

Supplementary table 5. Complete results of the Pathway-Phenotype Study

A. Results of binary logistic regression analysis for all 7 pathways and the phenotypes: GA, CNV, pseudoregular drusen, and calcified drusen. B. Results of linear regression for all 7 pathways and the phenotypes: drusen area in ETDRS grid and the AREDS Extended Severity Scale.

GA = geographic atrophy, CNV = choroidal neovascularization, OR = odds ratio, CI = confidence interval, ECM = extracellular matrix.

A.

Pathway	Phenotype	Rare variant carriers	Non-carriers	p	OR [95% CI]
Complement	GA	20/36 (55.6%)	507/1391 (36.4%)	0.023	2.17 [1.12, 4.24]
	CNV	22/36 (61.1%)	712/1391 (51.2%)	0.242	1.50 [0.76, 2.96]
	Pseudo-reticular Drusen	5/36 (13.9%)	274/1391 (19.7%)	0.393	0.66 [0.25, 1.71]
	Calcified Drusen	26/36 (72.2%)	578/1391 (41.6%)	4.6*10 ⁻⁴	3.75 [1.79, 7.86]
ECM	GA	25/52 (48.1%)	507/1391 (36.4%)	0.120	1.56 [0.89, 2.71]
	CNV	34/52 (65.4%)	712/1391 (51.2%)	0.062	1.74 [0.97, 3.12]
	Pseudo-reticular Drusen	14/52 (26.9%)	274/1391 (19.7%)	0.230	1.47 [0.78, 2.75]
	Calcified Drusen	23/52 (44.2%)	578/1391 (41.6%)	0.721	1.11 [0.63, 1.94]
Lipids	GA	13/49 (26.5%)	507/1391 (36.4%)	0.135	0.61 [0.32, 1.17]
	CNV	30/49 (61.2%)	712/1391 (51.2%)	0.199	1.47 [0.82, 2.64]
	Pseudo-reticular Drusen	10/49 (20.4%)	274/1391 (19.7%)	0.934	1.03 [0.51, 2.09]
	Calcified Drusen	21/49 (42.6%)	578/1391 (41.6%)	0.854	1.06 [0.59, 1.88]

Cell Survival	GA	12/28 (42.9%)	507/1391 (36.4%)	0.476	1.32 [0.62, 2.81]
	CNV	15/28 (53.6%)	712/1391 (51.2%)	0.792	1.11 [0.52, 2.35]
	Pseudo- reticular Drusen	8/28 (28.6%)	274/1391 (19.7%)	0.245	1.64 [0.71, 3.76]
	Calcified Drusen	13/28 (46.4%)	578/1391 (41.6%)	0.608	1.22 [0.57, 2.58]
Immune System	GA	3/14 (21.4%)	507/1391 (36.4%)	0.225	0.45 [0.13, 1.63]
	CNV	7/14 (50.0%)	712/1391 (51.2%)	0.872	0.92 [0.32, 2.63]
	Pseudo- reticular Drusen	2/14 (14.3%)	274/1391 (19.7%)	0.594	0.66 [0.15, 2.99]
	Calcified Drusen	4/14 (28.6%)	578/1391 (41.6%)	0.317	0.55 [0.17, 1.77]
Metabolism	GA	6/13 (46.2%)	507/1391 (36.4%)	0.523	1.43 [0.48, 4.29]
	CNV	6/13 (46.2%)	712/1391 (51.2%)	0.652	0.78 [0.26, 2.33]
	Pseudo- reticular Drusen	1/13 (7.7%)	274/1391 (19.7%)	0.286	0.33 [0.04, 2.54]
	Calcified Drusen	5/13 (38.5%)	578/1391 (41.6%)	0.737	0.83 [0.27, 2.54]
Unknown/ other	GA	60/126 (47.6%)	507/1391 (36.4%)	0.014	1.58 [1.10, 2.28]
	CNV	76/126 (60.3%)	712/1391 (51.2%)	0.052	1.45 [1.00, 2.10]
	Pseudo- reticular Drusen	27/126 (21.4%)	274/1391 (19.7%)	0.648	1.11 [0.71, 1.73]
	Calcified Drusen	64/126 (50.8%)	578/1391 (41.6%)	0.046	1.45 [1.01, 2.09]

B.

Pathway	Phenotype	p	B [95% CI]
Complement	AREDS extended severity scale	0.283	0.38 [-0.31, 1.07]
	Drusen area within grid	0.708	0.06 [-0.26, 0.39]
ECM	AREDS extended severity scale	0.035	0.62 [0.04, 1.20]
	Drusen area within grid	0.219	0.17 [-0.10, 0.44]
Lipids	AREDS extended severity scale	0.506	0.20 [-0.40, 0.80]
	Drusen area within grid	0.223	-0.18 [-0.46, 0.11]
Cell Survival	AREDS extended severity scale	0.550	0.24 [-0.55, 1.02]
	Drusen area within grid	0.842	-0.04 [-0.41, 0.33]
Immune System	AREDS extended severity scale	0.423	-0.452 [-1.56, 0.66]
	Drusen area within grid	0.930	-0.023 [-0.55, 0.50]
Metabolism	AREDS extended severity scale	0.877	0.09 [-1.06, 1.24]
	Drusen area within grid	0.680	-0.11 [-0.66, 0.43]
Unknown/ other	AREDS extended severity scale	0.004	0.55 [0.17, 0.93]
	Drusen area within grid	0.489	0.06 [-0.12, 0.24]