

Supplementary Data

Association of HSP70 and its Co-Chaperones with Alzheimer's Disease

Linda Broer^a, Mohammad Arfan Ikram^a, Maaïke Schuur^d, Anita L. DeStefano^{e,f,g}, Joshua C. Bis^h, Fan Liu^a, Fernando Rivadeneira^{a,b,k}, Andre G. Uitterlinden^{a,b,k}, Alexa S. Beiser^{e,f,g}, William T. Longstreth^{i,j}, Albert Hofman^a, Yurii Aulchenko^a, Sudha Seshadri^{e,f}, Annette L. Fitzpatrick^j, Ben A. Oostra^c, Monique M.B. Breteler^a and Cornelia M. van Duijn^{a,k,*}

^aDepartment of Epidemiology, Erasmus Medical Center, Rotterdam, The Netherlands

^bDepartment of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands

^cDepartment of Clinical Genetics, Erasmus Medical Center, Rotterdam, The Netherlands

^dDepartment of Neurology, Erasmus Medical Center, Rotterdam, The Netherlands

^eDepartment of Neurology, Boston University School of Medicine, Boston, MA, USA

^fThe National Heart Lung and Blood Institute's Framingham Heart Study, Framingham, MA, USA

^gDepartment of Biostatistics, Boston University School of Public Health, Boston, MA, USA

^hCardiovascular Health Research Unit and Department of Medicine, University of Washington, Seattle, WA, USA

ⁱDepartment of Neurology, University of Washington, Seattle, WA, USA

^jDepartment of Epidemiology, University of Washington, Seattle, WA, USA

^kNetherlands Genomics Initiative (NGI)-sponsored Netherlands Consortium for Healthy Aging (NCHA), Rotterdam, The Netherlands

Accepted 26 January 2011

Supplementary Table 1
Overview of all genes tested in RS1 and the number of SNPs per gene

Gene (HGNC)	Gene (2009)	Family	Chr	Start gene	End gene	Total SNPs
HSPA6	HSPA6	HSP70	1	159760660	159763311	139
HSPA4L	HSPH3	HSP70	4	128922903	128973976	84
HSPA4	HSPH2	HSP70	5	132415561	132468608	138
HSPA9	HSPA9	HSP70	5	137918923	137939014	129
HSPA1L	HSPA1L	HSP70	6	31885375	31890786	
HSPA1A	HSPA1A	HSP70	6	31891316	31893698	148
HSPA1B	HSPA1B	HSP70	6	31903503	31906010	
HSPA5	HSPA5	HSP70	9	127036953	127043430	79
HSPA14	HSPA14	HSP70	10	14920267	14953746	161
HSPA12A	HSPA12A	HSP70	10	118419930	118492786	304
HYOU1	HSPH4	HSP70	11	118420110	118433122	122
HSPA8	HSPA8	HSP70	11	122433410	122438054	218
HSPH1	HSPH1	HSP70	13	30608762	30634117	263
HSPA2	HSPA2	HSP70	14	64072376	64079708	118

*Correspondence to: C.M. van Duijn, Department of Epidemiology, Erasmus University Medical Center, Dr. Molewaterplein 50, PO-Box 2040, 3000 CA Rotterdam, The Netherlands. Tel.: +31 10 7043394; Fax: +31 10 7044657; E-mail: c.vanduijn@erasmusmc.nl.

Supplementary Table 1
(Continued)

Gene (HGCNC)	Gene (2009)	Family	Chr	Start gene	End gene	Total SNPs
HSPA12B	HSPA12B	HSP70	20	3661356	3681758	203
HSPA13	HSPA13	HSP70	21	14665307	14677380	277
BAG2	BAG2	BAG	6	57145293	57157694	112
BAG4	BAG4	BAG	8	38153263	38187694	65
BAG1	BAG1	BAG	9	33242469	33254744	165
BAG3	BAG3	BAG	10	121400872	121427321	164
BAG5	BAG5	BAG	14	103092642	103098904	110
DNAJA1	DNAJA1	HSP40-A	9	33015209	33029062	258
DNAJA4	DNAJA4	HSP40-A	15	76343551	76361591	203
DNAJA3	DNAJA3	HSP40-A	16	4415883	4446777	127
DNAJA2	DNAJA2	HSP40-A	16	45547796	45565036	60
DNAJB4	DNAJB4	HSP40-B	1	78243224	78255586	110
DNAJB2	DNAJB2	HSP40-B	2	219852284	219859866	118
DNAJB8	DNAJB8	HSP40-B	3	129663972	129668781	170
DNAJB11	DNAJB11	HSP40-B	3	187771161	187786283	200
DNAJB14	DNAJB14	HSP40-B	4	101039576	101086775	146
DNAJB9	DNAJB9	HSP40-B	7	107997592	108002530	142
DNAJB6	DNAJB6	HSP40-B	7	156822471	156902894	243
DNAJB5	DNAJB5	HSP40-B	9	34979785	34988428	139
DNAJB12	DNAJB12	HSP40-B	10	73762594	73784875	88
DNAJB13	DNAJB13	HSP40-B	11	73339012	73358980	176
DNAJB1	DNAJB1	HSP40-B	19	14486582	14490201	109
DNAJB7	DNAJB7	HSP40-B	22	39585499	39588076	67
DNAJC11	DNAJC11	HSP40-C	1	6616818	6684460	161
DNAJC16	DNAJC16	HSP40-C	1	15725939	15770814	191
DNAJC8	DNAJC8	HSP40-C	1	28399655	28432122	114
DNAJC6	DNAJC6	HSP40-C	1	65503018	65654140	349
DNAJC27	DNAJC27	HSP40-C	2	25020009	25048328	207
DNAJC5 G	DNAJC5 G	HSP40-C	2	27351793	27357800	97
DNAJC10	DNAJC10	HSP40-C	2	183289244	183351500	244
DNAJC13	DNAJC13	HSP40-C	3	133619194	133740565	239
DNAJC19	DNAJC19	HSP40-C	3	182184197	182190224	100
GAK	DNAJC26	HSP40-C	4	833065	916174	199
DNAJC21	DNAJC21	HSP40-C	5	34965455	34994826	244
DNAJC18	DNAJC18	HSP40-C	5	138775279	138803038	54
SEC63	DNAJC23	HSP40-C	6	108298215	108386086	288
DNAJC30	DNAJC30	HSP40-C	7	72733184	72735717	73
DNAJC2	DNAJC2	HSP40-C	7	102740157	102772556	91
DNAJC5B	DNAJC5B	HSP40-C	8	67096345	67175309	259
DNAJC25	DNAJC25	HSP40-C	9	113433453	113456452	239
DNAJC1	DNAJC1	HSP40-C	10	22085513	22332476	128
DNAJC12	DNAJC12	HSP40-C	10	69226433	69267943	146
DNAJC9	DNAJC9	HSP40-C	10	74672588	74677031	144
DNAJC24	DNAJC24	HSP40-C	11	31347953	31410958	120
DNAJC4	DNAJC4	HSP40-C	11	63746212	63757092	97
DNAJC22	DNAJC22	HSP40-C	12	48027308	48031964	91
DNAJC14	DNAJC14	HSP40-C	12	54501011	54509603	56
SACS	DNAJC29	HSP40-C	13	22800966	22840626	289
DNAJC15	DNAJC15	HSP40-C	13	42495362	42581306	348
DNAJC3	DNAJC3	HSP40-C	13	95127484	95241285	159
DNAJC17	DNAJC17	HSP40-C	15	38847363	38886947	110
DNAJC7	DNAJC7	HSP40-C	17	37382006	37422956	91
DNAJC5	DNAJC5	HSP40-C	20	61996962	62035839	135
DNAJC28	DNAJC28	HSP40-C	21	33782108	33785893	105
HSCB	DNAJC20	HSP40-C	22	27468043	27483498	125
STIP1	Hop	CHIP-like	11	63710248	63728591	133
STUB1	CHIP	CHIP-like	16	670116	672769	111
ST13	Hip	CHIP-like	22	39550545	39582633	95
PFDN6L	PFDN6L	Prefoldin	1	42774743	42892922	233
PFDN2	PFDN2	Prefoldin	1	159336970	159354490	114
PFDN1	PFDN1	Prefoldin	5	139604819	139662873	130

Supplementary Table 1
(Continued)

Gene (HGNC)	Gene (2009)	Family	Chr	Start gene	End gene	Total SNPs
PFDN6	PFDN6	Prefoldin	6	33365356	33366689	129
PFDN5	PFDN5	Prefoldin	12	51975502	51979501	75
PDRG1	PDRG1	Prefoldin	20	29996419	30003544	107
PFDN4	PFDN4	Prefoldin	20	52257909	52269899	278
Total	(79 genes)					12053

Genes made bold in the second column are genes that are subjected to name-change for the new HSP nomenclature.

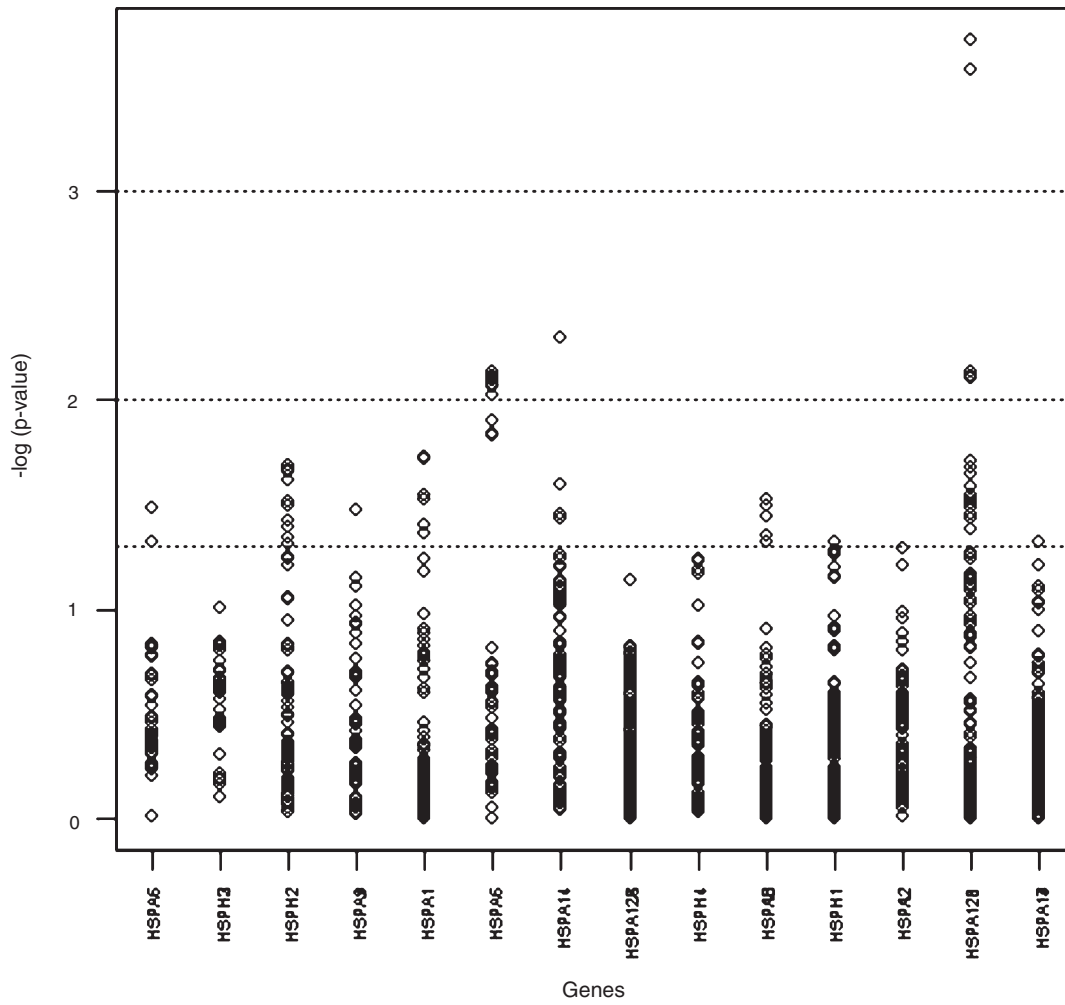
Supplementary Table 2
All SNPs in PFDN2

Chr	ROI	SNP	Position	Location	Eff. allele	EAF	Rsq	p-val	OR (95% CI)
1	PFDN2	rs2297221	159237592	-99378	G	0,72	1,00	7,83E-03	1.25 (1.06-1.47)
1	PFDN2	rs2297220	159237639	-99331	G	0,72	1,00	7,86E-03	1.25 (1.06-1.47)
1	PFDN2	rs790055	159237770	-99200	G	0,79	1,00	4,25E-03	0.79 (0.66-0.93)
1	PFDN2	rs2247459	159242624	-94346	C	0,72	1,00	7,88E-03	1.25 (1.06-1.47)
1	PFDN2	rs2481080	159242961	-94009	G	0,72	1,00	7,89E-03	1.25 (1.06-1.47)
1	PFDN2	rs17388108	159244326	-92644	A	0,72	1,00	7,91E-03	1.25 (1.06-1.47)
1	PFDN2	rs2247671	159244455	-92515	G	0,72	1,00	7,92E-03	1.25 (1.06-1.47)
1	PFDN2	rs2481081	159245198	-91772	A	0,72	1,00	7,93E-03	1.25 (1.06-1.47)
1	PFDN2	rs2247790	159245684	-91286	C	0,72	1,00	7,95E-03	1.25 (1.06-1.47)
1	PFDN2	rs11807930	159248881	-88089	A	0,72	1,00	7,97E-03	1.25 (1.06-1.47)
1	PFDN2	rs2039223	159252332	-84638	G	0,79	1,00	4,19E-03	0.78 (0.66-0.93)
1	PFDN2	rs2481084	159256238	-80732	T	0,72	1,00	5,33E-03	1.26 (1.07-1.49)
1	PFDN2	rs6695707	159258445	-78525	A	0,86	0,99	7,87E-01	0.97 (0.80-1.19)
1	PFDN2	rs7546890	159262016	-74954	T	0,51	1,00	8,72E-01	1.01 (0.88-1.17)
1	PFDN2	rs12030262	159267088	-69882	G	0,51	1,00	8,65E-01	1.01 (0.88-1.17)
1	PFDN2	rs11576837	159270498	-66472	G	0,61	1,00	8,65E-03	0.83 (0.72-0.95)
1	PFDN2	rs11265544	159272643	-64327	C	0,33	1,00	9,66E-01	1.00 (0.86-1.16)
1	PFDN2	rs10908821	159275159	-61811	C	0,87	0,96	5,54E-02	0.82 (0.67-1.01)
1	PFDN2	rs3737787	159276147	-60823	G	0,72	0,98	4,48E-03	1.27 (1.08-1.50)
1	PFDN2	rs2073656	159277979	-58991	G	0,72	0,98	4,48E-03	1.27 (1.08-1.50)
1	PFDN2	rs2774276	159278340	-58630	C	0,74	0,98	5,42E-03	0.80 (0.68-0.94)
1	PFDN2	rs2073653	159279384	-57586	T	0,87	1,00	9,36E-01	0.99 (0.81-1.21)
1	PFDN2	rs1556260	159281070	-55900	C	0,87	1,00	9,37E-01	0.99 (0.81-1.21)
1	PFDN2	rs1556259	159281273	-55697	A	0,87	1,00	9,37E-01	0.99 (0.81-1.21)
1	PFDN2	rs2516837	159281351	-55619	G	0,61	0,99	1,09E-02	0.83 (0.72-0.96)
1	PFDN2	rs2774279	159284180	-52790	T	0,33	1,00	9,63E-01	1.00 (0.86-1.17)
1	PFDN2	rs3813609	159285664	-51306	C	0,61	0,99	1,09E-02	0.83 (0.72-0.96)
1	PFDN2	rs11588189	159286245	-50725	T	0,33	1,00	9,62E-01	1.00 (0.87-1.17)
1	PFDN2	rs3813610	159289263	-47707	G	0,61	0,98	1,10E-02	0.83 (0.72-0.96)
1	PFDN2	rs7516231	159292703	-44267	A	0,87	0,99	9,43E-01	0.99 (0.81-1.22)
1	PFDN2	rs12130871	159293114	-43856	G	0,32	0,98	7,48E-01	0.98 (0.84-1.14)
1	PFDN2	rs10737178	159294116	-42854	G	0,92	1,00	5,69E-02	0.80 (0.63-1.01)
1	PFDN2	rs7556492	159295759	-41211	T	0,87	0,98	9,77E-01	1.00 (0.81-1.23)
1	PFDN2	rs17384360	159297430	-39540	T	0,71	0,94	1,43E-02	1.23 (1.04-1.46)
1	PFDN2	rs4617422	159303096	-33874	G	0,87	0,95	9,12E-01	1.01 (0.82-1.25)
1	PFDN2	rs10797092	159303666	-33304	C	0,79	1,00	4,78E-04	0.75 (0.63-0.88)
1	PFDN2	rs16832617	159304481	-32489	A	0,87	0,93	8,08E-01	1.03 (0.83-1.27)
1	PFDN2	rs12118313	159304603	-32367	A	0,78	0,99	1,21E-04	0.73 (0.62-0.86)
1	PFDN2	rs6671492	159305391	-31579	C	0,78	1,00	5,28E-04	0.75 (0.64-0.88)
1	PFDN2	rs12116949	159308687	-28283	A	0,28	0,87	7,48E-01	0.97 (0.82-1.15)
1	PFDN2	rs4656285	159310359	-26611	C	0,75	1,00	2,38E-03	0.78 (0.67-0.92)
1	PFDN2	rs4656978	159310388	-26582	A	0,75	1,00	2,39E-03	0.78 (0.67-0.92)
1	PFDN2	rs4559524	159311752	-25218	G	0,88	1,00	4,13E-02	0.81 (0.65-0.99)
1	PFDN2	rs11265548	159313844	-23126	T	0,89	0,99	4,07E-02	0.80 (0.65-0.99)
1	PFDN2	rs3820097	159315982	-20988	A	0,88	0,98	1,69E-01	0.86 (0.70-1.06)
1	PFDN2	rs1467742	159317475	-19495	G	0,88	0,98	1,69E-01	0.86 (0.70-1.06)
1	PFDN2	rs1556257	159317758	-19212	C	0,75	0,97	2,08E-03	0.78 (0.66-0.91)

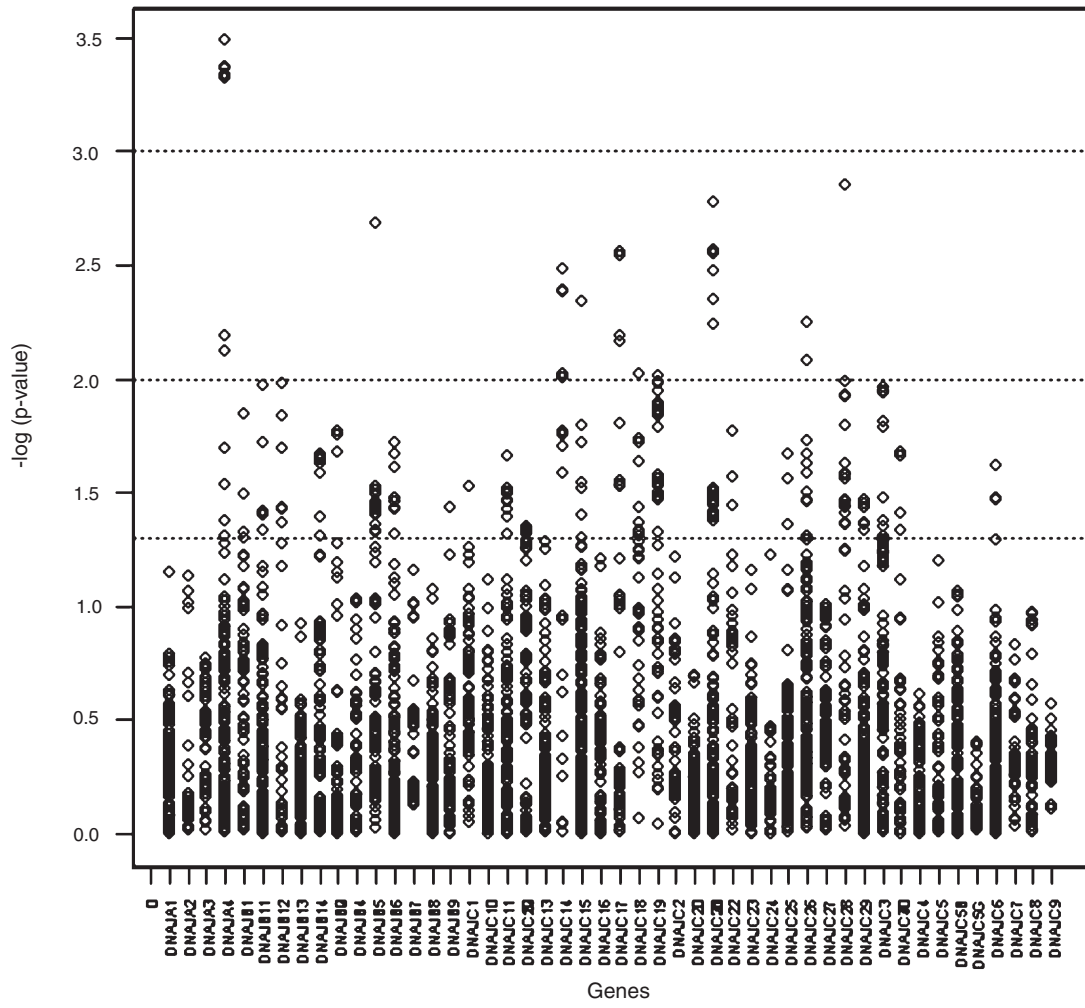
Supplementary Table 2
(Continued)

Chr	ROI	SNP	Position	Location	Eff. allele	EAF	Rsq	<i>p</i> -val	OR (95% CI)
1	PFDN2	rs11265549	159318150	-18820	G	0,88	0,99	1,64E-01	0.86 (0.70-1.06)
1	PFDN2	rs12401309	159318182	-18788	T	0,92	0,97	6,59E-02	0.80 (0.63-1.02)
1	PFDN2	rs3892376	159320397	-16573	C	0,87	1,00	5,71E-02	0.83 (0.68-1.01)
1	PFDN2	rs3892375	159320678	-16292	C	0,27	0,98	9,53E-01	1.00 (0.85-1.17)
1	PFDN2	rs4233364	159320847	-16123	A	0,89	0,98	1,58E-01	0.86 (0.70-1.06)
1	PFDN2	rs10159127	159323242	-13728	A	0,26	0,90	6,79E-01	1.04 (0.88-1.23)
1	PFDN2	rs11590097	159323613	-13357	G	0,88	0,88	4,11E-02	0.80 (0.64-0.99)
1	PFDN2	rs1411614	159324533	-12437	G	0,26	0,87	8,87E-01	1.01 (0.85-1.20)
1	PFDN2	rs11265550	159327014	-9956	A	0,46	0,88	3,17E-02	1.18 (1.01-1.37)
1	PFDN2	rs4656287	159330632	-6338	T	0,91	0,99	6,88E-02	0.81 (0.64-1.02)
1	PFDN2	rs11576830	159335460	-1510	C	0,29	1,00	5,04E-01	1.06 (0.90-1.23)
1	PFDN2	rs4078017	159340716	intronic	G	0,91	0,96	3,79E-02	0.79 (0.63-0.99)
1	PFDN2	rs4656289	159341216	intronic	C	0,91	0,96	3,79E-02	0.79 (0.63-0.99)
1	PFDN2	rs4233365	159341225	intronic	A	0,39	0,99	3,98E-02	1.16 (1.01-1.34)
1	PFDN2	rs4347230	159341253	intronic	A	0,39	0,99	4,00E-02	1.16 (1.01-1.34)
1	PFDN2	rs4656985	159345779	intronic	C	0,39	0,99	4,06E-02	1.16 (1.01-1.34)
1	PFDN2	rs11265554	159350631	intronic	C	0,39	0,99	4,07E-02	1.16 (1.01-1.34)
1	PFDN2	rs4523530	159351397	intronic	T	0,39	0,99	3,81E-02	1.17 (1.01-1.35)
1	PFDN2	rs17389237	159359385	4895	A	0,91	0,97	3,97E-02	0.79 (0.63-0.99)
1	PFDN2	rs1135783	159360814	6324	A	0,91	0,97	3,98E-02	0.79 (0.63-0.99)
1	PFDN2	rs12727614	159363865	9375	A	0,25	1,00	3,19E-01	1.09 (0.92-1.28)
1	PFDN2	rs7517289	159368514	14024	C	0,37	0,97	7,17E-03	1.22 (1.06-1.41)
1	PFDN2	rs10797093	159370069	15579	G	0,27	0,99	1,22E-01	1.13 (0.97-1.33)
1	PFDN2	rs4288617	159370646	16156	A	0,38	0,95	7,64E-03	1.22 (1.05-1.41)
1	PFDN2	rs11265558	159373805	19315	G	0,36	1,00	8,11E-03	1.22 (1.05-1.40)
1	PFDN2	rs10908824	159378555	24065	G	0,26	1,00	3,27E-01	1.08 (0.92-1.27)
1	PFDN2	rs10732962	159381939	27449	G	0,36	1,00	8,08E-03	1.22 (1.05-1.4)
1	PFDN2	rs4656988	159389527	35037	A	0,36	1,00	8,05E-03	1.22 (1.05-1.41)
1	PFDN2	rs12031437	159393599	39109	G	0,36	1,00	8,05E-03	1.22 (1.05-1.41)
1	PFDN2	rs3402	159402045	47555	T	0,10	0,88	9,45E-01	1.01 (0.78-1.31)
1	PFDN2	rs2502806	159402183	47693	G	0,57	0,91	1,34E-02	1.21 (1.04-1.41)
1	PFDN2	rs2301286	159402848	48358	A	0,36	0,99	7,89E-03	1.22 (1.05-1.41)
1	PFDN2	rs6779	159408056	53566	G	0,26	0,99	3,27E-01	1.09 (0.92-1.28)
1	PFDN2	rs3813619	159410425	55935	G	0,93	1,00	2,41E-01	0.86 (0.67-1.11)
1	PFDN2	rs3813620	159411629	57139	C	0,91	1,00	4,48E-02	0.79 (0.63-1.00)
1	PFDN2	rs17392570	159414395	59905	A	0,92	0,99	1,83E-02	0.76 (0.60-0.95)
1	PFDN2	rs4575098	159422016	67526	A	0,22	0,98	4,05E-01	1.08 (0.91-1.27)
1	PFDN2	rs4233366	159425771	71281	C	0,75	1,00	7,82E-01	1.02 (0.87-1.20)
1	PFDN2	rs7512012	159428797	74307	A	0,58	1,00	2,21E-02	1.19 (1.03-1.37)
1	PFDN2	rs4233367	159429661	75171	C	0,58	1,00	2,06E-02	1.19 (1.03-1.38)
1	PFDN2	rs4589131	159434322	79832	G	0,57	0,98	4,17E-02	1.16 (1.01-1.35)
1	PFDN2	rs3813623	159435789	81299	G	0,87	1,00	5,25E-01	0.94 (0.77-1.15)
1	PFDN2	rs3813624	159437601	83111	C	0,87	1,00	5,28E-01	0.94 (0.77-1.15)
1	PFDN2	rs10908826	159439149	84659	C	0,87	1,00	5,29E-01	0.94 (0.77-1.15)
1	PFDN2	rs4656993	159442761	88271	G	0,57	0,98	4,37E-02	1.16 (1.00-1.34)
1	PFDN2	rs16832694	159443430	88940	A	0,92	1,00	4,01E-02	0.79 (0.63-0.99)
1	PFDN2	rs3924264	159445308	90818	C	0,35	1,00	7,28E-01	1.03 (0.89-1.19)
1	PFDN2	rs4656994	159446501	92011	G	0,78	1,00	6,23E-02	0.86 (0.73-1.01)
1	PFDN2	rs11576415	159448832	94342	G	0,10	0,99	4,49E-01	1.10 (0.87-1.39)
1	PFDN2	rs10797094	159449296	94806	A	0,57	1,00	5,64E-02	1.15 (1.00-1.33)
1	PFDN2	rs1136207	159450140	95650	C	0,87	1,00	5,89E-01	0.95 (0.77-1.16)
1	PFDN2	rs11587213	159451499	97009	G	0,19	1,00	3,93E-02	1.20 (1.01-1.43)
1	PFDN2	rs12094497	159452927	98437	A	0,10	0,99	4,58E-01	1.09 (0.86-1.38)
1	PFDN2	rs2070902	159454289	99799	C	0,76	1,00	8,62E-01	1.02 (0.86-1.20)

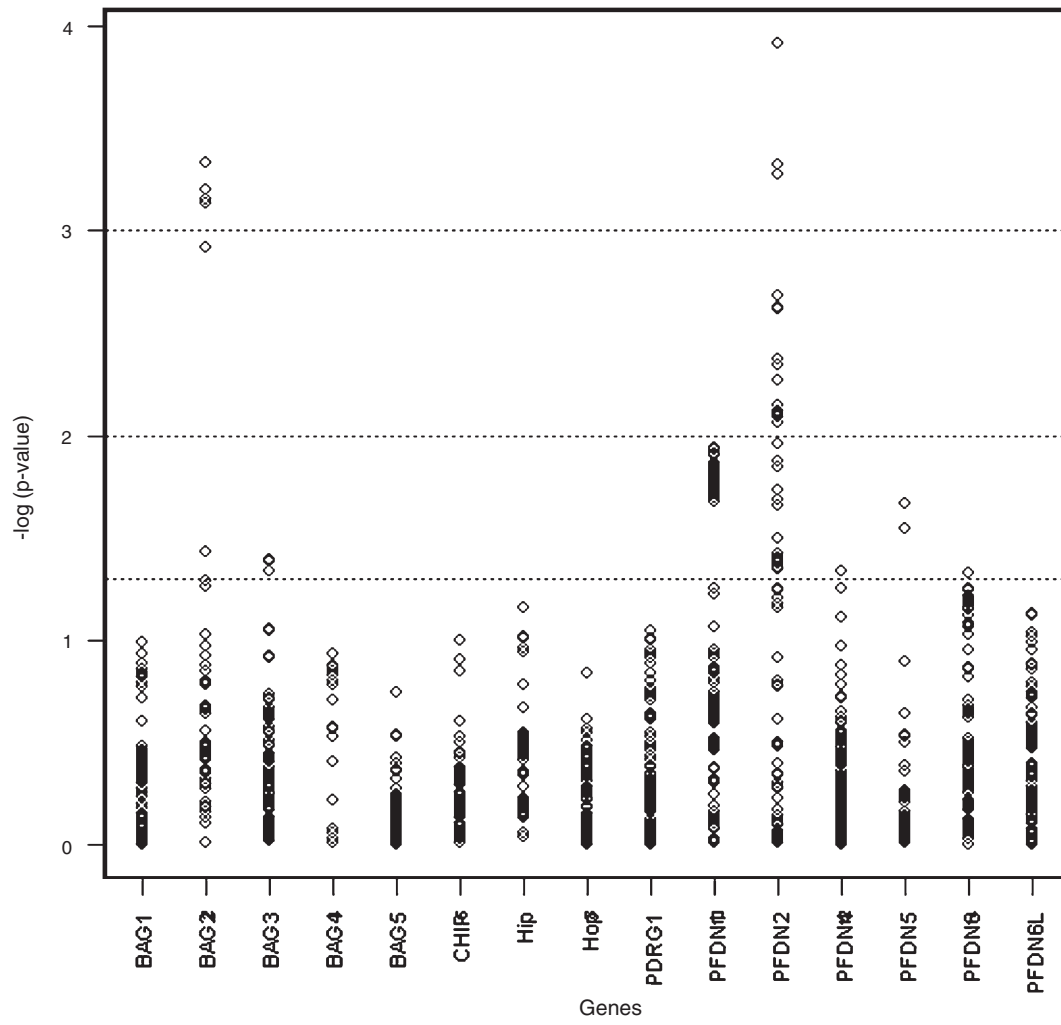
Chr: chromosome; ROI: Region of Interest; Eff. allele: Effective allele; Rsq: imputation quality value; *p*-val: *p*-value; OR (95% CI): Odds Ratio (95% confidence interval).



Supplementary Figure 1a. $-\log(p\text{-values})$ of all SNPs tested. Each gene tested is a bar. HSP70 genes.



Supplementary Figure 1b. $-\log(p\text{-values})$ of all SNPs tested. Each gene tested is a bar. HSP40 genes, ordered on subclass A, B, and C.



Supplementary Figure 1c. $-\log(p\text{-values})$ of all SNPs tested. Each gene tested is a bar. BAG genes, CHIP-like genes and Prefoldin genes.