

**Supplementary Table S1: Association results in the South European GWAS cohort of the 133 previously reported UC risk loci.**

SNP	Chr	Position(Mb)	Genes	RAF	P-val(1)	OR(1)	MAF(2)	P-val(2)	OR(2)
rs12103	1	1.24	<i>TNFRSF18,TNFRSF4,(30)</i>	0.18	7.66E-13	1.10	0.36	0.119	1.25(0.94-1.66)
rs10797432	1	2.5	<i>TNFRSF14,MME1,PLCH2,(8)</i>	0.52	2.62E-12	1.08	0.46	0.359	0.94(0.83-1.07)
rs35675666	1	8.02	<i>TNFRSF9,(6)</i>	0.84	1.12E-15	1.11	0.13	0.1967	0.89(0.74-1.06)
rs6426833	1	20.15	<i>(9)</i>	0.54	2.39E-68	1.27	0.42	0.08359	0.9(0.79-1.01)
rs12568930	1	22.7	<i>(3)</i>	0.82	1.26E-17	1.10	0.16	0.002037	0.78(0.66-0.91)
rs11209026	1	67.68	<i>IL23R,IL12RB2,(4)</i>	0.93	8.12E-161	2.01	0.05	0.002878	0.67(0.51-0.87)
rs2651244	1	70.99	<i>(3)</i>	0.60	2.29E-08	1.02	0.39	0.3434	1.06(0.94-1.2)
rs4845604	1	151.79	<i>RORC,(14)</i>	0.86	3.52E-16	1.14	0.15	0.2371	0.9(0.76-1.07)
rs670523	1	155.67	<i>UBQLN4,RIT1,MSTO1,(28)</i>	0.32	5.79E-11	1.06	0.33	0.8709	1.01(0.88-1.16)
rs1801274	1	161.47	<i>FCGR2A,FCGR2B,FCGR3A,HSPA6,FCGR3B,FCRLA,(9)</i>	0.51	2.12E-38	1.12	0.45	0.03255	0.88(0.77-0.99)
rs4656958	1	160.85	<i>CD48,SLAMF1,ITLN1,CD244,F11R,USF1,SLAMF7,ARHGAP30,(8)</i>	0.69	6.80E-09	1.06	0.29	0.4538	0.95(0.83-1.09)
rs2488389	1	197.6	<i>C1orf53,(2)</i>	0.22	8.45E-13	1.12	0.24	0.3344	1.07(0.93-1.24)
rs2816958	1	200.09	<i>(3)</i>	0.89	1.98E-17	1.23	0.10	0.006225	0.76(0.63-0.93)
rs7554511	1	200.87	<i>KIF21B,(6)</i>	0.73	1.24E-32	1.16	0.20	5.19E-06	0.71(0.61-0.82)
rs3024505	1	206.93	<i>IL10,IL20,IL19,IL24,PIGR,MAPKAPK2,FAIM3,RASSF5,(3)</i>	0.16	6.66E-42	1.21	0.15	0.05886	1.18(0.99-1.41)
rs6545800	2	25.12	<i>ADCY3,(6)</i>	0.45	6.14E-16	1.11	0.46	0.5934	1.03(0.91-1.17)
rs925255	2	28.61	<i>FOSL2,BRE,(1)</i>	0.56	2.67E-15	1.09	0.44	0.6299	1.03(0.91-1.17)
rs10495903	2	43.81	<i>(5)</i>	0.13	8.03E-12	1.09	0.13	0.6734	1.04(0.87-1.25)
rs7608910	2	61.2	<i>REL,C2orf74,KIAA1841,AHSA2,(6)</i>	0.39	8.65E-32	1.14	0.44	0.1646	1.09(0.96-1.24)
rs6740462	2	65.67	<i>SPRED2,(1)</i>	0.74	2.35E-08	1.08	0.22	0.02022	0.84(0.73-0.97)
rs917997	2	102.86	<i>IL1R2,IL18RAP,IL18R1,IL1R1,IL1RL1,IL1RL2,(3)</i>	0.23	3.12E-20	1.10	0.26	0.7625	1.02(0.89-1.17)
rs2111485	2	163.1	<i>IFIH1,(5)</i>	0.40	1.93E-08	1.07	0.41	0.8836	1.01(0.89-1.14)
rs1517352	2	191.92	<i>STAT1,STAT4,(2)</i>	0.60	3.28E-11	1.08	0.42	0.5913	1.03(0.91-1.17)
rs1016883	2	198.65	<i>RFTN2,PLCL1,(7)</i>	0.82	2.87E-08	1.10	0.21	0.09924	0.88(0.76-1.02)
rs17229285	2	199.7	<i>0</i>	0.50	1.73E-13	1.12	0.52	0.05072	1.13(1-1.29)
rs2382817	2	219.14	<i>SLC11A1,CXCR2,CXCR1,PNKD,ARPC2,TMBIM1,CTDSP1,(8)</i>	0.41	3.70E-12	1.07	0.45	0.9804	1(0.88-1.13)
rs3749171	2	241.57	<i>GPR35,(12)</i>	0.17	3.07E-21	1.14	0.18	3.99E-05	1.42(1.2-1.68)
rs4256159	3	18.76	<i>0</i>	0.14	9.00E-15	1.11	0.11	0.1377	1.16(0.95-1.41)
rs3197999	3	48.96	<i>MST1,PFKFB4,MST1R,UCN2,GPX1,IP6K2,BSN,IP6K1,USP4,(56)</i>	0.30	1.01E-47	1.18	0.38	7.68E-07	1.38(1.21-1.56)
rs9847710	3	53.05	<i>PRKCD,ITIH4,(8)</i>	0.42	1.05E-08	1.06	0.44	0.5556	1.04(0.92-1.17)
rs2472649	4	74.85	<i>CXCL5,CXCL1,CXCL3,IL8,CXCL6,PF4,CXCL2,PF4V1,(3)</i>	0.82	2.57E-08	1.10	0.17	0.1918	0.9(0.77-1.05)
rs3774959	4	103.51	<i>NFKB1,MANBA,(2)</i>	0.36	3.66E-12	1.12	0.37	0.0971	1.11(0.98-1.26)
rs7657746	4	123.22	<i>IL2,IL21,(2)</i>	0.75	2.76E-13	1.12	0.24	0.04696	0.87(0.75-1)
rs11739663	5	0.59	<i>SLC9A3,(8)</i>	0.76	1.81E-08	1.07	0.21	0.4525	0.94(0.81-1.1)
rs2930047	5	10.69	<i>DAP,(2)</i>	0.38	1.03E-08	1.07	0.40	0.356	1.06(0.94-1.2)

rs11742570	5	40.38	PTGER4,(1)	0.61	1.81E-82	1.20	0.36	0.2962	0.93(0.82-1.06)
rs1363907	5	96.24	ERAP2,ERAP1,LNPEP,(2)	0.41	5.62E-13	1.07	0.39	0.8792	0.99(0.87-1.12)
rs4836519	5	130.005	(1)	0.77	4.24E-10	1.07	0.22	0.1879	1.11(0.95-1.28)
rs2188962	5	131.19	IRF1,IL13,CSF2,SLC22A4,IL4,IL3,IL5,PDLIM4,SLC22A5,ACSL6,(8)	0.43	1.35E-52	1.16	0.45	0.679	1.03(0.91-1.16)
rs254560	5	134.44	(6)	0.40	2.55E-09	1.06	0.41	0.02311	1.16(1.02-1.31)
rs6863411	5	141.51	SPRY4,NDFIP1,(5)	0.63	3.59E-14	1.09	0.35	0.6387	0.97(0.85-1.1)
rs11741861	5	150.27	TNIP1,IRGM,ZNF300P1,(8)	0.09	2.94E-37	1.25	0.14	0.9999	1(0.84-1.19)
rs6871626	5	158.8	IL12B,(3)	0.34	1.43E-42	1.18	0.31	0.17	1.13(0.95-1.34)
rs12654812	5	176.79	DOK3,(17)	0.34	1.68E-08	1.07	0.33	0.1982	1.11(0.95-1.31)
rs17119	6	14.71	0	0.79	3.08E-11	1.07	0.25	0.7109	0.97(0.84-1.12)
rs9358372	6	20.77	(2)	0.38	8.66E-14	1.09	0.43	0.03632	1.14(1.01-1.29)
rs6927022	6	32.595	HLA-DQB1,HLA-DRB1,HLA-DQA1,HLA-DRA,(12)	0.54	4.71E-133	1.44	0.23	0.001459	0.71(0.57-0.88)
rs1847472	6	90.96	(1)	0.66	1.57E-10	1.06	0.37	0.9403	1(0.88-1.13)
rs6568421	6	106.43	(2)	0.30	8.24E-20	1.11	0.29	0.01874	1.21(1.03-1.42)
rs3851228	6	111.82	TRAF3IP2,FYN,REV3L,(2)	0.07	1.08E-13	1.15	0.08	0.002071	1.47(1.15-1.87)
rs6920220	6	138	TNFAIP3,(1)	0.21	1.40E-21	1.10	0.23	0.0008788	1.29(1.11-1.49)
rs12199775	6	143.9	PHACTR2,(5)	0.93	1.99E-08	1.13	0.06	0.7914	0.97(0.75-1.24)
rs1819333	6	167.37	CCR6,RPS6KA2,RNASET2,(3)	0.52	6.76E-21	1.08	0.45	0.6765	0.97(0.86-1.1)
rs798502	7	2.78	CARD11,GNA12,TTYH3,(4)	0.71	6.09E-17	1.13	0.28	0.0002821	0.78(0.68-0.89)
rs4722672	7	27.22	(14)	0.18	2.06E-08	1.09	0.22	0.005842	1.24(1.06-1.44)
rs1456896	7	50.245	ZBPB,IKZF1,(4)	0.69	7.28E-15	1.09	0.30	0.1272	0.9(0.79-1.03)
rs9297145	7	98.75	SMURF1,(6)	0.27	8.21E-12	1.08	0.28	0.7503	0.98(0.85-1.12)
rs1734907	7	100.335	EPO,(21)	0.15	1.67E-13	1.11	0.13	0.5534	1.06(0.88-1.27)
rs4380874	7	107.45	DLD,(9)	0.41	2.07E-26	1.14	0.42	0.00636	1.19(1.05-1.35)
rs38904	7	116.89	(6)	0.53	1.31E-08	1.05	0.48	0.1019	0.9(0.8-1.02)
rs4728142	7	128.57	IRF5,TNPO3,TSPAN33,(11)	0.44	4.37E-14	1.10	0.49	0.03467	1.14(1.01-1.29)
rs921720	8	126.53	TRIB1,(1)	0.61	8.30E-20	1.08	0.42	0.1644	0.92(0.81-1.04)
rs1991866	8	130.62	(2)	0.42	1.65E-09	1.05	0.42	0.8574	1.01(0.89-1.15)
rs10758669	9	4.98	JAK2,(4)	0.35	7.88E-45	1.17	0.38	0.0001039	1.28(1.13-1.46)
rs4743820	9	93.92	NFIL3,(2)	0.70	3.60E-09	1.06	0.24	0.1442	0.9(0.78-1.04)
rs4246905	9	117.6	TNFSF8,TNFSF15,TNC,(2)	0.71	2.80E-32	1.14	0.31	0.9192	0.99(0.87-1.14)
rs10781499	9	139.32	CARD9,PMPCA,SDCCAG3,INPP5E,(19)	0.41	4.38E-56	1.19	0.42	0.0004352	1.25(1.1-1.42)
rs12722515	10	6.08	IL2RA,IL15RA,(6)	0.85	3.76E-10	1.10	0.11	0.1184	0.86(0.71-1.04)
rs1042058	10	30.72	MAP3K8,(3)	0.59	5.93E-11	1.08	0.39	0.02434	0.87(0.77-0.98)
rs11010067	10	35.295	CREM,(3)	0.35	2.49E-25	1.12	0.35	0.07884	1.12(0.99-1.28)
rs2790216	10	59.99	CISD1,IPMK,(2)	0.78	8.07E-09	1.07	0.21	0.6817	1.03(0.89-1.2)
rs10761659	10	64.51	(3)	0.54	6.37E-46	1.17	0.52	0.0001379	1.31(1.14-1.51)

rs2227564	10	75.67	(13)	0.77	6.75E-10	1.08	0.18	0.2429	0.91(0.78-1.07)
rs1250546	10	81.03	(5)	0.60	3.15E-18	1.10	0.33	0.8993	0.99(0.87-1.13)
rs6586030	10	82.25	TSPAN14,C10orf58,(4)	0.85	9.24E-16	1.12	0.13	0.5908	0.95(0.8-1.14)
rs7911264	10	94.43	(4)	0.52	2.98E-08	1.07	0.50	0.07018	1.12(0.99-1.27)
rs4409764	10	101.28	NKX2-3,(6)	0.49	1.03E-54	1.18	0.45	0.1501	0.91(0.81-1.03)
rs907611	11	1.87	TNNI2,LSP1,(17)	0.32	2.70E-10	1.07	0.33	0.4269	1.05(0.93-1.2)
rs10896794	11	58.33	CNTF,LPXN,(8)	0.76	6.80E-10	1.08	0.23	0.5749	0.96(0.83-1.11)
rs11230563	11	60.77	CD6,CD5,PTGDR2,(12)	0.65	9.03E-13	1.09	0.37	0.0004896	0.8(0.71-0.91)
rs4246215	11	61.56	C11orf9,FADS1,FADS2,(12)	0.34	1.93E-15	1.08	0.31	0.8146	0.98(0.86-1.13)
rs559928	11	64.12	CCDC88B,RPS6KA4,TRPT1,FLRT1,(20)	0.82	4.19E-11	1.10	0.15	0.4796	0.94(0.79-1.11)
rs2231884	11	65.65	RELA,FOSL1,CTSW,SNX32,(22)	0.16	2.91E-10	1.08	0.18	0.371	1.08(0.92-1.26)
rs2155219	11	76.29	(5)	0.51	4.24E-36	1.15	0.44	0.1483	0.91(0.8-1.03)
rs6592362	11	87.12	(1)	0.25	2.32E-08	1.08	0.22	0.3555	1.08(0.91-1.28)
rs483905	11	96.02	JRKL,MAML2,(2)	0.29	1.21E-08	1.06	0.30	0.2783	0.93(0.81-1.06)
rs561722	11	114.38	FAM55A,FAM55D,(5)	0.66	5.15E-17	1.12	0.31	0.0007577	0.79(0.7-0.91)
rs630923	11	118.74	CXCR5,(17)	0.85	7.07E-09	1.07	0.16	0.4659	0.94(0.8-1.11)
rs11612508	12	12.65	LOH12CR1,(8)	0.27	1.06E-08	1.06	0.25	0.9687	1(0.87-1.15)
rs11564258	12	40.77	LRRK2,MUC19	0.03	6.38E-29	1.33	0.03	0.01381	1.64(1.1-2.45)
rs11168249	12	48.2	VDR,(8)	0.47	7.78E-09	1.05	0.47	0.1479	0.91(0.81-1.03)
rs7134599	12	68.49	IFNG,IL26,IL22,(1)	0.38	8.51E-32	1.10	0.42	0.0855	1.12(0.98-1.26)
rs17085007	13	27.52	(2)	0.18	2.79E-19	1.11	0.17	0.1285	1.14(0.96-1.34)
rs941823	13	40.86	(3)	0.76	2.07E-14	1.07	0.24	0.05296	0.87(0.76-1)
rs9557195	13	99.95	GPR183,GPR18,(6)	0.77	2.37E-14	1.11	0.24	0.7611	0.98(0.85-1.13)
rs194749	14	69.27	ZFP36L1,(4)	0.23	2.70E-10	1.08	0.20	0.3002	1.09(0.93-1.27)
rs4899554	14	75.7	FOS,MLH3,(6)	0.82	2.71E-08	1.08	0.15	0.9744	1(0.84-1.18)
rs8005161	14	88.47	GPR65,GALC,(1)	0.09	2.35E-14	1.15	0.10	0.1366	1.17(0.95-1.43)
rs28374715	15	41.55	ITPKA,NDUFAF1,NUSAP1,(8)	0.74	2.43E-08	1.08	0.22	0.4387	0.94(0.81-1.09)
rs17293632	15	67.43	SMAD3,(2)	0.24	5.97E-16	1.07	0.26	0.01051	1.21(1.04-1.39)
rs7495132	15	91.17	CRTC3,(3)	0.89	9.48E-11	1.13	0.10	0.9834	1(0.81-1.23)
rs529866	16	11.54	SOCS1,LITAF,RMI2,(10)	0.80	1.73E-16	1.12	0.15	0.8622	0.99(0.83-1.17)
rs7404095	16	23.86	PRKCB,(5)	0.57	9.68E-10	1.06	0.42	0.1145	0.9(0.8-1.02)
rs26528	16	28.595	RABEP2,IL27,EIF3C,SULT1A1,SULT1A2,NUPR1,(9)	0.45	9.65E-22	1.10	0.40	0.1977	1.08(0.96-1.23)
rs11150589	16	30.47	ITGAL,(20)	0.46	6.04E-10	1.09	0.44	0.7062	0.97(0.85-1.11)
rs1728785	16	68.58	ZFP90,(6)	0.77	3.71E-08	1.08	0.23	0.9552	1(0.86-1.15)
rs10521318	16	86	IRF8,(4)	0.92	1.41E-09	1.16	0.05	0.9445	0.99(0.75-1.3)
rs3091316	17	32.59	CCL13,CCL2,CCL11,(4)	0.72	1.22E-26	1.12	0.23	0.7844	0.98(0.85-1.13)
rs12946510	17	37.91	IKZF3,ZBPB2,GSDMB,ORMDL3,GSDMA,(12)	0.47	4.10E-38	1.16	0.44	0.008795	1.19(1.04-1.35)

rs12942547	17	40.53	STAT3,STAT5B,STAT5A,(13)	0.58	5.51E-22	1.10	0.37	0.1569	0.91(0.8-1.04)
rs1292053	17	57.96	TUBD1,RPS6KB1,(9)	0.45	8.85E-13	1.08	0.45	0.7292	1.02(0.9-1.16)
rs7210086	17	70.64	(3)	0.80	1.89E-09	1.11	0.18	0.03517	0.85(0.72-0.99)
rs1893217	18	12.8	(6)	0.16	3.05E-26	1.17	0.15	0.4321	1.07(0.9-1.27)
rs7240004	18	46.39	SMAD7,(2)	0.62	1.31E-09	1.06	0.39	0.4574	0.95(0.84-1.08)
rs727088	18	67.53	CD226,(2)	0.48	4.65E-09	1.08	0.46	0.6957	1.02(0.91-1.16)
rs11879191	19	10.49	TYK2,PPAN-P2RY11,ICAM1,(25)	0.80	2.04E-18	1.14	0.18	0.2366	1.1(0.94-1.3)
rs17694108	19	33.73	CEBPG,(8)	0.28	5.85E-15	1.10	0.22	0.5616	1.06(0.87-1.29)
rs1126510	19	47.12	CALM3,(14)	0.36	1.55E-09	1.08	0.38	0.1615	1.09(0.96-1.24)
rs11672983	19	55.38	NLRP7,NLRP2,KIR2DL1,LILRB4,(15)	0.39	6.50E-11	1.09	0.41	0.2103	1.08(0.96-1.23)
rs6142618	20	30.75	HCK,(10)	0.56	6.05E-10	1.07	0.47	0.5658	1.04(0.92-1.17)
rs4911259	20	31.37	DNMT3B,(8)	0.38	1.20E-09	1.08	0.32	0.3123	1.07(0.94-1.22)
rs6088765	20	33.8	PROCR,UQCC,CEP250,(8)	0.44	2.21E-08	1.08	0.47	0.05839	1.14(1-1.31)
rs6017342	20	43.06	ADA,HNF4A,(9)	0.53	1.43E-43	1.23	0.36	0.9481	0.99(0.75-1.3)
rs1569723	20	44.74	CD40,MMP9,PLTP,(11)	0.26	9.95E-14	1.09	0.29	0.1511	1.1(0.96-1.26)
rs913678	20	48.95	CEBPB,(5)	0.66	4.59E-08	1.06	0.36	0.6658	1.03(0.91-1.17)
rs259964	20	57.82	ZNF831,CTSZ,(5)	0.46	1.01E-12	1.09	0.45	0.3988	1.05(0.93-1.19)
rs6062504	20	62.34	TNFRSF6B,LIME1,SLC2A4RG,ZGPAT,(23)	0.68	1.09E-23	1.10	0.24	0.01028	0.83(0.72-0.96)
rs2823286	21	16.81	0	0.71	9.28E-30	1.16	0.31	0.2405	0.92(0.81-1.05)
rs2836878	21	40.46	(3)	0.73	4.62E-48	1.18	0.22	0.002151	0.8(0.69-0.92)
rs7282490	21	45.62	ICOSLG,(9)	0.39	2.35E-26	1.11	0.41	0.01328	1.17(1.03-1.33)
rs2266959	22	21.92	MAPK1,YDJC,UBE2L3,RIMBP3,CCDC116,(8)	0.19	1.39E-16	1.11	0.21	0.1496	1.12(0.96-1.31)
rs2412970	22	30.425	LIF,OSM,MTMR3,(8)	0.46	2.70E-14	1.08	0.49	0.1398	1.1(0.97-1.24)
rs2413583	22	39.69	ATF4,TAB1,APOBEC3G,(16)	0.83	4.40E-33	1.21	0.16	0.06078	0.85(0.73-1.01)

Replication results of 133 reported UC risk loci. Chr: Chromosome; Mb: Megabase (middle of locus window as described in Jostins et al. Nature 2012)

Genes: Key gene/genes in the risk locus. In parenthesis (number of additional genes in locus)

RAF: Risk allele frequency in metaanalysis of Northern European ancestry populations

P-value(1): association significance in metaanalysis of Northern European ancestry populations

OR(1): Odds ratio of associated SNP in metaanalysis of Northern European ancestry populations

MAF(2): Minor allele frequency in Southern European UC GWAS

P-value(2): association significance in Southern European UC GWAS

OR(2): Odds ratio of associated SNP in Southern European UC GWAS

**Supplementary Table S2: 61 GWAS loci with significant association with UC (P<5e-4) and replication results in the independent dataset.**

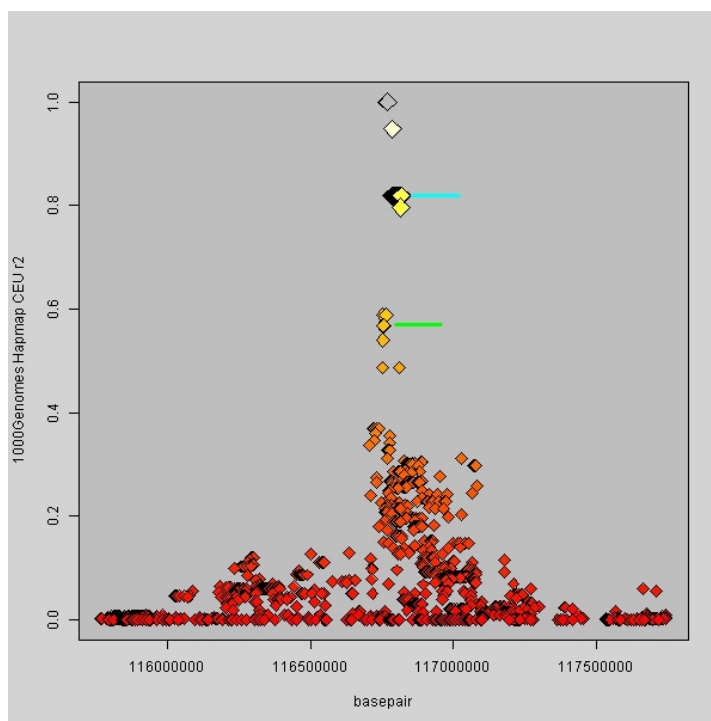
CHR	SNP	Locus	location	pb	OR_GWAS	OR_REPL	P_GWAS	P_REPL	P_COMB
1	rs11804649	<i>FLJ36116</i>	flanking 3'UTR	113348570	1.47	1.1	0.0000316	0.143	0.00006
1	rs964555	<i>SELL</i>	intron	169671088	0.67	0.99	0.000064	0.48	0.00035
1	rs9659337	<i>SIPA1L2</i>	flanking 3'UTR	232379496	0.73	1.01	0.000082	0.56	0.0005
<b>2</b>	<b>rs11679592</b>	<b><i>MYT1L</i></b>	<b>flanking 5'UTR</b>	<b>2406488</b>	<b>1.28</b>	<b>1.16</b>	<b>0.000064</b>	<b>0.0097</b>	<b>0.0000094</b>
2	rs12990137	<i>LOC729769</i>	flanking 3'UTR	26223547	1.29	0.97	0.000058	0.67	0.00043
2	rs17537701	<i>LOC130865</i>	flanking 5'UTR	60928367	0.74	0.95	0.000077	0.277	0.000251
<b>2</b>	<b>rs8179646</b>	<b><i>GPD2</i></b>	<b>flanking 3'UTR</b>	<b>157598678</b>	<b>1.31</b>	<b>1.17</b>	<b>0.000037</b>	<b>0.0094</b>	<b>0.0000055</b>
2	rs11694601	<i>OLA1</i>	intron	174949358	1.28	1	0.00012	0.48	0.00062
2	rs6756374	<i>SLC39A10</i>	intron	196587670	1.29	0.91	0.000199	0.92	0.00176
3	rs4234517	<i>FBLN2</i>	flanking 3'UTR	13756808	0.75	1.01	0.000107	0.59	0.00067
<b>3</b>	<b>rs358803</b>	<b><i>CACNA2D3-WNT5A</i></b>	<b>flanking 3'UTR</b>	<b>55318709</b>	<b>1.27</b>	<b>1.13</b>	<b>0.00033</b>	<b>0.034</b>	<b>0.000141</b>
3	rs11130567	<i>SPATA12</i>	flanking 5'UTR	57074119	0.78	1.03	0.000071	0.69	0.00053
3	rs1835898	<i>PRICKLE2</i>	intron	64121290	0.78	1.07	0.000092	0.86	0.00082
3	rs169059	<i>MAGI1</i>	intron	65780364	1.44	1.13	0.000049	0.095	0.000061
3	rs9288930	<i>PLCXD2</i>	intron	111538899	1.3	1.05	0.000026	0.233	0.000079
<b>4</b>	<b>rs11133504</b>	<b><i>Chr4q12</i></b>	<b>flanking 3'UTR</b>	<b>58380322</b>	<b>0.71</b>	<b>0.75</b>	<b>0.0000248</b>	<b>0.000237</b>	<b>0.000000117</b>
4	rs10022714	<i>ATOH1</i>	flanking 5'UTR	94741522	1.26	0.89	0.00035	0.97	0.00308
4	rs11724903	<i>ODZ3</i>	flanking 5'UTR	183200145	0.75	1.01	0.000124	0.56	0.00073
5	rs1030191	<i>ODZ2</i>	flanking 5'UTR	166743702	1.27	1.08	0.000122	0.113	0.000168
6	rs1737766	<i>LOC646800</i>	flanking 5'UTR	1361844	0.74	0.95	0.000008	0.234	0.0000267
<b>6</b>	<b>rs1924466</b>	<b><i>KIF13A</i></b>	<b>intron</b>	<b>17772764</b>	<b>1.28</b>	<b>1.16</b>	<b>0.000098</b>	<b>0.0104</b>	<b>0.000015</b>
6	rs2745639	<i>KRT18P50</i>	intron	96376639	0.74	0.96	0.00000299	0.258	0.0000117
6	rs4440501	<i>FRK</i>	flanking 3'UTR	116058859	1.25	0.97	0.00045	0.72	0.00293
7	rs6953766	<i>TWIST1</i>	flanking 3'UTR	19134119	0.77	1.01	0.00033	0.59	0.00183
7	rs2041017	<i>7A5</i>	flanking 5'UTR	20280329	0.66	0.93	0.000032	0.252	0.000104
7	rs6462063	<i>JAZF1</i>	intron	28099570	1.27	0.86	0.000111	0.99	0.00111
7	rs701308	<i>SEMA3A</i>	flanking 3'UTR	83562164	1.28	0.97	0.000082	0.7	0.00061
<b>7</b>	<b>rs4725479</b>	<b><i>ACTR3B</i></b>	<b>flanking 3'UTR</b>	<b>152745810</b>	<b>0.75</b>	<b>0.84</b>	<b>0.0000049</b>	<b>0.0056</b>	<b>0.00000051</b>
8	rs2922861	<i>ANGPT2</i>	flanking 5'UTR	6435875	0.8	0.98	0.00043	0.4	0.00165
8	rs12156170	<i>WISP1</i>	flanking 5'UTR	134188778	1.34	0.92	0.000095	0.87	0.00086
9	rs12552514	<i>GLDC</i>	flanking 5'UTR	6665593	1.47	1.01	0.000079	0.46	0.00041
9	rs9695318	<i>LOC158345</i>	flanking 3'UTR	7348292	0.78	1.13	0.000085	0.97	0.00086

9	rs408960	<i>PTPRD</i>	flanking 5'UTR	9069839	0.76	1.03	0.000233	0.66	0.0015
9	rs843282	<i>CYLC2</i>	flanking 5'UTR	105625399	1.4	1.08	0.00008	0.191	0.000186
9	rs10817777	<i>41974</i>	flanking 3'UTR	118255516	0.79	0.97	0.000271	0.34	0.00095
<b>10</b>	<b>rs4747437</b>	<b><i>MLL710</i></b>	<b>intron</b>	<b>22030023</b>	<b>1.27</b>	<b>1.17</b>	<b>0.000174</b>	<b>0.0091</b>	<b>0.0000228</b>
10	rs2489701	<i>CCNYL2</i>	flanking 3'UTR	42896183	0.74	1.16	0.000118	0.98	0.00116
10	rs2642575	<i>COL13A1</i>	flanking 5'UTR	71543168	0.73	0.9	0.0000035	0.08	0.0000045
10	rs869244	<i>SHOC2</i>	flanking 3'UTR	112909105	0.77	1	0.000064	0.51	0.00037
<b>10</b>	<b>rs4246949</b>	<b><i>CPXM2</i></b>	<b>intron</b>	<b>125517080</b>	<b>0.76</b>	<b>0.82</b>	<b>0.000106</b>	<b>0.004</b>	<b>0.0000067</b>
11	rs2450129	<i>GAB2</i>	intron	77940385	0.67	0.98	0.0000041	0.41	0.0000239
11	rs12223674	<i>DSCAML1</i>	intron	117451256	0.75	1.12	0.000036	0.95	0.00038
12	rs5745879	<i>RFC5</i>	intron	118467645	0.64	1.17	0.000122	0.91	0.00112
12	rs10774497	<i>CCDC60</i>	intron	119837041	1.31	1.02	0.00007	0.4	0.00032
13	rs985035	<i>SLITRK1</i>	flanking 3'UTR	84262897	1.3	0.96	0.0000282	0.77	0.000254
13	rs6492073	<i>LOC728215</i>	intron	108387359	1.43	1.01	0.000112	0.48	0.00059
13	rs2477466	<i>C13orf16</i>	flanking 5'UTR	111971579	1.34	1.06	0.000078	0.245	0.000228
14	rs12892100	<i>RGS6</i>	intron	72478034	1.33	1.01	0.0000135	0.47	0.000082
15	rs1975242	<i>RYR3</i>	intron	33801207	1.28	0.98	0.000086	0.65	0.0006
<b>15</b>	<b>rs4776239</b>	<b><i>UNC13C</i></b>	<b>flanking 3'UTR</b>	<b>54967175</b>	<b>1.4</b>	<b>1.2</b>	<b>0.000068</b>	<b>0.017</b>	<b>0.000017</b>
15	rs10851649	<i>MYO1E</i>	intron	59610743	1.43	0.89	0.000097	0.9	0.00091
15	rs7180683	<i>LOC728163</i>	flanking 5'UTR	85926546	0.72	0.87	0.000078	0.059	0.000061
16	rs1159778	<i>RBFOX1-TMEM114</i>	intergenic	8224988	1.43	0.91	0.000059	0.86	0.00055
17	rs7221150	<i>PIPOX</i>	flanking 3'UTR	27387415	1.71	1.01	0.000042	0.49	0.00024
17	rs4098686	<i>FZD2</i>	flanking 5'UTR	42629737	1.34	0.94	0.0000159	0.82	0.00016
18	rs10503022	<i>NEDD4L</i>	intron	55991546	1.34	0.92	0.000119	0.89	0.00107
19	rs945704	<i>LONP1</i>	intron	5704353	1.62	1.16	0.000047	0.114	0.000071
20	rs2229205	<i>OPRL1</i>	coding	62729431	0.73	0.93	0.000094	0.224	0.000247
21	rs2014791	<i>NCAM2</i>	flanking 3'UTR	23145950	0.78	1.02	0.000056	0.65	0.00041
21	rs2833400	<i>TIAM1</i>	intron	32790952	0.74	0.91	0.000275	0.133	0.00041
21	rs7279991	<i>DIP2A</i>	intron	47905496	0.78	0.99	0.000053	0.42	0.000261

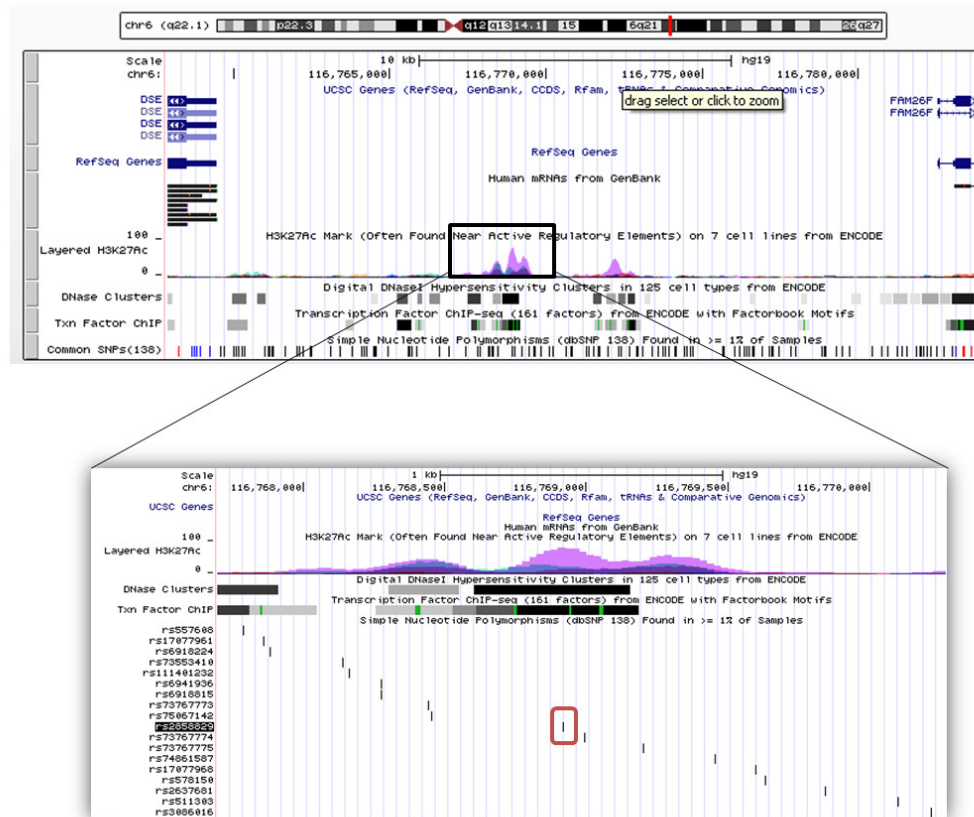
In light grey, SNPs replicated at  $P < 0.05$  with the same effect size as in the GWAS.

CHR: chromosome; pb: pairbase; P\_COMB: combined P-value of GWAS and replication cohorts

**Supplementary Figure S1. LD patterns of SNP rs2858829 with SNPs at +/- 200 kb**



**Supplementary Figure S1. Linkage disequilibrium plot for rs2858829.** All SNPs identified in the 1KG project are plotted according to their  $r^2$  values with respect to rs2858829 (grey diamond). Heat colors go from 0 (no LD,  $r^2 = 0$ ) to yellow and white (highest LD,  $r^2 > 0.8$ ). SNPs showing significant association with the regulation of *FAM26F* gene expression are rs2858829 (blue arrow), and rs479454 (green arrow).



**Supplementary Figure S2. University of California Santa Cruz (UCSC) genome browser visualization of the ENCODE elements in the rs2858829 region in chromosome 6q22.1.** In the upper figure, the location of the rs2858829 SNP region in relation to the two flanking genes *DSE* and *FAM26F*. The lower figure represents the zoomed visualization of the ENCODE elements that overlap the SNP associated with risk to UC. rs2858829 SNP location is highlighted with a red box. Several regulatory elements can be found to be enriched in this particular region including high acetylation of histone H3 at lysine 27 (associated to enhancer activity), clustering of DNase hypersensitive areas (associated to gene expression regulation) and ChIP-seq derived evidence of DNA-binding motifs (associated to transcription factor function).

Supplementary Table S3: List of UC microarray studies and FAM26F differential expression results					
GEO ID	Species	Comparison	Probe	Significance	Sense
GDS4365	<i>H. sapiens</i>	UCActiveInvolvedMucosavsControl	229391_s_at	1.88E-05	overexpr. in UC
GDS4365	<i>H. sapiens</i>	UCActiveInvolvedMucosavsControl	229390_at	2.93E-05	overexpr. in UC
GDS4365	<i>H. sapiens</i>	UCActiveInvolvedMucosavsUCActiveNon-InvolvedMucosa(pairec	229390_at	3.73E-05	overexpr. in involved mucosa
GDS3859	<i>M. musculus</i>	Day6vsDay0	1436576_at	6.00E-05	overexpr. in UC
GDS4365	<i>H. sapiens</i>	UCActiveInvolvedMucosavsUCActiveNon-InvolvedMucosa(pairec	229391_s_at	2.58E-04	overexpr. in involved mucosa
GDS3859	<i>M. musculus</i>	Day4vsDay0	1436576_at	0.00093	overexpr. in UC
GDS3268	<i>H. sapiens</i>	UC_inflamed_descendingcolonvsNormal_uninflamed_descending	28352	0.00095	overexpr. in UC
GDS3119	<i>H. sapiens</i>	UC_inflamedvsNormal	229390_at	0.0022	overexpr. in UC
GDS3119	<i>H. sapiens</i>	UC_inflamedvsNormal	229391_s_at	0.0026	overexpr. in UC
GDS3119	<i>H. sapiens</i>	UC_inflamedvsNormal	228362_s_at	0.0037	overexpr. in UC
GDS4367	<i>M. musculus</i>	UCvsNormal	1436576_at	0.0103	overexpr. in UC
GDS4365	<i>H. sapiens</i>	UCActiveInvolvedMucosavsControl	229543_at	0.022	overexpr. in UC
GDS4365	<i>H. sapiens</i>	UCActiveInvolvedMucosavsControl	228362_s_at	0.033	overexpr. in UC
GDS3119	<i>H. sapiens</i>	UC_Non-inflamedvsNormal	229390_at	0.033	overexpr. in UC
GDS3119	<i>H. sapiens</i>	UC_Non-inflamedvsNormal	229391_s_at	0.046	overexpr. in UC
GDS3859	<i>M. musculus</i>	Day2vsDay0	1436576_at	NS	NA
GDS4270	<i>H. sapiens</i>	RespondervsNon-Responder	8121596	NS	NA
GDS4365	<i>H. sapiens</i>	UCActive_NonInvolvedMucosavsControl	228362_s_at	NS	NA
GDS4365	<i>H. sapiens</i>	UCRemissionInvolvedMucosavsControl	228362_s_at	NS	NA
GDS4365	<i>H. sapiens</i>	UCActive_NonInvolvedMucosavsControl	229390_at	NS	NA
GDS4365	<i>H. sapiens</i>	UCRemissionInvolvedMucosavsControl	229390_at	NS	NA
GDS4365	<i>H. sapiens</i>	UCActive_NonInvolvedMucosavsControl	229391_s_at	NS	NA
GDS4365	<i>H. sapiens</i>	UCRemissionInvolvedMucosavsControl	229391_s_at	NS	NA
GDS4365	<i>H. sapiens</i>	UCActive_NonInvolvedMucosavsControl	229543_at	NS	NA
GDS4365	<i>H. sapiens</i>	UCRemissionInvolvedMucosavsControl	229543_at	NS	NA
GDS4365	<i>H. sapiens</i>	UCActiveInvolvedMucosavsControl	229915_at	NS	NA
GDS4365	<i>H. sapiens</i>	UCActive_NonInvolvedMucosavsControl	229915_at	NS	NA
GDS4365	<i>H. sapiens</i>	UCRemissionInvolvedMucosavsControl	229915_at	NS	NA
GDS4365	<i>H. sapiens</i>	UCActiveInvolvedMucosavsUCActiveNon-InvolvedMucosa(pairec	228362_s_at	NS	NA
GDS4365	<i>H. sapiens</i>	UCActiveInvolvedMucosavsUCActiveNon-InvolvedMucosa(pairec	229543_at	NS	NA
GDS4365	<i>H. sapiens</i>	UCActiveInvolvedMucosavsUCActiveNon-InvolvedMucosa(pairec	229915_at	NS	NA
GDS3268	<i>H. sapiens</i>	UC_inflamed_ascendingcolonvsNormal_uninflamed_ascendingcc	28352	NS	NA
GDS3268	<i>H. sapiens</i>	UC_inflamed_sigmoidcolonvsNormal_uninflamed_sigmoidcolon	28352	NS	NA
GDS3119	<i>H. sapiens</i>	UC_Non-inflamedvsNormal	228362_s_at	NS	NA
GDS3119	<i>H. sapiens</i>	UC_Non-inflamedvsNormal	229543_at	NS	NA

**Supplementary Table S5: Common genes in human and mouse FAM26F network**

<b>Gene_Name*</b>	<b>mouse_GDS4367</b>	<b>mouse_GDS3859</b>	<b>human_GDS4365</b>	<b>human_GDS3268</b>	<b>human_GDS3119</b>
<b>ARHGAP25</b>	2.35E-05	0.000118312	0.014399671	<1E-23	6.30E-09
<b>ARHGDIB</b>	0.000128147	9.52E-05	0.001599385	<1E-23	0.021863148
<b>CD300A</b>	0.000817717	1.36E-06	1.17E-12	<1E-23	1.23E-10
<b>CD40</b>	4.90E-06	3.38E-06	4.22E-12	<1E-23	1.65E-08
<b>CD53</b>	0.000272753	0.000208231	5.31E-13	<1E-23	6.06E-09
<b>CD84</b>	0.007528962	5.35E-06	2.42E-07	0.004612808	1.26E-08
<b>CIITA</b>	0.00024629	0.000816589	6.98E-10	0.01688149	4.58E-08
<b>CORO1A</b>	7.30E-06	7.06E-05	1.22E-10	<1E-23	8.73E-08
<b>CXCL10</b>	6.45E-08	3.61E-07	7.55E-15	<1E-23	1.29E-08
<b>CXCL9</b>	8.15E-06	2.21E-08	8.44E-15	<1E-23	2.45E-11
<b>CYTIP</b>	9.41E-05	0.00019031	1.96E-11	<1E-23	7.81E-08
<b>DOCK2</b>	7.67E-06	3.53E-08	1.67E-10	<1E-23	7.24E-08
<b>GBP2</b>	0.000485104	2.61E-07	7.63E-11	1.01E-12	7.99E-10
<b>GIMAP4</b>	1.33E-08	0.001731292	2.34E-09	<1E-23	5.18E-08
<b>GIMAP6</b>	6.28E-05	0.000360336	9.09E-07	3.51E-11	1.99E-06
<b>GMFG</b>	0.000388185	0.000896592	2.39E-12	<1E-23	5.96E-09
<b>IL18BP</b>	0.00072555	2.18E-05	0.030569386	0.001525193	5.19E-08
<b>LAIR1</b>	5.22E-07	0.000106098	9.10E-11	8.88E-16	6.58E-08
<b>LAPTM5</b>	1.92E-05	2.35E-05	3.73E-11	<1E-23	3.04E-09
<b>LCP1</b>	0.000626194	3.54E-07	1.67E-11	<1E-23	6.17E-10
<b>LYN</b>	0.001059532	8.98E-05	4.42E-11	<1E-23	2.30E-07
<b>NCKAP1L</b>	0.00059753	5.98E-05	2.19E-12	<1E-23	6.75E-10
<b>PSMB9</b>	0.00092084	2.22E-06	4.98E-09	2.66E-15	5.63E-09
<b>PTPRC</b>	4.02E-06	1.94E-06	1.88E-10	<1E-23	0.008497052
<b>RASSF5</b>	0.000297352	0.00056142	2.39E-07	<1E-23	1.85E-07
<b>SLAMF8</b>	1.90E-06	0.000223502	1.97E-09	<1E-23	1.32E-07
<b>TNFSF13B</b>	0.002914637	0.005789256	1.44E-11	<1E-23	1.30E-07
<b>WIPF1</b>	0.000619911	3.45E-06	7.00E-06	<1E-23	1.02E-08

\*Genes strongly correlated with *FAM36F* expression in all human UC studies AND in all mouse UC model studies

**Supplementary Table S7: Association results of the new UC risk candidate loci in the Northern European ancestry GWAS**

Gene	Location	SNP	CHR	BP	RISK	COF	SCAN-P	OR(95%)
MYT1L	3' flanking region	rs11679592	2	2406488	T	0.488	0.811	1.01(0.96-1.05)
GPD2	3' flanking region	rs8179646	2	157598678	C	0.606	0.763	1.01(0.96-1.05)
CACNA2D3-WNT5A	intergenic	rs358803	3	55318709	G	0.293	0.0603	1.04(1.00-1.09)
Chr4q12	intergenic	rs11133504	4	58380322	G	0.825	0.0281	1.06(1.00-1.12)
KIF13A	intron	rs1924466	6	17772764	C	0.553	0.595	1.01(0.97-1.05)
ACTR3B	3' flanking region	rs4725479	7	152745810	T	0.427	0.999	1.00(0.96-1.04)
MLLT10	intron	rs4747437	10	22030023	G	0.6	0.179	1.03(0.99-1.07)
CPXM2	intron	rs4246949	10	125517080	T	0.234	0.521	1.02(0.96-1.08)

*CHR: Chromosome, BP: Basepair; RISK: Risk Allele; COF: Frequency of risk allele in control cohort.*

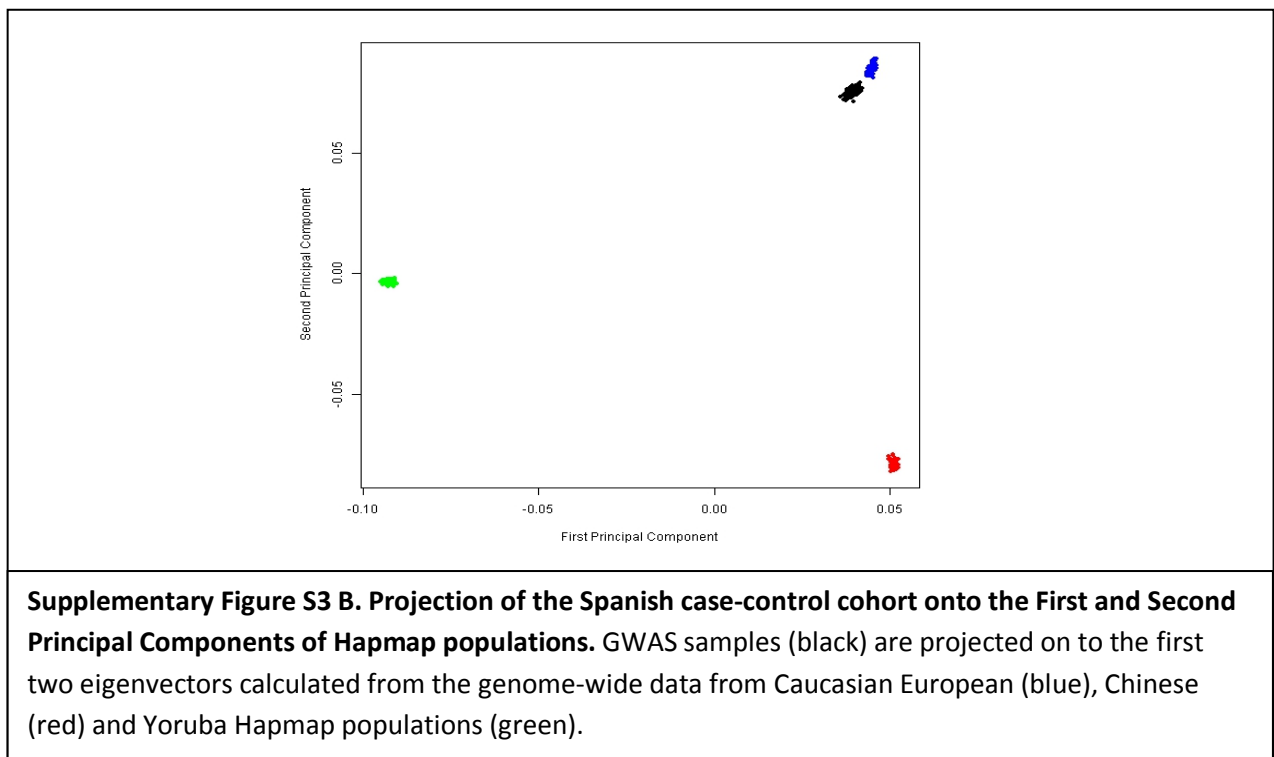
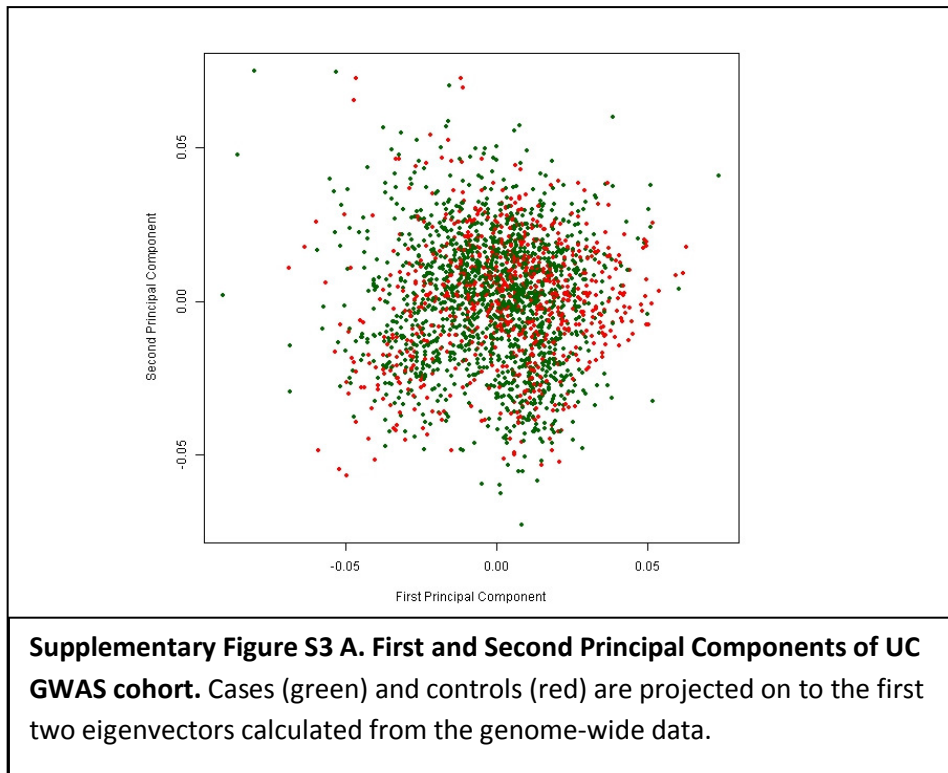
*SCAN-P: P-value of association to UC risk; OR: Odds Ratio.*

**Supplementary Table S8. List of the gastroenterology departments form Spanish University Hospitals participating in the IMIDC project and in the present study**

<b>Hospital Name</b>	<b>Spanish Province</b>	<b>PI</b>
Hospital Clínico Universitario de Santiago	La Coruña	Manuel Barreiro
Hospital Universitari Germans Trias i Pujol	Barcelona	Eugeni Domènech
Hospital Universitario Reina Sofía	Córdoba	Valle García
Hospital de la Santa Creu i Sant Pau	Barcelona	Esther García-Planella
Hospital General de Alicante	Alicante	Ana Gutiérrez
Hospital Clínico San Carlos	Madrid	Juan Luís Mendoza
Hospital Universitario de la Princesa	Madrid	Javier Pérez-Gisbert
Hospital Clínic i Provincial de Barcelona	Barcelona	Julià Panés
Hospital Universitari i Politècnic La Fe	Valencia	Pilar Nos Mateu
Hospital Clínico Universitario Lozano Blesa	Zaragoza	Fernando Gomollón
Complejo Hospitalario de León	León	Fernando Muñoz
Hospital Universitario Puerta de Hierro	Madrid	Maribel Vera
Mútua de Terrasa	Barcelona	Maria Esteve Comas
Hospital Clínico Universitario de Santiago	La Coruña	Manuel Barreiro

Gastroenterology departments participating in the IMIDC and their respective University Hospitals and geographic location in Spain (i.e. province). PI: Principal Investigator/s.

### **Supplementary Figures S3 A and S3B**



**Supplementary Table S9. List of microarray studies in ulcerative colitis and study design**

<b>GEO Accession#</b>	<b>Reference Publ. (Pmed ID)</b>	<b>Sample origin</b>	<b>Study Design</b>	<b>Sample size</b>	<b>Differential expression?</b>
<b>GDS4367</b>	22610167	Mouse	DSS induced UC vs saline (control); colorectal tissue obtained at 0-2-6-4-8-20 weeks.	3 replicates each subgroup.	Yes.
<b>GDS3859</b>	20923862	Mouse	Time-series DSS-induced UC (0-2-4-6 days). Colorrectal tissue.	3 replicates each subgroup.	Yes.
<b>GDS4270</b>	20941359	Human	Whole blood RNA, from pediatric UC patients responder vs non responder to IVCS therapy (day 3 of treatment)	20 replicates each subgroup.	Yes.
<b>GDS4365</b>	23135761	Human	Colonic biopsies from controls and UC patients (involved, non- involved mucosa).	12 controls, 15 UC involved mucosa, 7 UC non-involved mucosa and 8 UC in remission.	Yes.

<b>GDS3268</b>	18523026	Human	Colonic biopsies from normal controls and UC patients: inflamed/uninflamed ascending colon/descending colon/sigmoid colon/terminal ileum.	Normal (n=73: AC=17, DC=23, SC=27, TI=6),  Uninflamed UC (n=66: AC=21, DC=15, SC=15, TI=5), Inflamed UC (n=63: AC=11, DC=19, SC=32, TI=1).	Yes.
<b>GDS3119</b>	19177426	Human	Colonic mucosa from UC patients (inflamed & non-inflamed) and controls	5 Controls and 21 UC patients (8 inflamed).	Yes.