GENE	POSITION	cDNA change	Aa change	rs ID	MAF cases-ctrls	ExAC	MA	SIFT	POLYPHEN	aa/Aa/AA cases	aa/Aa/AA ctrls	P-VALUE	OR
ABCA7	19:1043103	c.G643A	p.G215S	rs72973581	0.04669-0.07249	0.04316	A	Tolerated	Benign	0/31/301	1/96/579	0.026	0.615
ABCA7	19:1050996	c.G2629A	p.A877T	rs74176364	0.003012-0.01183	0.01692	A	Deleterious	Benign	0/2/330	0/16/660	0.072	0.25
ABCA7	19:1059056	c.G5435A	p.R1812H	rs114782266	0.01506-0.008136	0.01057	A	Tolerated	Benign	0/10/322	0/11/665	0.162	1.87
ABCA7	19:1057343	c.G4795A	p.V1599M	rs117187003	0.006024-0.002219	0.003085	A	Deleterious	Probably damaging	0/4/328	0/3/673	0.226	2.73
ABCA7	19:1047537	c.A2153C	p.N718T	rs3752239	0.01657-0.02448	0.07028	C	Deleterious	Benign	0/11/321	0/33/641	0.325	0.665
ABCA7	19:1043794	c.G1001A	p.R334Q	rs147846250	0.001506-0	0.0001995	A	Tolerated	Benign	0/1/331	0/0/676	0.329	Inf
ABCA7	19:1044619	c.C1091G	p.P364R	rs146982710	0.001506-0	0.0003843	G	Tolerated	Possibly damaging	0/1/331	0/0/676	0.329	Inf
ABCA7	19:1046239	c.C1456G	p.P486A	rs141428162	0.001506-0	0.0003212	G	Deleterious	Possibly damaging	0/1/331	0/0/676	0.329	Inf
ABCA7	19:1047372	c.G2062A	p.A688T	rs376686030	0.001506-0		A	Tolerated	Possibly damaging	0/1/331	0/0/676	0.329	Inf
ABCA7	19:1053521	c.C3414G	p.S1138R	rs1053521	0.001506-0	0.00002865	G	Deleterious	Possibly damaging	0/1/331	0/0/676	0.329	Inf
ABCA7	19:1056372	c.T4460G	p.V1487G	rs200825702	0.001506-0	0.0001245	G	Deleterious	Probably damaging	0/1/331	0/0/676	0.329	inf
ABCA7	19:1056941	c.G4622A	p.C1541Y	rs145632609	0.001506-0	0.00004131	A	Deleterious	Probably damaging	0/1/331	0/0/676	0.329	Inf
ABCA7	19:1056958	c.T4639C	p.S1547P	rs778244634	0.001506-0	0.00000826	C	Deleterious	Probably damaging	0/1/331	0/0/676	0.329	Inf
ABCA7	19:1057366	c.G4818T	p.Q1606H	NOVEL	0.001506-0		T	Deleterious	Probably damaging	0/1/331	0/0/676	0.329	Inf
ABCA7	19:1058655	c.G5188A	p.V1730I	NOVEL	0.001506-0		A	Tolerated	Benign	0/1/331	0/0/676	0.329	inf
ABCA7	19:1044712	c.A1184G	p.H395R	rs3764647	0.0256-0.03333	0.06298	G	Tolerated	Benign	0/17/315	0/45/630	0.403	0.755
ABCA7	19:1043748	c.A955G	p.T319A	rs3752232	0.0256-0.03264	0.06039	G	Tolerated	Benign	0/17/315	0/44/630	0.403	0.77
ABCA7	19:1058176	c.A5057G	p.Q1686R	rs4147918	0.0256-0.0318	0.04785	G	Tolerated	Benign	0/17/315	0/43/633	0.481	0.794
ABCA7	19:1056109	c.C4283T	p.S1428L	rs145232000	0.001506-0.0007396	0.0001994	T	Tolerated	Benign	0/1/331	0/1/675	0.550	2.037
ABCA7	19:1053382	c.T3275G	p.V1092G	rs201213180	0.00303-0.0007452	0.0008056	G	Deleterious	Possibly damaging	1/0/329	0/1/670	0.550	2.034
ABCA7	19:1041922	c.C253A	p.L85M	rs146597357	0-0.0007396	0.0002568	A	Deleterious	Benign	0/0/332	0/1/675	1	0
ABCA7	19:1041950	c.T281C	p.L94P	NOVEL	0-0.0007396		C	Deleterious	Probably damaging	0/0/332	0/1/675	1	0
ABCA7	19:1041971	c.T302G	p.L101R	rs201665195	0.001506-0.001479	0.0006849	G	Deleterious	Possibly damaging	0/1/331	0/2/674	1	1.018

ABCA7	19:1044708	c.G1180C	p.G394R	rs781692277	0-0.0007396	0.000009175	C	Deleterious	Possibly damaging	0/0/332	0/1/675	1	0
ABCA7	19:1046944	c.C1766G	p.A589G	rs144979723	0-0.0007396	0.0007465	G	Tolerated	Possibly damaging	0/0/332	0/1/675	1	0
ABCA7	19:1047169	c.T1859C	p.L620P	rs144852598	0-0.001479	0.0003622	C	Deleterious	Probably damaging	0/0/331	0/2/674	1	0
ABCA7	19:1047336	c.G2026A	p.A676T	rs59851484	0-0.0007396	0.01294	A	Deleterious	Probably damaging	0/0/332	0/1/675	1	0
ABCA7	19:1049312	c.C2428G	p.R810G	rs747154333	0-0.0007396	0.000008437	G	Deleterious	Possibly damaging	0/0/332	0/1/675	1	0
ABCA7	19:1049318	c.C2434A	p.L812M	NOVEL	0-0.0007396		A	Deleterious	Probably damaging	0/0/332	0/1/675	1	0
ABCA7	19:1056126	c.C4300T	p.R1434C	rs137888610	0-0.0007396	0.0001541	T	Tolerated	Possibly damaging	0/0/332	0/1/675	1	0
ABCA7	19:1057056	c.C4737G	p.Y1579X	rs148266574	0-0.0007396	0.0000252	G	NA	NA	0/0/332	0/1/675	1	0
ABCA7	19:1058635	c.C5168T	p.S1723L	rs73505232	0-0.0007396	0.01161	T	Deleterious	Probably damaging	0/0/332	0/1/675	1	0
ABCA7	19:1059029	c.G5408A	p.R1803H	rs143615723	0-0.0007396	0.000168	A	Tolerated	Benign	0/0/332	0/1/675	1	0
ABCA7	19:1063574	c.T5744C	p.L1915P	NOVEL	0-0.0007407		C	Deleterious	Probably damaging	0/0/332	0/1/674	1	0
ABCA7	19:1063651	c.G5821A	p.V1941I	rs151130083	0-0.0007396	0.0004578	A	Tolerated	Benign	0/0/332	0/1/675	1	0
ABCA7	19:1056492	c.G4580C	p.G1527A	rs3752246	0.1767-0.1629	0.159	C	Tolerated	Benign	13/91/227	13/193/466	0.827	1.036
ABCA7	19:1063831	c.G5920T	p.E1974X	NOVEL	0-0.0007396		T	NA	NA	0/0/332	0/1/675	1	0
ABCA7	19:1042809	c.A563G	p.E188G	rs3764645	0.4517-0.4697	0.4838	G	Tolerated	Benign	67/165/99	154/327/195	0.768	0.950
ABCA7	19:1065018	c.G6133T	p.A2045S	rs4147934	0.4613-0.4163	0.268	T	Tolerated	Benign	114/70/139	179/179/287	0.680	1.061
ABCA7	19:1055191	c.G4046A	p.R1349Q	rs3745842	0.2987-0.385	0.4433	A	Tolerated	Benign	38/111/164	119/261/268	0.001	0.641
BIN1	2:127811524	c.C1196T	p.P399L	rs558530329	0.001506-0		T	Deleterious	Benign	0/1/331	0/0/676	0.329	Inf
BIN1	2:127806110	c.G1774T	p.V592F	rs199908147	0-0.001479	0.0000165	T	Deleterious	Probably damaging	0/0/332	0/2/674	1	0
BIN1	2:127808064	c.C1607A	p.T536K	rs773732601	0-0.0007396	0.0000165	T	Deleterious	Possibly damaging	0/0/332	0/1/675	1	0
BIN1	2:127808076	c.C1595T	p.T532M	rs112318500	0-0.0007396	0.009155	A	Deleterious	Possibly damaging	0/0/332	0/1/675	1	0
BIN1	2:127808458	c.T1492C	p.F498L	rs368238742	0-0.0007396	0.00003322	C	Tolerated	Benign	0/0/332	0/1/675	1	0
BIN1	2:127825804	c.C547T	p.P183S	NOVEL	0-0.0007396		T	Deleterious	Probably damaging	0/0/332	0/1/675	1	0
BIN1	2:127808046	c.A1625G	p.K542R	rs138047593	0.00753-0.01109	0.01122	G	Deleterious	Probably damaging	0/5/327	1/13/662	0.629	0.723
BIN1	2:127834212	c.A155G	p.N52S	rs369549551	0.001506-0	0.000008237	G	Tolerated	Probably damaging	0/1/331	0/0/676	0.329	Inf
CD2AP	6:47573971	c.G1488A	p.M496I	rs143297472	0.003012-0.0007396		A	Tolerated	Benign	0/2/330	0/1/675	0.253	4.084

CD2AP	6:47567069	c.A1307G	p.K436R	NOVEL	0.001506-0		G	Deleterious	Probably damaging	0/1/331	0/0/676	0.329	Inf
CD2AP	6:47563608	c.A1120G	p.T374A	rs138727736	0.00753-0.006657		G	Tolerated	Benign	0/5/327	0/9/667	0.782	1.13
CD2AP	6:47512351	c.A329C	p.K110T	NOVEL	0-0.0007396		C	Deleterious	Benign	0/0/332	0/1/675	1	0
CD2AP	6:47541940	c.C682T	p.R228W	rs150851309	0-0.0007396	0	T	Deleterious	Probably damaging	0/0/332	0/1/675	1	0
CD2AP	6:47544775	c.A839G	p.Y280C	rs765702919	0-0.0007396		G	Deleterious	Benign	0/0/332	0/1/675	1	0
CD2AP	6:47547209	c.T992A	p.L331H	rs140188898	0-0.0007396	0	A	Tolerated	Benign	0/0/332	0/1/675	1	0
CD2AP	6:47548605	c.A1014G	p.P338P	NOVEL	0-0.0007396		G	NA	NA	0/0/332	0/1/675	1	0
CD33	19:51728635	c.A199G	p.I67V	rs746818326	0.001506-0	0.00004119	G	Tolerated	Benign	0/1/331	0/0/676	0.329	Inf
CD33	19:51728629	c.G193C	p.A65P	rs115684563	0-0.001479	0.003262	C	Tolerated	Benign	0/0/332	0/2/674	1	0
CD33	19:51728729	c.G293A	p.R98K	rs148118239	0-0.0007396	0.001	A	Tolerated	Benign	0/0/332	0/1/675	1	0
CD33	19:51729594	c.T727C	p.F243L	rs11882250	0-0.0007396	0.01017	C	Tolerated	Benign	0/0/332	0/1/675	1	0
CD33	19:51738465	c.G799A	p.V267I	rs58981829	0-0.0007396	0.01103	A	Tolerated	Benign	0/0/332	0/1/675	1	0
CD33	19:51738920	c.T913C	p.S305P	rs61736475	0.01355-0.01479	0.04688	C	Tolerated	Benign	0/9/323	0/20/656	1	0.914
CD33	19:51728815	c.T379C	p.Y127H	rs146181856	0.001506-0.003704		C	Tolerated	Benign	0/1/331	0/5/670	0.669	0.4
CD33	19:51738917	c.G910A	p.G304R	rs35112940	0.2009-0.2151	0.1603	A	Tolerated	Benign	10/113/208	27/236/411	0.581	0.924
CD33	19:51728477	c.C41T	p.A14V	rs12459419	0.3106-0.3207	0.2939	T	Deleterious	Benign	29/147/154	75/281/316	0.946	1.014
CD33	19:51728641	c.A205G	p.R69G	rs2455069	0.4258-0.4302	0.3577	G	Tolerated	Benign	60/161/109	131/317/225	0.943	1.018
CLU	8:27461872	c.C870G	p.H290Q	NOVEL	0-0.0007396		G	Deleterious	Possibly damaging	0/0/332	0/1/675	1	0
CLU	8:27466474	c.A227C	p.E76A	rs372043736	0-0.0007396	0.00001647	C	Deleterious	Benign	0/0/332	0/1/675	1	0
CLU	8:27457512	c.A949C	p.N317H	rs9331936	0.001506-0	0.01922	C	Deleterious	Probably damaging	0/1/331	0/0/676	0.329	Inf
CLU	8:27462725	c.G545A	p.R182H	rs201670453	0.001506-0	0.000511	A	Tolerated	Benign	0/1/331	0/0/676	0.329	Inf
CLU	8:27462744	c.A526G	p.M176V	NOVEL	0.001506-0		G	Deleterious	Benign	0/1/331	0/0/676	0.329	Inf
CLU	8:27462662	c.C608T	p.T203I	rs41276297	0.001506-0.003698	0.001673	T	Tolerated	Benign	0/1/331	0/5/671	0.669	0.4
CR1	1:207741336	c.C2770G	p.P924A	rs760418677	0.001506-0	0.00007469	G	Tolerated	Possibly damaging	0/1/331	0/0/676	0.329	Inf
CR1	1:207782916	c.A4828T	p.T1610S	rs4844609	0.03313-0.02515	0.0147	T	Tolerated	Benign	1/20/311	0/34/642	0.460	1.27
CR1	1:207679348	c.G221A	p.R74H	rs200913967	0.001506-0.002219	0.0008698	A	Tolerated	Benign	0/1/331	0/3/673	1	0.677

CR1	1:207680071	c.G314A	p.R105H	rs56102840	0-0.0007396	0.00004973	A	Tolerated	Benign	0/0/332	0/1/675	1	0
CR1	1:207680127	c.G370A	p.G124R	rs55962594	0-0.0007396	0.00005806	A	Tolerated	Possibly damaging	0/0/332	0/1/675	1	0
CR1	1:207680154	c.A397G	p.K133E	rs183171969	0-0.0007396	0.0002253	G	Tolerated	Benign	0/0/332	0/1/675	1	0
CR1	1:207739203	c.C2537T	p.S846F	rs199990810	0-0.0007396	0.000365	T	Tolerated	Possibly damaging	0/0/332	0/1/675	1	0
CR1	1:207741193	c.T2627C	p.V876A	rs149099494	0-0.0007396	0.00595	C	Tolerated	Benign	0/0/332	0/1/675	1	0
CR1	1:207751179	c.G3217A	p.A1073T	rs187750583	0-0.0007396	0.0004809	A	Tolerated	Possibly damaging	0/0/332	0/1/675	1	0
CR1	1:207751252	c.T3290C	p.L1097P	rs200111726	0-0.0007407	0.003333	C	Tolerated	Possibly damaging	0/0/332	0/1/674	1	0
CR1	1:207751260	c.A3298G	p.R1100G	rs202070239	0-0.0007407	0.003284	G	Tolerated	Benign	0/0/332	0/1/674	1	0
CR1	1:207760830	c.G4280A	p.R1427H	rs373049995	0-0.0007396	0.0001491	A	Tolerated	Benign	0/0/332	0/1/675	1	0
CR1	1:207760852	c.G4302A	p.M1434I	rs140566582	0-0.001479	0.0006462	A	Tolerated	Benign	0/0/332	0/2/674	1	0
CR1	1:207785022	c.T4946C	p.V1649A	rs541247689	0-0.0007396	0.00004155	C	Tolerated	Benign	0/0/332	0/1/675	1	0
CR1	1:207785099	c.G5023T	p.V1675L	rs202148801	0.003012-0.003698	0.001747	T	Tolerated	Benign	0/2/330	0/5/671	1	0.81
CR1	1:207787763	c.G5240A	p.G1747D	rs200692346	0-0.0007396	0.0007873	A	Deleterious	Benign	0/0/332	0/1/675	1	0
CR1	1:207790017	c.C5409G	p.C1803W	rs749885738	0-0.0007396	0.00003312	G	Deleterious	Probably damaging	0/0/332	0/1/675	1	0
CR1	1:207790110	c.C5502A	p.S1834R	NOVEL	0-0.0007396		A	Deleterious	Probably damaging	0/0/332	0/1/675	1	0
CR1	1:207782856	c.A4768G	p.K1590E	rs17047660	0-0.002219	0.02141	G	Tolerated	Possibly damaging	0/0/332	0/3/673	0.554	0
CR1	1:207782769	c.G4681A	p.V1561M	rs41274768	0.0256-0.02959	0.02487	A	Tolerated	Possibly damaging	0/17/315	1/38/637	0.770	0.88
CR1	1:207791434	c.A5558G	p.K1853R	rs41274770	0.03464-0.02441	0.0153	G	Tolerated	Benign	0/23/309	1/31/644	0.183	1.49
CR1	1:207680157	c.G400A	p.G134R	rs767211812	0.003012-0.0007396	0.00008366	A	Deleterious	Probably damaging	0/2/330	0/1/675	0.253	4.084
CR1	1:207680070	c.C313T	p.R105C	rs11587944	0.009036-0.01479	0.007601	T	Tolerated	Possibly damaging	0/6/326	1/18/657	0.395	0.636
CR1	1:207782889	c.A4801G	p.R1601G	rs17047661	0.001506-0.004438	0.05483	G	Tolerated	Benign	0/1/331	0/6/670	0.436	0.33
CR1	1:207760772	c.A4222G	p.T1408A	rs61734514	0.03464-0.03107	0.01843	G	Tolerated	Benign	1/21/310	1/40/635	0.782	1.099
CR1	1:207782707	c.A4619G	p.N1540S	rs17259045	0.1099-0.1095	0.08897	G	Tolerated	Benign	4/65/263	8/132/536	1	1
CR1	1:207795320	c.A5905G	p.T1969A	rs2296160	0.2078-0.1711	0.1841	G	Tolerated	Benign	22/94/216	17/197/461	0.317	1.15
CR1	1:207782931	c.A4843G	p.I1615V	rs6691117	0.2274-0.2101	0.3341	G	Tolerated	Benign	17/117/198	33/218/425	0.334	1.14

CR1	1:207760773	c.C4223T	p.T1408M	rs3737002	0.2831-0.2911	0.275	T	Tolerated	Possibly damaging	26/136/170	54/285/336	0.687	0.944
CR1	1:207790088	c.C5480G	p.P1827R	rs3811381	0.1955-0.1748	0.2403	G	Tolerated	Benign	13/103/214	24/188/463	0.251	1.18
CR1	1:207753621	c.A3623G	p.H1208R	rs2274567	0.1973-0.1778	0.251	G	Tolerated	Possibly damaging	13/105/214	26/187/459	0.225	1.18
EPHA1	7:143095907	c.G1123A	p.G375S	rs149370167	0.001506-0	0.0001187	A	Tolerated	Benign	0/1/331	0/0/676	0.329	Inf
EPHA1	7:143092269	c.C2090T	p.P697L	rs34372369	0.04669-0.04882	0.04929	T	Tolerated	Possibly damaging	2/27/303	3/60/613	0.816	0.931
EPHA1	7:143088576	c.T2905C	p.C969R	rs61732993	0.001506-0.002219	0.0003652	C	Tolerated	Possibly damaging	0/1/331	0/3/673	1	0.677
EPHA1	7:143088779	c.G2786A	p.R929H	rs201365734	0-0.0007396	0.0002313	A	Tolerated	Possibly damaging	0/0/332	0/1/675	1	0
EPHA1	7:143095849	c.C1181T	p.P394L	rs140236236	0-0.0007396	0.0003166	T	Deleterious	Probably damaging	0/0/332	0/1/675	1	0
EPHA1	7:143095979	c.C1051T	p.R351C	rs56006153	0-0.0007396	0.0001114	T	Deleterious	Benign	0/0/332	0/1/675	1	0
EPHA1	7:143096369	c.C973T	p.P325S	NOVEL	0-0.0007396		T	Tolerated	Benign	0/0/332	0/1/675	1	0
EPHA1	7:143096809	c.T770G	p.V257G	rs201380861	0-0.0007418		G	Deleterious	Possibly damaging	0/0/329	0/1/673	1	0
EPHA1	7:143098598	c.A251G	p.N84S	rs142191815	0-0.0007396	0.0002481	G	Tolerated	Benign	0/0/332	0/1/675	1	0
EPHA1	7:143098605	c.C244T	p.R82C	rs74721927	0-0.0007396	0.00002481	T	Deleterious	Possibly damaging	0/0/332	0/1/675	1	0
EPHA1	7:143105828	c.G71A	p.R24H	rs79587607	0.003012-0.003704		A	Tolerated	Benign	0/2/330	1/3/671	1	1.016
EPHA1	7:143088584	c.G2897A	p.R966H	rs139482378	0.001506-0.0007396	0.0006136	A	Deleterious	Probably damaging	0/1/331	0/1/675	0.550	2.037
EPHA1	7:143095153	c.G1475A	p.R492Q	rs11768549	0.0256-0.01479	0.0121	A	Tolerated	Benign	0/17/315	1/18/657	0.071	1.864
EPHA1	7:143096020	c.G1010A	p.R337Q	rs201581948	0.001506-0	0.000357	A	Tolerated	Benign	0/1/331	0/0/676	0.329	Inf
EPHA1	7:143088867	c.A2698G	p.M900V	rs6967117	0.06949-0.0638	0.0634	C	Tolerated	Benign	4/38/289	3/80/591	0.919	1.031
EPHA1	7:143097100	c.T479C	p.V160A	rs149370167	0.07553-0.06899		G	Tolerated	Benign	3/44/284	2/89/583	0.770	1.6
MS4A6A	11:59949058	c.T143C	p.I48T	rs61742546	0.02711-0.02885	0.01537	C	Deleterious	Possibly damaging	0/18/314	0/39/637	0.885	0.936
MS4A6A	11:59940599	c.A553T	p.T185S	rs7232	0.3313-0.3741	0.3131	A	Deleterious	Benign	36/148/148	103/299/273	0.221	0.844
MS4A6A	11:59940532	c.G620A	p.R207Q	rs146398167	0.001506-0	0.00004118	A	Tolerated	Benign	0/1/331	0/0/676	0.329	Inf
PICALM	11:85685839	c.G1835T	p.S612I	rs370710573	0-0.0007396	0.00004119	T	Deleterious	Benign	0/0/332	0/1/675	1	0
PICALM	11:85687719	c.C1765G	p.P589A	rs147556602	0-0.0007396	0.0002729	G	Tolerated	Benign	0/0/332	0/1/675	1	0
PICALM	11:85707896	c.G1231C	p.A411P	rs34013602	0.001506-0.002219	0.001533	C	Tolerated	Benign	0/1/331	0/3/673	1	0.677

PICALM	11:85707933	c.G1194T	p.Q398H	rs372958249	0.001506-0	0.000008246	T			0/1/331	0/0/676	0.329	Inf
PICALM	11:85701307	c.A1373G	p.H458R	rs117411388	0.001506-0.0007396	0.0007449	G	Tolerated	Benign	0/1/331	0/1/675	0.550	2.037
PICALM	11:85779721	c.C102G	p.I34M	rs146840505	0.00303-0.002219	0.001638	G	Tolerated	Benign	0/2/328	0/3/673	0.665	1.36

Table S1. Common, low frequency and rare coding variants detected in our cohort. Position is in hg19/GRCh37. MAF, minor allele frequency; OR, odds ratio; Inf, infinity. Highlighted in grey and blue, singletons and common coding variants, respectively. These variants have been excluded from the study. If we would have included also the common coding variants (16 variants) in the single-variants based analysis, the p-value for the statistical significance would have been $p<8.9x10^{-4}$ (0.05/56 coding variants).

GENE	CHR	BP1	BP2	KB	N SNPS	SNPS
CR1	1	207753621	207795320	41.7	6	1:207753621|1:207760773|1:207782707|1:207782931|1:207790088|1:207795320
CR1	1	207812791	207813601	0.811	3	1:207812791|1:207813556|1:207813601
CR1	1	207814451	207872595	58.145	7	1:207814451|1:207814835|1:207850879|1:207851554|1:207851611|1:207857254|1:207872595
BIN1	2	127816632	127826533	9.902	2	2:127816632|2:127826533
CD2A6	6	47594002	47594722	0.721	2	6:47594002|6:47594722
EPHA1	7	143088085	143088526	0.442	2	7:143088085|7:143088526
EPHA1	7	143088823	143088867	0.045	2	7:143088823|7:143088867
CLU	8	27454682	27455442	0.761	2	8:27454682|8:27455442
CLU	8	27462481	27468862	6.382	2	8:27462481|8:27468862
MS4A6A	11	59940599	59945745	5.147	2	11:59940599|11:59945745
PICALM	11	85627108	85630837	3.73	3	11:85627108|11:85630411|11:85630837
ABCA7	19	1038871	1042809	3.939	5	19:1038871|19:1038893|19:1038995|19:1041352|19:1042809
ABCA7	19	1051214	1052005	0.792	2	19:1051214|19:1052005
ABCA7	19	1054060	1056065	2.006	3	19:1054060|19:1055191**|19:1056065
ABCA7	19	1056492	1068738	12.247	7	19:1056492*|19:1064193|19:1065018|19:1065044|19:1065563|19:1068734|19:1068738
CD33	19	51728477	51738917	10.441	3	19:51728477|19:51728641|19:51738917

Table S2. **Common haplotype blocks (Minor allele frequency >0.05) identified in our cohort**. CHR, chromosome; BP, base pair; KB, kilobases; N, number; SNPS, single nucleotide polymorphisms. Position is in hg19/GRCh37.*GWAS hit (rs3752246). **Common coding variant (rs3745842), nominal significant in our cohort.

Variants in the main GWAS genes (NIH-UCL series)

CTRLS ID	*ABCA7*	*BIN1*	*CD2AP*	*CD33*	*CLU*	*CR1*	*EPHA1*	*MS4A6A*	*PICALM*
019_11	G215S					T1408A			
033-11	G215S, R810G								
92-32						R105H, T1408A			
97-45	G215S, A877T					R74H		I48T	
C04_99	Q1686R			S305P					
C07_00	G215S							I48T	
C07_97		P183S				T1408A			
C09_97						K1853R		I48T	
C15_94						T1408A	P697L		
C19_93	G215S	K542R	L331H						
C33_93	G215S					T1408A			
N168	G215S, V1599M								
N176	Q1686R						P697L		
N181						V1561M		I48T	S612I
N183						R105H, V1561M			
N188						K1853R,	R492Q		
P23_07						T1408A	P697L		
SH-01-31	N718T, Q1686R				Q1686R				
SH-02-12	Q1686R					K1853R			
SH-04-19	N718T, Q1686R								
SH-06-05						V1561M	P697L		
UMARY-5088	G215S						P697L		

Table S3a. Cases carrying multiple low-frequency and rare variants in the GWAS loci studied, in the NIH-UCL cohort.

	Variants in the main GWAS genes (NIH-UCL series)								
CTRLS ID	***ABCA7***	***BIN1***	***CD2AP***	***CD33***	***CLU***	***CR1***	***EPHA1***	***MS4A6A***	***PICALM***
019_11	G215S					T1408A			
033-11	G215S, R810G								
92-32						R105H, T1408A			
97-45	G215S, A877T					R74H		I48T	
C04_99	Q1686R			S305P					
C07_00	G215S							I48T	
C07_97		P183S				T1408A			
C09_97						K1853R		I48T	
C15_94						T1408A	P697L		
C19_93	G215S	K542R	L331H						
C33_93	G215S					T1408A			
N168	G215S, V1599M								
N176	Q1686R						P697L		
N181						V1561M		I48T	S612I
N183						R105H, V1561M			
N188						K1853R	R492Q		
P23_07						T1408A	P697L		
SH-01-31	N718T, Q1686R				Q1686R				
SH-02-12	Q1686R					K1853R			
SH-04-19	N718T, Q1686R								
SH-06-05						V1561M	P697L		
UMARY-5088	G215S						P697L		

Table S3b. Controls carrying multiple low-frequency and rare variants in the GWAS loci studied, in the NIH-UCL cohort.

GENE	TRANSCRIPT	TOTAL VARIANT IN OUR COHORT	RELATIVE FREQ. OF TOTAL VARIANTS IN OUR COHORT	TOTAL VARIANT IN EVS IN European-American	RELATIVE FREQ. OF TOTAL VARIANTS IN EVS IN European-American
ABCA7	NM_019112	72/1008	0.106	369/4300	0.085
CD2AP	NM_012120	20/1008	0.029	87/4300	0.020
MS4A6A	NM_152851	11/1008	0.016	41/4300	0.0095
CR1	NM_000651	72/1008	0.106	170/4300	0.039
BIN1	NM_139343	27/1008	0.026	117/4300	0.027
PICALM	NM_007166	19/1008	0.018	106/4300	0.024
EPHA1	NM_005232	30/1008	0.029	167/4300	0.038
CLU	NM_001831	29/1008	0.028	75/4300	0.017
CD33	NM_001772	13/1008	0.012	63/4300	0.014

Table S4. **Relative frequency of total variants in the 9 AD GWAS loci in our cohort and EVS**. Freq., frequency; EVS, exome variant server.

Gene	Transcript	Kbps of coding sequence	Relative freq coding variants (coding variants/kbps of coding sequence)	Relative freq rare low freq coding variants (low frequency and rare coding variants/kbps of coding sequence)	relative frequency of damaging variants (damaging variants/kbps of coding sequence)
ABCA7	NM_019112	6.441	6.21 (40/6.441)	5.27 (34/6.44)	3.72 (24/6.44)
CD2AP	NM_012120	1.920	3.64 (7/1.92)	3.64 (7/1.92)	2.08 (4/1.92)
MS4A6A	NM_152851	0.538	5.57 (3/0.538)	3.71 (2/0.538)	1.85 (1/0.538)
CR1	NM_000651	7.470	4.14 (31/7.47)	3.21 (24/7.47)	1.87 (14/7.47)
BIN1	NM_139343	1.783	4.48 (8/1.78)	4.49 (8/1.783)	3.92 (7/1.783)
PICALM	NM_007166	1.960	3.06 (6/1.96)	3.06 (6/1.96)	0.51 (1/1.96)
EPHA1	NM_005232	2.932	5.45 (16/2.93)	5.11 (15/2.932)	2.72 (8/2.93)
CLU	NM_001831	1.350	4.44 (6/1.35)	4.44 (6/1.35)	2.96 (4/1.35)
CD33	NM_001772	1.093	9.14 (10/1.093)	7.31 (8/1.093)	0.91 (1/1.093)

Table S5. Relative frequency of coding and damaging variants in the 9 AD GWAS loci in our cohort. Freq., frequency; kbps, kilobase pairs.

Position	MA	RS ID	Aa change	aa/Aa/AA cases	aa/Aa/AA controls	ExAC MAF	P-Value*	OR
19:1047002	G	rs3752234	p.A608A	57/95/163	148/254/264	0.5547	0.0004289	0.612
19:1055191	A	rs3745842	p.R1349Q	38/111/164	119/261/268	0.4433	0.001448	0.641
19:1061804	C	rs78320196	p.N1829N	0/17/315	1/65/608	0.05847	0.01049	0.497
19:1053524	G	rs3752241	p.L1139L	5/71/253	12/192/467	0.2525	0.01647	0.687
19:1041347	C	rs182233998	c.7-7T>C	0/5/327	0/30/646	0.01511	0.0166	0.329
19:1043103	A	rs72973581	p.G215S	0/31/301	1/96/579	0.04316	0.02665	0.615
19:1065044	T	rs4147935	p.G2053G	30/102/193	72/244/349	0.4049	0.04164	0.755
19:1050996	A	rs74176364	p.A877T	0/2/330	0/16/660	0.01692	0.07264	0.25
19:1059056	A	rs114782266	p.R1812H	0/10/322	0/11/665	0.01057	0.1625	1.87
19:1064193	G	rs4147930	p.L1995L	19/115/191	34/275/363	0.7303	0.1739	0.824
19:1041352	G	rs3752229	c.-7-2A>G	2/36/294	1/59/616	0.06973	0.2136	1.326
19:1057343	A	rs117187003	p.V1599M	0/4/328	0/3/673	0.003085	0.2269	2.73
19:1041909	T	rs144546979	p.T80T	0/2/330	0/1/675	0.000144	0.2538	4.08
19:1052086	A	rs61576791	p.T1036T	0/2/330	0/1/675	0.01736	0.2538	4.084
19:1065563	G	rs2242437	3'UTR	18/119/190	36/270/363	0.395	0.2774	0.855
19:1047537	C	rs3752239	p.N718T	0/11/321	0/33/641	0.07028	0.3251	0.665
19:1043794	A	rs147846250	p.R334Q	0/1/331	0/0/676	0.0002	0.329	Inf
19:1044619	G	rs146982710	p.P364R	0/1/331	0/0/676	0.000384	0.329	Inf
19:1046239	G	rs141428162	p.P486A	0/1/331	0/0/676	0.000321	0.3294	Inf
19:1047372	A	NOVEL	p.A688T	0/1/331	0/0/676	NA	0.3294	Inf
19:1053521	G	NOVEL	p.S1138R	0/1/331	0/0/676	2.87E-05	0.3294	Inf
19:1056372	G	NA	p.V1487G	0/1/331	0/0/676	0.000125	0.3294	inf
19:1056941	A	rs145632609	p.C1541Y	0/1/331	0/0/676	4.13E-05	0.3294	Inf
19:1056958	C	NA	p.S1547P	0/1/331	0/0/676	8.26E-06	0.3294	Inf
19:1057366	T	NOVEL	p.Q1606H	0/1/331	0/0/676	NA	0.3294	Inf
19:1058655	A	NOVEL	p.V1730I	0/1/331	0/0/676	NA	0.3294	inf
19:1044712	G	rs3764647	p.H395R	0/17/315	0/45/630	0.06298	0.4032	0.755
19:1043748	G	rs3752232	p.T319A	0/17/315	0/44/630	0.06039	0.4035	0.77

19:1058176	G	rs4147918	p.Q1686R	0/17/315	0/43/633	0.04785	0.4812	0.794
19:1049269	A	rs4147914	p.L795L	6/65/255	12/147/511	0.1781	0.5221	0.894
19:1056109	T	rs145232000	p.S1428L	0/1/331	0/1/675	0.000199	0.5505	2.037
19:1056918	T	NA	p.S1533S	0/1/331	0/1/675	0.000925	0.5505	2.037
19:1053382	G	NA	p.V1092G	1/0/329	0/1/670	0.000806	0.5509	2.034
19:1062192	C	rs4147921	A1864A	0/16/315	0/40/635	0.04819	0.5592	0.8
19:1043747	T	rs149023827	p.L318L	0/3/329	0/10/665	0.001779	0.5623	0.6
19:1065018	T	rs4147934	p.A2045S	114/70/139	179/179/287	0.7317	0.6808	1.061
19:1041852	T	rs3764644	p.L61L	0/16/315	0/36/631	0.05701	0.7641	0.89
19:1042809	G	rs3764645	p.E188G	67/165/99	154/327/195	0.4838	0.768	0.9500902
19:1051214	G	rs3752240	p.V915V	42/157/132	86/313/275	0.3361	0.785	1.039
19:1056492	C	rs3752246	p.G1527A	13/91/227	13/193/466	0.16	0.8276	1.036
19:1052005	T	rs3764652	p.A1009A	61/162/104	130/330/210	0.4256	0.8848	0.978
19:1041289	T	NOVEL	c.231-12C>A	0/0/332	0/1/675	NA	1	0
19:1041922	A	NOVEL	p.L85M	0/0/332	0/1/675	0.000257	1	0
19:1041950	C	NOVEL	p.L94P	0/0/332	0/1/675	NA	1	0
19:1041951	A	NOVEL	p.L94L	0/0/332	0/1/675	NA	1	0
19:1041971	G	NA	p.L101R	0/1/331	0/2/674	0.000685	1	1.018
19:1043350	T	NA	p.L270L	0/0/332	0/1/675	0.000906	1	0
19:1044692	T	NA	p.D388D	0/0/332	0/1/675	5.28E-05	1	0
19:1044708	C	NA	p.G394R	0/0/332	0/1/675	9.18E-06	1	0
19:1046944	G	rs144979723	p.A589G	0/0/332	0/1/675	0.000747	1	0
19:1047169	C	rs144852598	p.L620P	0/0/331	0/2/674	0.000362	1	0
19:1047336	A	rs59851484	p.A676T	0/0/332	0/1/675	0.01294	1	0
19:1048982	T	rs9282560	p.C786C	0/1/331	0/2/674	0.001928	1	1.018
19:1049305	A	rs4147915	p.V807V	3/74/248	24/133/508	0.1792	1	1
19:1049312	G	NA	p.R810C	0/0/332	0/1/675	8.44E-06	1	0
19:1049318	A	NOVEL	p.L812M	0/0/332	0/1/675	NA	1	0
19:1051944	A	rs139214131	p.R989H	0/0/332	0/2/674	0.00068	1	0
19:1052017	A	NOVEL	p.G1013G	0/0/332	0/1/675	0.000204	1	0
19:1054060	G	rs3752243	p.L1176L	54/173/105	127/334/212	0.4723	1	0.99

19:1054791	G	NOVEL	p.P1288P	0/0/332	0/1/675	NA	1	0
19:1055249	A	NA	p.P1368P	0/0/332	0/1/675	8.79E-05	1	0
19:1056065	G	rs881768	p.R1413R	54/161/107	128/317/221	0.4451	1	0.99
19:1056110	A	NA	p.S1428S	0/0/332	0/1/675	0.000121	1	0
19:1056126	T	rs137888610	p.R1434C	0/0/332	0/1/675	0.000154	1	0
19:1056421	A	rs113711363	p.P1503P	0/0/332	0/1/675	0.00593	1	0
19:1057047	A	NA	p.P1576P	0/0/332	0/1/675	3.34E-05	1	0
19:1057056	G	rs148266574	p.Y1579X	0/0/332	0/1/675	2.52E-05	1	0
19:1058635	T	rs73505232	p.S1723L	0/0/332	0/1/675	0.01161	1	0
19:1059029	A	rs143615723	p.R1803H	0/0/332	0/1/675	0.000168	1	0
19:1063574	C	NOVEL	p.L1915P	0/0/332	0/1/674	NA	1	0
19:1063651	A	rs151130083	p.V1941I	0/0/332	0/1/675	0.000458	1	0
19:1063831	T	NOVEL	p.E1974X	0/0/332	0/1/675	NA	1	0

Table S6. Collection of all the variants included in the *ABCA7* gene-based analysis. Position is in hg19/GRCh37. MAF, minor allele frequency; OR, odds ratio; Inf, infinity.*non corrected. In light blue are the nominal significant variants.

GENE	Position	rsID	cDNA change	PROTEIN VARIATION	EFFECT	AD CARRIER	CONTROL CARRIER	MAF cases-controls (%)	MAF in EVS European-American (%)	MAF in ExAC European-non Finnish (%)	P-value	OR
ABCA7	19:1057056	rs148266574	c.C4737G	p.Y1579X	stop gained	0/0/332	0/1/675	0-0.74	0.0116	4.592e-7	1	0
ABCA7	19:1063831	NOVEL	c.G5920T	p.E1974X	stop gained	0/0/332	0/1/675	0-0.74	NA	NA	1	0
ABCA7	19:1041347	rs182233998	c.7-7T>C	NA	near splice site	0/5/327	0/30/646	0.753-2.21	1.61	1.67	0.0166	0.329
ABCA7	19:1041352	rs3752229	c.7-2 A>G	NA	splice acceptor	2/36/294	1/59/616	6-4.51	4.732	4.472	0.2136	1.326
ABCA7	19:1041289	NOVEL	c.231-12C>A	NA	near splice site	0/0/332	0/1/675	0-0.74	NA	NA	1	0

Table S7. **Loss of function mutations in *ABCA7* detected in our discovery set**. Position is in hg19/GRCh37. MAF, minor allele frequency; EVS, exome variant server, OR, odds ratio.

GENE	POSITION	cDNA change	Aa change	rs ID	MAF cases-ctrls	MA	SIFT	POLYPHEN	aa/Aa/AA cases	aa/Aa/AA ctrls	P-VALUE	OR	
ABCA7	19:1057366	c.G4818T	p.Q1606H	NOVEL	0.001506-0	T	Deleterious	Probably damaging	0/1/331	0/0/676	0,329	Inf	WES
ABCA7	19:1058655	c.G5188A	p.V1730I	NOVEL	0.001506-0	A	Tolerated	Benign	0/1/331	0/0/676	0,329	inf	WES
ABCA7	19:1041950	c.T281C	p.L94P	NOVEL	0-0.0007396	C	Deleterious	Probably damaging	0/0/332	0/1/675	1	0	WES
ABCA7	19:1049318	c.C2434A	p.L812M	NOVEL	0-0.0007396	A	Deleterious	Probably damaging	0/0/332	0/1/675	1	0	WES
ABCA7	19:1063574	c.T5744C	p.L1915P	NOVEL	0-0.0007407	C	Deleterious	Probably damaging	0/0/332	0/1/674	1	0	WGS
ABCA7	19:1063831	c.G5920T	p.E1974X	NOVEL	0-0.0007396	T	NA	NA	0/0/332	0/1/675	1	0	WGS
BIN1	2:127825804	c.C547T	p.P183S	NOVEL	0-0.0007396	T	Deleterious	Probably damaging	0/0/332	0/1/675	1	0	WES
CD2AP	6:47567069	c.A1307G	p.K436R	NOVEL	0.001506-0	G	Deleterious	Probably damaging	0/1/331	0/0/676	0,329	Inf	WES
CD2AP	6:47512351	c.A329C	p.K110T	NOVEL	0-0.0007396	C	Deleterious	Benign	0/0/332	0/1/675	1	0	WES
CD2AP	6:47548605	c.A1014G	p.P338P	NOVEL	0-0.0007396	G	NA	NA	0/0/332	0/1/675	1	0	WES
CLU	8:27461872	c.C870G	p.H290Q	NOVEL	0-0.0007396	G	Deleterious	Possibly damaging	0/0/332	0/1/675	1	0	WES
CLU	8:27462744	c.A526G	p.M176V	NOVEL	0.001506-0	G	Deleterious	Benign	0/1/331	0/0/676	0,329	Inf	WES
CR1	1:207790110	c.C5502A	p.S1834R	NOVEL	0-0.0007396	A	Deleterious	Probably damaging	0/0/332	0/1/675	1	0	WGS
EPHA1	7:143096369	c.C973T	p.P325S	NOVEL	0-0.0007396	T	Tolerated	Benign	0/0/332	0/1/675	1	0	WGS

Table S8. *ABCA7* novel coding variants detected in our cohort. Position is in hg19/GRCh37. MA, minor allele; WES, whole exome sequencing; WGS; whole genome sequencing; OR, odds ratio; Inf, infinity.

GENE	Position	rsID	cDNA change	PROTEIN VARIATION	EFFECT	AD CARRIER (n = 127)	CONTROLS CARRIER (n = 204)	MAF cases-controls (%)	MAF in EVS European-American (%)	MAF in ExAC European-non Finnish (%)	P-value	OR	95% CI	Comment
ABCA7	19:1055907	NA	c.4208del1	p.1402delT	frameshift	1	1	0.39-0.24	0.0969	0.163	1	1.6	0.02-126.9	reported in the Belgian and Islandic cohort but not associated to LOAD (1) (2)
ABCA7	19:1057946	NA	c.4914_4916del3	p.1638delCTT	inframe deletion	0	1	0-0.24	0.0242	0	1	0	0.00-62.58	
ABCA7	19:1058711	NA	c.5475del6	p.1749delCTACTG	frameshift	0	1	0-0.24	NA	NA	1.00	0.00	0.00-62.58	

Table S9. **Indels detected in *ABCA7* detected in the NIH-UCL cohort**. Position is in hg19/GRCh37. MAF, minor allele frequency; OR, odds ratio; CI, confidential interval; del, deletion; TOT, total.

GENE	Position	rsID	cDNA change	PROTEIN VARIATION	Comment
ABCA7	19:1058727	rs556286113	c.C5260T	p.R1754X	
ABCA7	19:1051178	rs200408449	c.G2709A	p.W903X	
ABCA7	19:1047631	NA	c.G2247A	p.W749X	
ABCA7	19:1056244	rs113809142	c.4416+2T>G	NA	associated with LOAD Islandic population (2), reported in the Belgian population but not associated to LOAD (1)

Table S10. **Nonsense mutations in *ABCA7* detected in our cohort and eliminated by the QC filter**. Position is in hg19/GRCh37.

GENE	TRANSCRIPT	POSITION	MA	Aa change	Rs ID	ExAC MAF(%)	POLYPHEN	GERP* score	Grantham** score	P-value	OR (95% CI)	Disease	Ref.
IL23R	NM_144701.2	1:67635211	G>A	p.R86Q	rs76575803	0.2776	Benign	-2.52	43	0.010	0.40 (0.000-1.031)	CD	(3)
IL23R	NM_144701.2	1:67648596	G>A	p.G149R	rs76418789	0.7084	Probably-damaging	5.24	125	$1.46x10^{-3}$	0.335 (0.000–0.843)	CD, UL	(3)(4)
IL23R	NM_144701.2	1:67705900	G>A	p.V362I	rs41313262	1.168	Benign	-6.22	29	$2.89x10^{-4}$	0.567 (0.000–0.821)	CD, UL	(3)(4)
IL23R	NM_144701.2	1:67705958	G>A	p.R381Q	rs11209026	4.221	Probably-damaging	5.19	43	$<1.00x10^{-6}$	0.363 (0.000–0.452)	CD, UL	(3)
IFIH1	NM_022168.3	2:163124637	T>C	I923V	rs35667974	1.156	Probably-damaging	5.13	29	$2.1x10^{-16}$	0.51 (0.43 – 0.61)	T1D	(5)
IFIH1	NM_022168.3	2:163134090	C>A	E627X	rs35744605	0.0008288	NA	2.87	NA	$1.3x10^{-3}$	0.69 (0.52 – 0.91)	T1D	(5)
G6PC2	NM_021176.2	2:169764176	G>C	p.V219L	rs492594	48.65	Benign	3.06	32	NA	NA	T2D	(6)
TMEM106B	NM_001134232.1	7:12269417	C>G	p.T185S	rs3173615	46.16	Benign	5.36	58	NA	NA	FTLD	(7)
ABCA7	NM_019112	19:1043103	G>A	p.G215S	rs72973581	4.31	Benign	-5.86	56	$6x10^{-4}$	0.57 (0.41-0.80)		

Table S11. **Protective variants reported at the GWAS loci**. Position is in hg19/GRCh37. MAF, minor allele frequency; Aa, amino acid; OR, odds ratio; Ref., reference; CD, Crohn's disease; UL, ulcerative colitis; FTLD, frontotemporal lobar degeneration. .*GERP score >5 indicates high conservation among different species.**Grantham score < 50 indicates an amino acid substitution that does not importantly alter the protein sequence.

GENE	TRANSCRIPT	POSITION	MA	Aa change	rs ID	ExAC MAF(%)	POLYPHEN	GERP* score	Grantham** score	P-value	OR	EFFECT	Ref.
ABCA1	NM_005502.3	9:107599376	A>G	V399A	rs9282543	0.3520	Benign	5.7	64	0.6273	0.38	Potential protective factor for AD	(8)
ABCA1	NM_005502.3	9:107589255	C>T	V771M	rs2066718	5.11	Benign	4.55	21	0.1495	0.43	Potential protective factor for AD	(8)
ABCA1	NM_005502.3	9:104819652	G>A	P1059S	rs371168450	NA	Probably damaging	NA	NA	0.04705	0.49	Potential protective factor for AD	(8)
ABCA1	NM_005502.3	9:107579632	C>G	E1172D	rs33918808	3.82	Benign	4.68	45	1	0.96	Potential protective factor for AD	(8)

Table S12. **Potential protective variants for AD reported in *ABCA1*** (8). Position is in hg19/GRCh37. MAF, minor allele frequency; Aa, amino acid; OR, odds ratio; Ref., reference; AD, Alzheimer's disease.

*GERP score >5 indicates high conservation among different species
**Grantham score < 50 indicates an amino acid substitution that does not importantly alter the protein sequence

Homo Sapiens	197	L-R-S-L-V-E-L-R-A-L-L-Q-R-P-R-G-T-S-**G**-P-L-E-L-L-S-E-A-L-C-S-V-R-G-P-S-S-T
Gorilla	197	L-R-S-L-V-E-L-Q-A-L-L-R-R-P-R-G-T-S-**G**-P-L-E-L-L-S-E-A-L-C-S-A-R-G-P-S-S-T
Macaca mulatta	195	L-P-S-L-G-E-L-W-A-L-L-Q-R-P-H-R-P-G-**G**-P-L-E-A-V-A-E-A-L-C-S-A-R-G-P-S-K-P
Bos Taurus	197	L-P-S-L-V-E-L-Q-A-L-L-H-R-P-R-G-T-G-**G**-P-L-E-L-L-S-E-A-L-C-S-A-R-G-P-S-S-T
Rattus norvegicus	193	L-P-S-L-V-E-L-R-A-L-L-R-R-P-Q-G-P-G-**G**-P-L-E-A-V-S-E-A-L-C-G-A-R-G-P-G-I-P
Mus musculus	194	L-P-S-L-M-E-L-R-A-L-L-R-R-P-R-G-S-A-**G**-S-L-E-L-V-S-E-A-L-C-S-T-K-G-P-S-S-P
Canis lupus	194	L-P-S-L-V-E-L-R-A-L-L-R-R-P-Q-G-T-R-**S**-P-L-Q-L-V-S-E-A-F-C-S-A-K-G-P-S-S-P
Pteropus vampyrus	191	L-P-S-L-A-E-L-Q-A-L-L-P-R-L-R-E-T-D-**S**-T-L-A-V-V-S-E-A-L-C-S-A-K-G-P-S-V-P-G-G-P-S
Cavia porcellus	272	L-P-S-L-A-E-L-Q-A-L-L-Q-R-P-W-G-T-S-**S**-S-L-E-L-V-S-E-A-L-C-S-A-K-G-P-S-S-P-G-G

Figure S1. **Conservation of ABCA7 p.G215 in different species**

ABCA7	197	L-R-S-L-V-E-L-R-A-L-L-Q-R-P-R-G-T-S-**G**-P-L-E-L-L-S-E-A-L-C-S-V-R-G-P-S-S-T
ABCA2	241	T-P-G-S-G-E-L-G-R-I-L-T-V-P-E-S-Q-K-**G**-A-L-Q-G-Y-R-D-A-V-C-S-G-Q-A
ABCA12	701	R-S-V-P-L-T-Q-A-M-Y-R-S-N-R-M-N-T-P-Q-**G**-S-F-S-T-I-S-Q-A-L-C
ABCA13	3217	L-L-E-T-L-D-F-Q-Q-V-S-Q-N-V-Q-A-R-S-S-A-F-**G**-S-F-Q-F-V-M-K-M-V-C—K-D-Q-A-S-F
ABCA1	274	M-R-S-W-S-D-M-R-Q-E-V-M-F-L-T-N-V-N-S-**S**-S-S-S-T-Q-I-Y-Q-A-V-S-R

Figure S2. **Conservation of ABCA7 p.G215 in homologous proteins**

Bioinformatic

Each of the samples in our dataset consisted of paired-end 100 base pair reads. We used the Burrows-Wheeler Aligner (BWA)(9) to map the reads to build of the human genome (hg19/GRCh37). Following read mapping, we used SAMtools (10), Picard (http://picard.sourceforge.net), and the Genome Analysis Toolkit (GATK) (11)(12) to refine the resulting alignments by removing duplicates, performing realignment around InDels, and recalibrating base quality scores. We then used the GATK's UnifiedGenotyper to identify sequence variants, and subsequently filtered the variants and recalibrated variant quality scores (11). Our final dataset consisted of variant call format (VCF) files containing variants that passed all filters. Since our dataset consisted of a mix of exomes captured using different kits, and whole genome sequences, we employed a highly conservative approach to variant selection to increase our confidence that analyzed variants are true positives. We limited our dataset of variants to only those genomic regions we expected to have been sequenced in each of the exomes (based on capture probes used for exome library preparation) and whole genomes. Next, we compiled a list of all the variants present in at least a single sample. We examined each of the variants from the list of total variants in each sample, whether or not the variant was called by the GATK, and reassigned the genotype for that variant according to the following criteria. (1) If the variant was called by the GATK and passed all filters, we used the GATK genotype. (2) If no variant was called at the genomic position in question, we returned to the raw VCF file and if there were reads containing the variant, but the variant was not called because of failing filters or because only a small number of reads contain the variant, we set the genotype to missing for the sample. (3) Finally, if all the reads at this position for the sample indicated reference alleles, we set the genotype to homozygous reference. Resulting sequence files were converted to Plink format (13) using VCFTools (14). Lastly, we removed all variants not in our pre-defined list of candidate genes (*ABCA7* [NM_019112]; *CD2AP* [NM_012120]; *MS4A6A* [NM_152851]; *CR1* [NM_000573]; *BIN1* [NM_139343]; *PICALM* [NM_001206946]; *EPHA1* [NM_005232]; *CLU* [NM_001831]; *CD33* [NM_001772]. Remaining variants were annotated using ANNOVAR (15). Each variant was annotated with gene information (gene name, transcript ID, and transcript and protein positions of the variant), genomic location (exon, intron, UTR, intergenic, etc.), one or more variant classes (5'-UTR, 3'-UTR, intergenic, intronic, splice site,

nonsynonymous, stop-gain, stop-loss, or synonymous), the 1000 Genomes minor allele frequency (16), dbSNP identifier(17), and PolyPhen-2 (18).

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