Supplementary Information

DNA methylation landscape of ocular tissue relative to matched peripheral blood.

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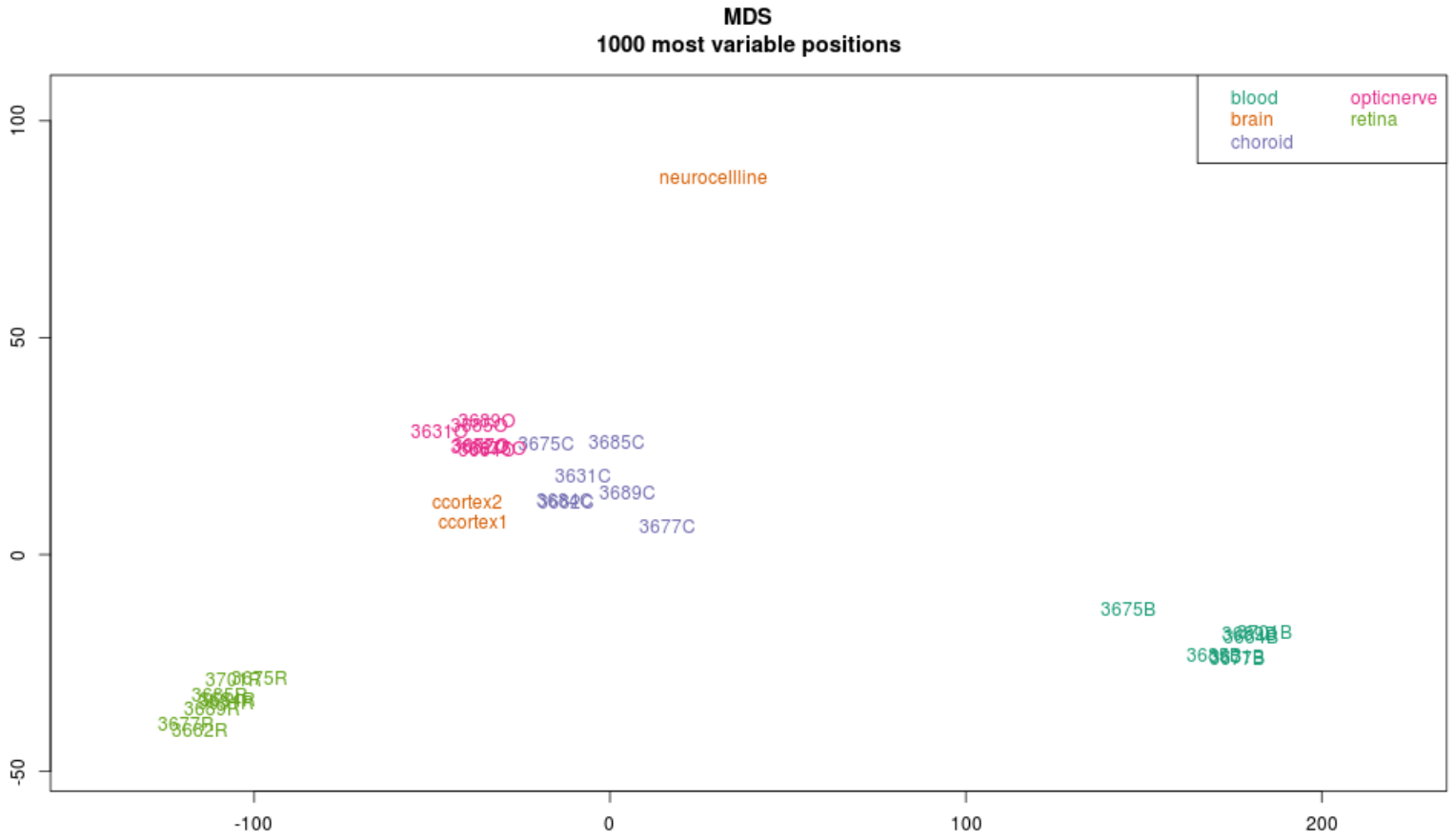
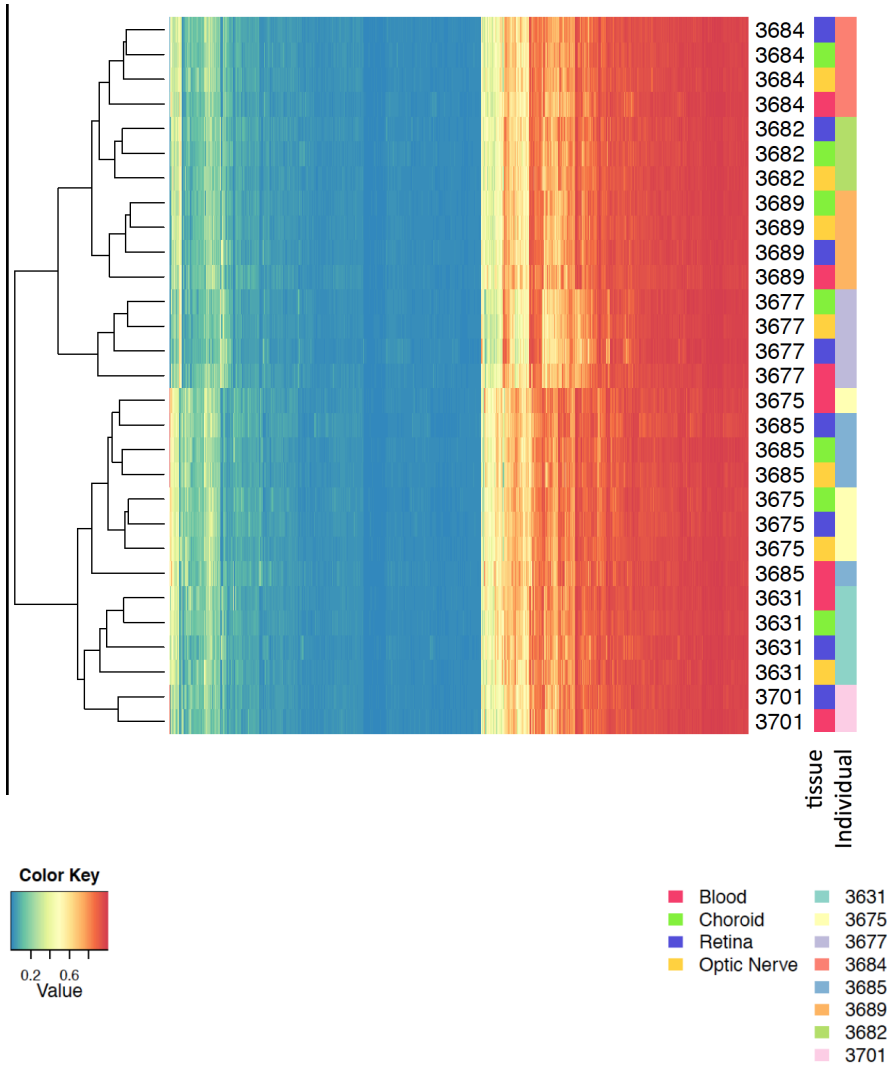
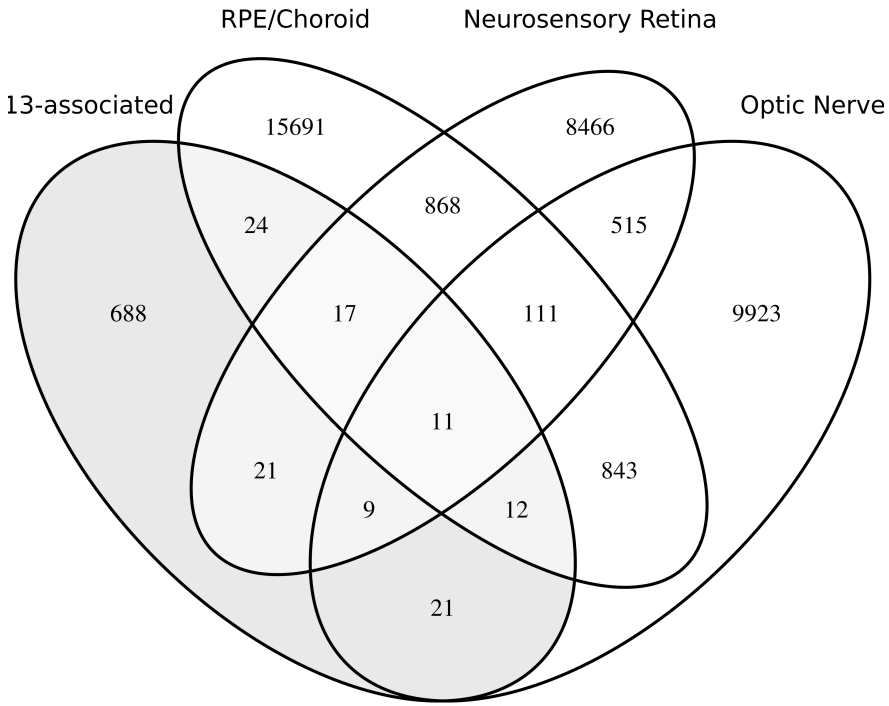


Supp Figure 1

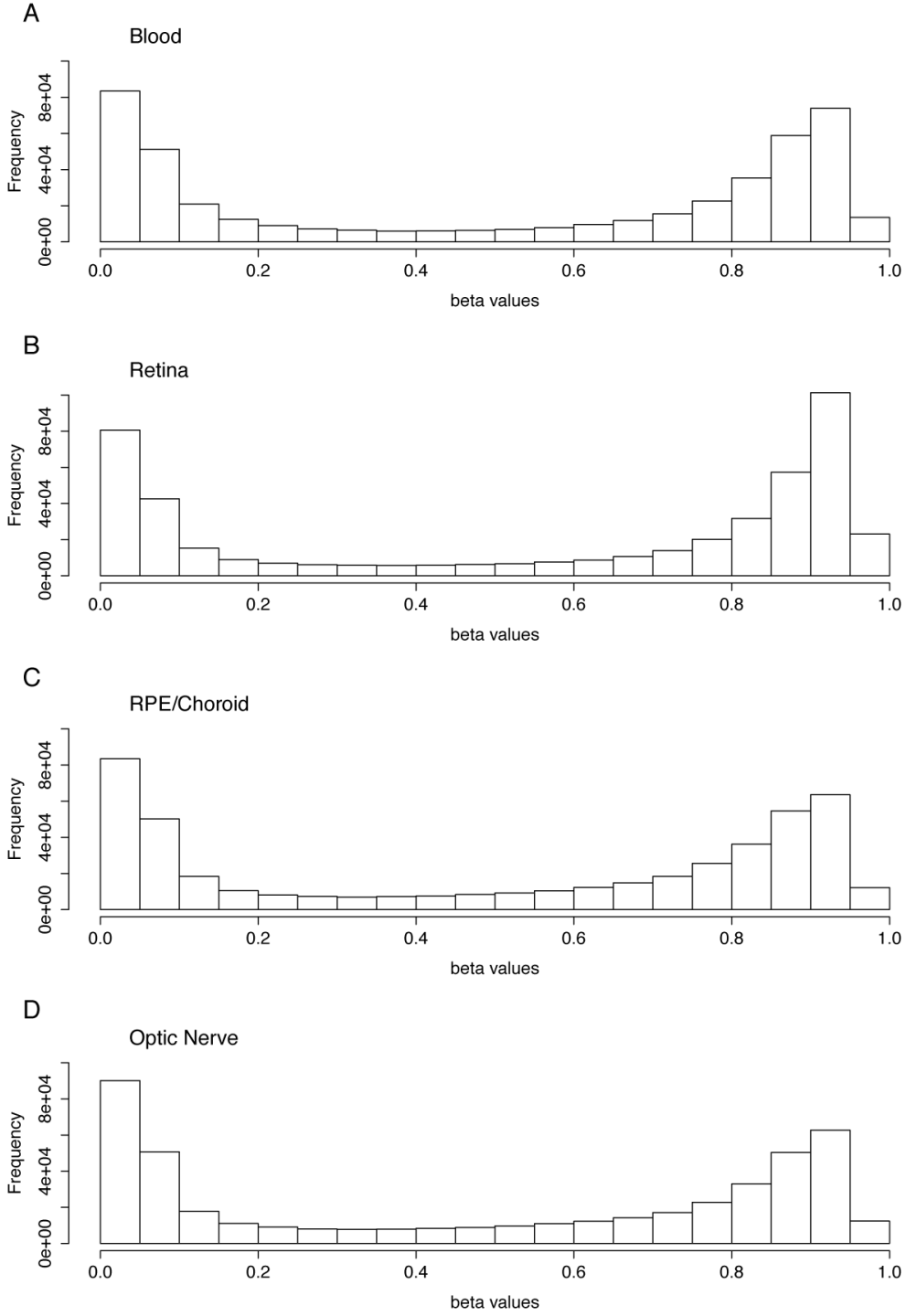
A.



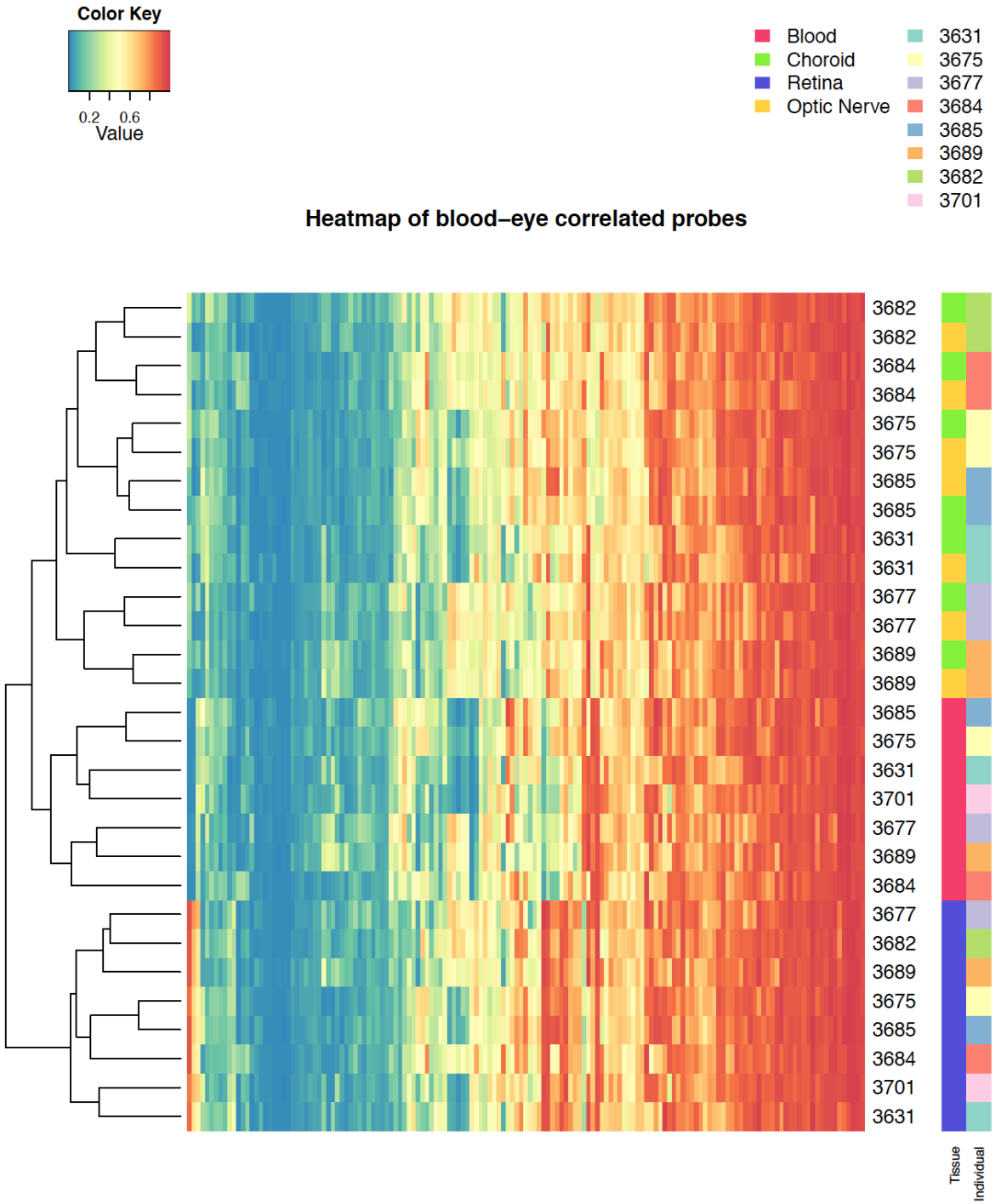
B.



Supp Figure 2



Supp Figure 3



Supp Figure 4

Supplementary Figure 1. Multi Dimensional Scaling plot showing the relationship between samples based on 1000 most variable probes. Whereas RPE/choroid (C) and optic nerve (O) tissue cluster together, with methylation profiles similar to adult cortex tissue, retinal (R) methylation profile is distinct, with blood (B) being least similar to all other tissues. A neuronal cell line is included for comparative purposes.

Supplementary Figure 2. (A) Heatmap of probes associated with PC13 at $|r| > 0.5$, showing some clustering according to individual rather than tissue type. Blue denotes fully unmethylated (0 or 0% methylation), while red fully methylated (1 or 100% methylated) probes. (B) Venn diagram showing the overlap of PC13-associated probes with each of the 3 ocular tissues.

Supplementary Figure 3. Distribution of mean HM450K methylation b-values (in 5% bins) across each tissue tested in the current study. All tisseus show a bimodal distribution. X-axis b-values correspond to methylation levels approximating 0-100%. Y-axis is the frequency of probes within each bin.

Supplementary Figure 4.
Heatmap of 122 probes showing inter-individual variation in blood that show a degree of correlation between blood and all three eye tissues within individuals. Whereas clear inter-individual differences are apparent in the choroid and optic nerve, blood and retina remain clustered by tissue type. Blue denotes fully unmethylated (0 or 0% methylation), while red fully methylated (1 or 100% methylated) probes.

Supplementary Table 1.
Demographic details of samples included in analysis.

ID	Age at Death (years)	PTI (hours)	Cause of Death	Known Co-morbidities	Samples Passing QC			
					Whole Blood	Neurosensory Retina	Choroid/RPE	Optic Nerve
3684	37	3.1	Hanging	Depression, Asthma	X	X	X	X
3675	56	9.3	AMI	Type II Diabetes, Hypercholesterolaemia, Peptic Ulcer Disease	X	X	X	X
3631	58	8.2	AMI	Hypertension, Hypercholesterolaemia, Peptic Ulcer Disease	X	X	X	X
3685	63	11.3	AMI	Type II Diabetes,Hypertension, Hypercholesterolaemia, Asthma	X	X	X	X
3701	62	6.0	SAH	Type II Diabetes,Hypertension, Hypercholesterolaemia, Ischaemic Heart Disease	X	X		
3682	66	9.4	Respiratory Failure	Oesophogeal adenocarcinoma, Type II diabetes		X	X	X
3689	67	9.1	AMI	Prostate cancer	X	X	X	X
3677	76	10.1	AMI	Hypercholesterolaemia	X	X	X	X

Abbreviations: PTI, preservation time interval; AMI, Acute myocardial infarction; SAH, Subarachnoid haemorrhage.

Supplementary Table 3.
Genes linked to probes that variation exclusively associated with individuals at $p < 0.05$ (PC13), which have been previously implicated in eye disease.

Gene	Disease / Trait													Reference
	AMD	Age-related nuclear cataracts	Corneal curvature	PXF	Eye color	Glaucoma	Myopia (pathological)	Optic cup area	VCDR	Syndromic Retinal Dystrophy	RP	LCA	Recessive optic atrophy	
ACBD5										X				1
ADAMTS18										X				2,3
ASB7								X						4
B3GALTL	X													5,6
CACNA1A				X										7
CHEK2								X	X					4,8,9
CPLX2		X												10
DNAJC24						X								11
EIF2AK4			X											12
EXOC2									X					8
EXOSC2										X				13
FBXL17					X									14
GPR125											X			1
HARS										X				15
IQCB1										X		X		16,17
LRRK1			X											18
NOTCH4	X													19
PANK2										X				20-23
PDE2A								X						24
PTPRN2							X							25
TMEM126A													X	26
TOPORS											X			27
TRNT1										X				28,29
TUBGCP4										X				30
WFS1										X				31-33

Abbreviations: AMD, Age-related macular degeneration; PXF, Exfoliation syndrome; VCDR, Vertical cup-disc ratio; RP, Retinitis pigmentosa; LCA, Leber congenital amaurosis;

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