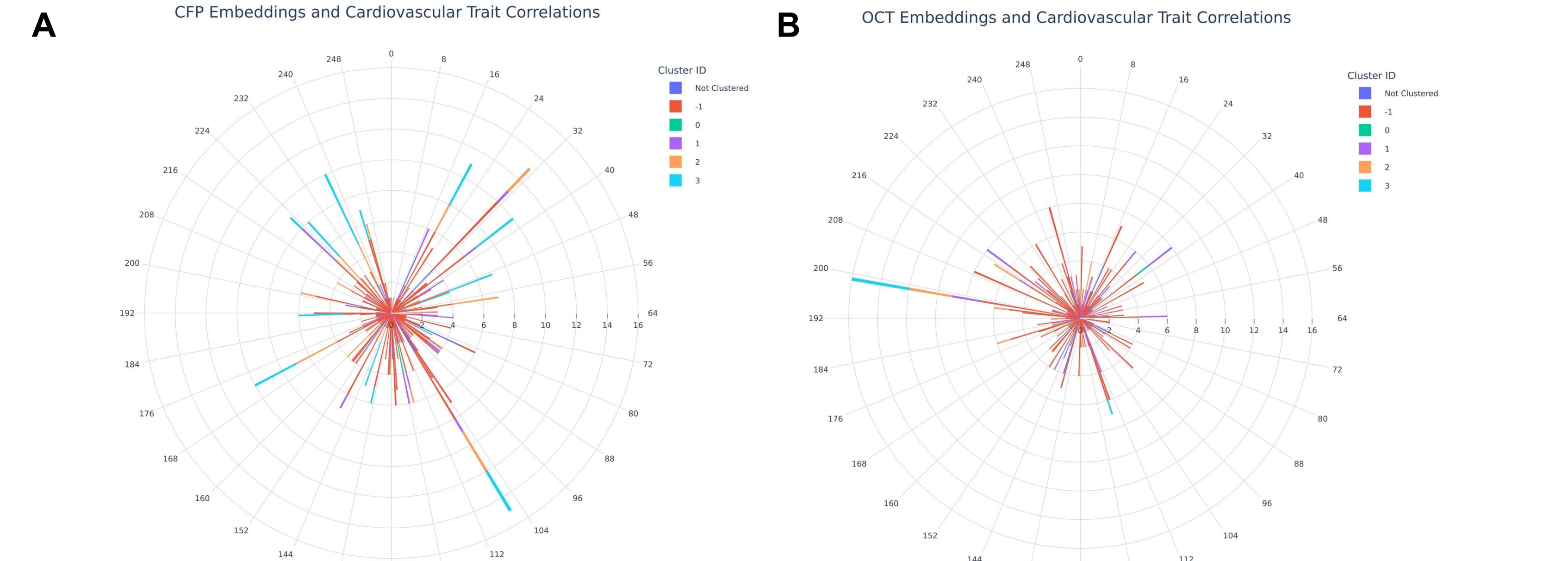


A Miami plot illustrating the genetic associations of CFP and OCT features. Key genes relate to pigmentation, vascular physiology, and accelerated aging.

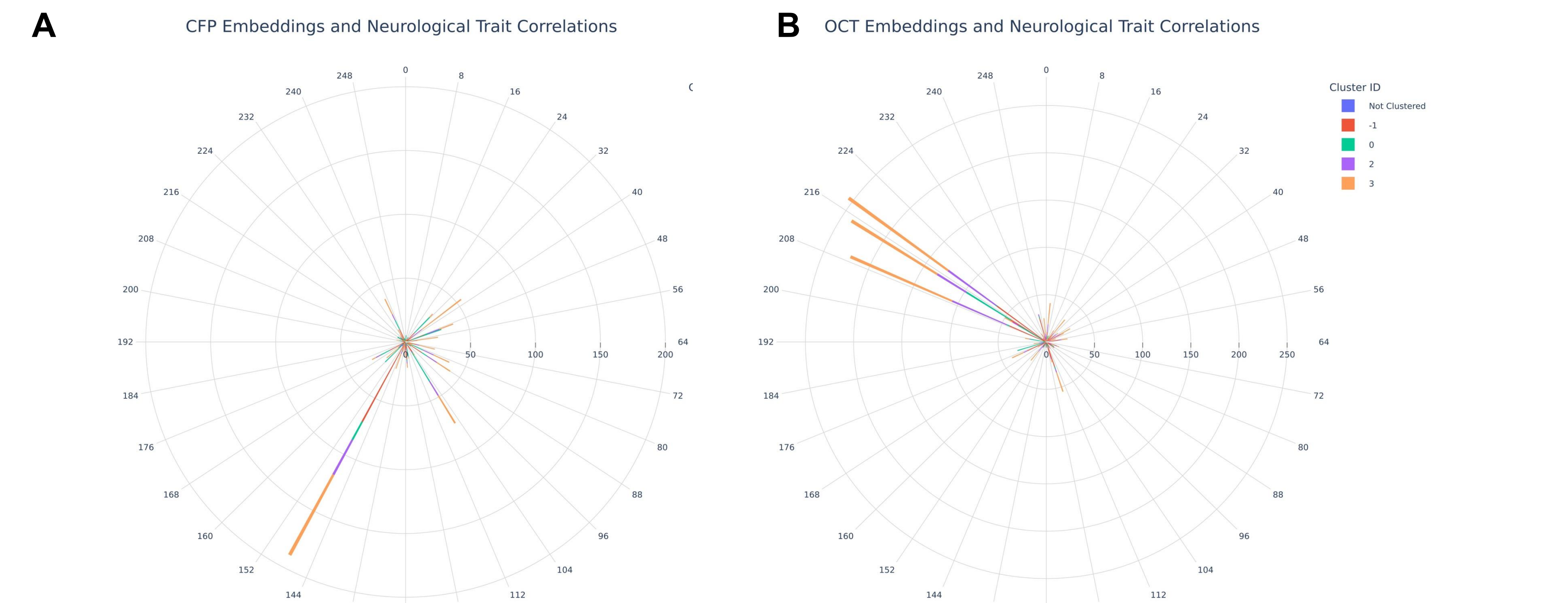


The OCT gene set analysis with MAGMA identified associations between OCT features and pathways known to be linked to neurodegenerative disease.

Results



Polar plots displaying the number of significant relationships (Pearson correlation) between Ret-AAE and cardiovascular traits. The bars are colour coded according to the cluster of traits the significant relationship belongs to. 'Cluster 0' was comprised of electrocardiogram (ECG) intervals ('PP interval', 'RR interval', 'QT interval'); 'cluster 1' grouped heart rate measures; 'cluster 2' included central pulse pressure, peripheral pulse pressure, and stroke volume; and 'cluster 3' encompassed blood pressure measures.



Polar plots displaying the number of significant relationships (Pearson correlation) between Ret-AAE embeddings and neurological traits. The bars are colour coded according to the cluster of traits the significant relationship belongs to. 'Cluster 0' was principally constituted of grey matter volumes assessed using magnetic resonance imaging (MRI); 'clusters 1-3' were largely constituted of diffusion MRI values.

Finally, metabolomic studies using canonical correlation analysis and sparse partial least squares indicated that ophthalmic features are associated with serum high density lipoprotein, low density lipoprotein, and very low-density lipoprotein compositional measures.

Conclusions

Leveraging comprehensive physiological, anatomical, radiomic, metabolomic and genomic analyses, we provide converging evidence that the observed association between ophthalmic features and systemic disease reflect diverse processes.