Supplementary Notes

FibroGENE Cohort Descriptions

Women's Genome Health Study (WGHS)

WGHS is part of the Women's Health Study (WHS), a prospective cohort of female North American health-care professionals, who provided a blood sample at baseline and consented for blood-based analyses. All participants were at least 45 years of age, free of cardiovascular disease, cancer, or other major chronic illnesses at the time of consent. Health- and lifestyle-related information were collected via questionnaires at enrollment and follow-up time points. WHS participants were asked whether they had ever been diagnosed with UL and their age at diagnosis. Cases were defined as women who self-reported 'yes' to having a history of UL, while controls were classified as women who self-reported 'no'. Women who reported an age of UL diagnosis < 20 or > 70 years of age were excluded from the analysis. Participants in WGHS were recruited under an IRB-approved protocol by the Partners HealthCare System Human Research Committee. For this study, a total of 12,840 women of white European ancestry were included: 3,375 UL cases and 9,465 controls.

Northern Finland Birth Cohort (NFBC)

NFBC includes two longitudinal and prospective birth cohorts of white European women and offspring collected at 20-year intervals from the same provinces of Oulu and Lapland in Finland: NFBC1966 and NFBC1986. In this study, we utilized data from NFBC1966. Cases (n=363) with a history of UL were identified through national outpatient and inpatient hospital discharge registers and self-reported diagnosis through postal questionnaire at age 46. The hospital discharge

registers include WHO ICD codes for identification of disease diagnoses and dates for each hospital visit. Controls (n=5,000) were drawn from the rest of the cohort population. Informed consent was obtained from all participants using protocols approved by the Ethical Committee of the Northern Ostrobothnia Hospital District.

QIMR Berghofer Medical Research Institute (QIMR)

In the QIMR cohort women were originally recruited into a study examining predisposition to endometriosis[1] and a twin study of gynecological health[2]. For both studies, women completed questionnaires on various aspects of their reproductive health. Participants who answered "yes" to the "uterine fibroids" option of the question "Have you ever had any of the following conditions?" were selected as cases (n=1,484). Controls (n=3,701) were drawn from twin pairs in the gynecological health study in which both sisters answered "no" to a question about medical history of uterine fibroids (one sample per twin pair). Informed consent was obtained from all participants. Approval for the studies was granted by the Human Research Ethics Committee at the QIMR and the Australian Twin Registry.

UK Biobank

UK Biobank includes samples of over 500,000 individuals (aged 45-69 years) collected in 2006-2010 from across the United Kingdom along with data from electronic health records, interviews with trained research nurses, and web-based questionnaires[3]. For this study, altogether 220,936 women of European ancestry were considered. Based on both hospital-linked medical records and self-report (interview with research nurse), women with a history of UL were selected as cases (n=15,184), while controls (n=205,752) had no previous history of UL. Informed consent was

obtained from all participants. The UK Biobank project is approved by the North West Multi-centre Research Ethics Committee.

23andMe Cohort

Participants were drawn from the customer base of 23andMe (Mountain View, CA, USA). For this study, the 23andMe cohort included 58,655 unrelated European women. Data on participants' history of UL were collected via self-report in online surveys. Medical history of UL was determined with the research question, "Have you ever been diagnosed with uterine fibroids?", which had three response options: yes, no, and not sure. Females who answered "yes" were selected as cases, those who answered "no" as controls, and those who answered "not sure" were excluded from the study, resulting in 15,068 cases and 43,587 controls. All 23andMe research participants provided informed consent and answered surveys online according to a human subjects protocol approved by Ethical and Independent Review Services, an external institutional review board.

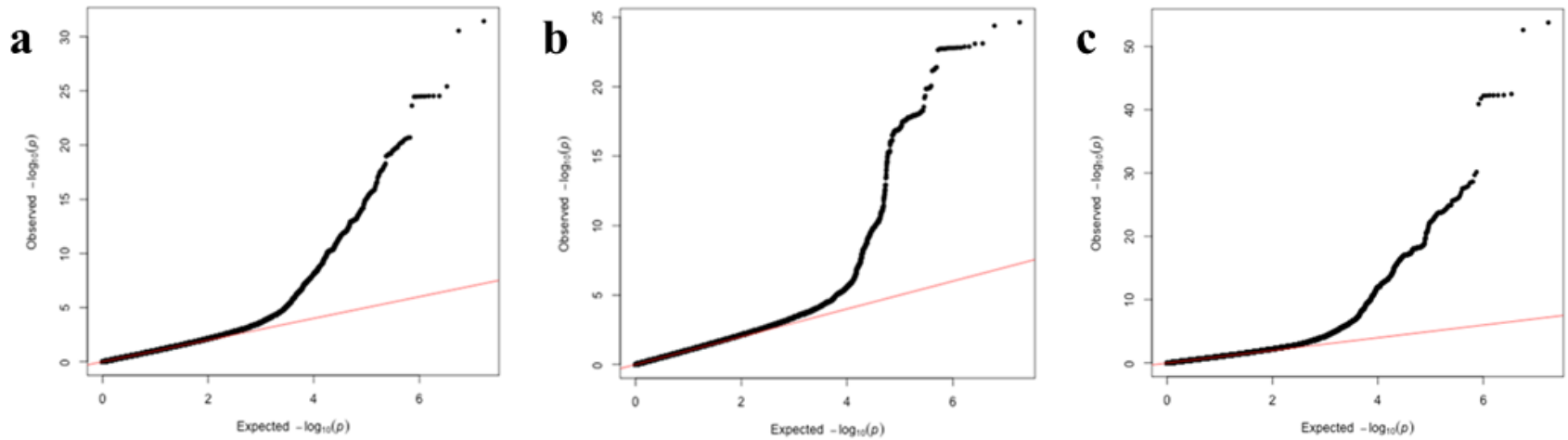
References

1. Treloar SA, Wicks J, Nyholt DR, et al. Genomewide linkage study in 1,176 affected sister pair families identifies a significant susceptibility locus for endometriosis on chromosome 10q26. Am J Hum Genet 2005;77:365-76.

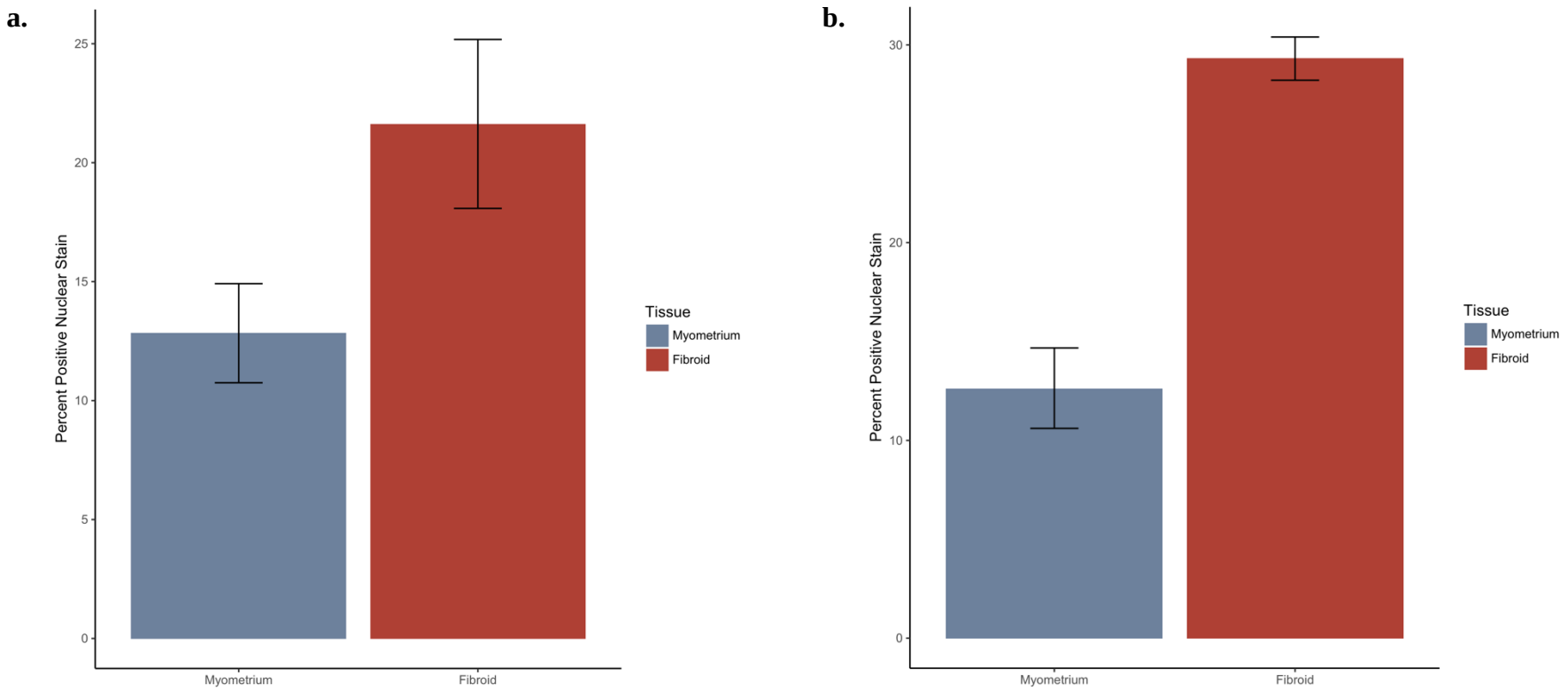
2. Treloar SA, Do KA, O'Connor VM, O'Connor DT, Yeo MA, Martin NG. Predictors of hysterectomy: an Australian study. Am J Obstet Gynecol 1999;180:945-54.

3. Sudlow C, Gallacher J, Allen N, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. PLoS Med 2015;12:e1001779.

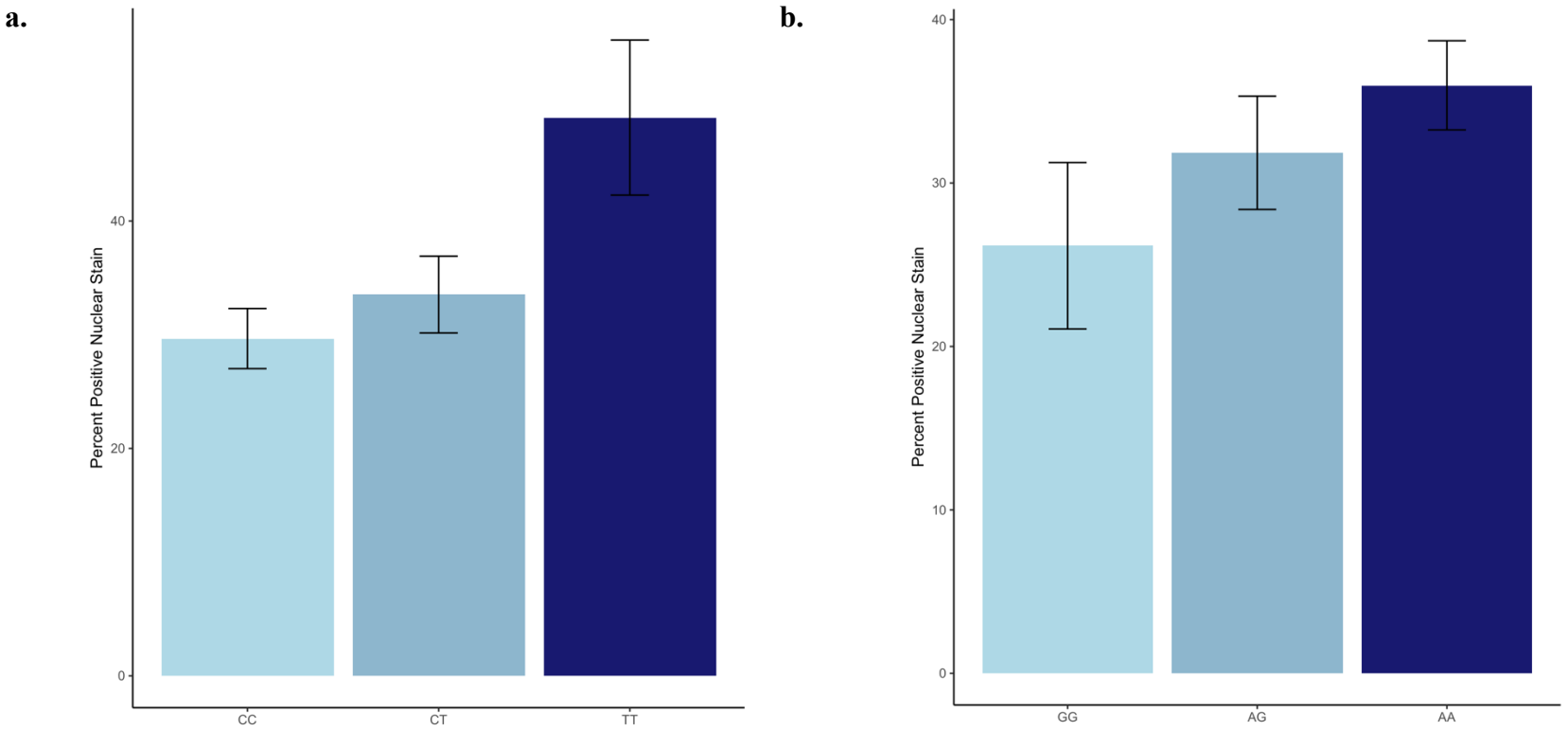
Supplementary Figures and Table



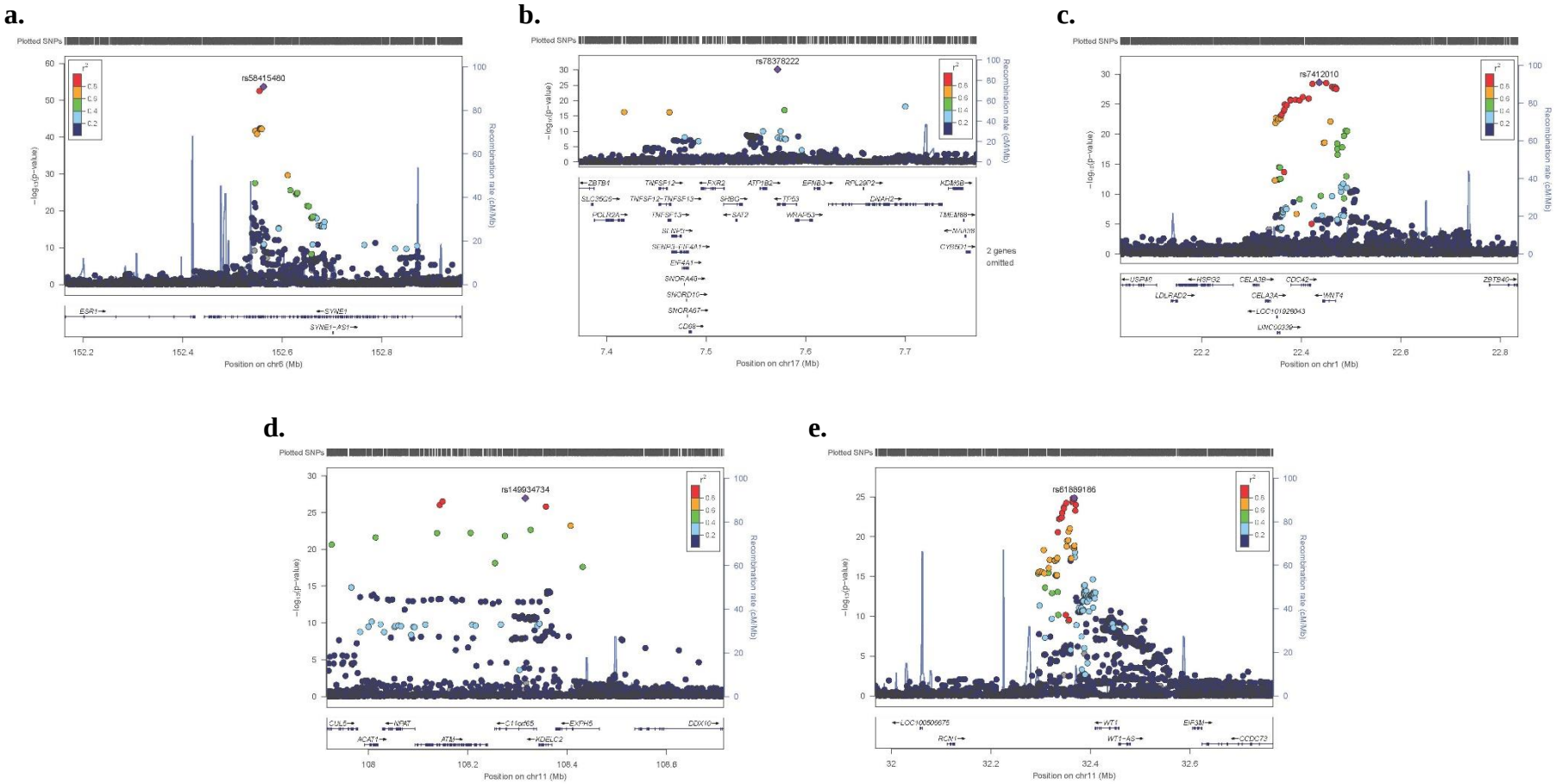
Supplementary Fig. 1 Quantile-quantile plots. a) Quantile-quantile plot of *P*-values observed in meta-analysis of UL GWAS conducted in 244,324 women from population-based cohorts. Genomic inflation factor (γ_{GC} = 1.025) indicates modest inflation in χ^2 test statistic. **b)** Quantile-quantile plot of *P*-values observed in UL GWAS conducted in 58,655 women from 23andMe direct-to-consumer cohort. Genomic inflation factor (γ_{GC} = 1.051) indicates modest inflation in the χ^2 test statistic. **c)** Quantile-quantile plot of *P*-values observed in meta-analysis of UL GWAS conducted in 302,979 women from the FibroGENE consortium. Genomic inflation factor (γ_{GC} = 1.020) indicates modest inflation in the χ^2 test statistic. The diagonal red line represents expected distribution of observed *P*-values under the null hypothesis of no association. Of note, scales of the y axis differ between plots.



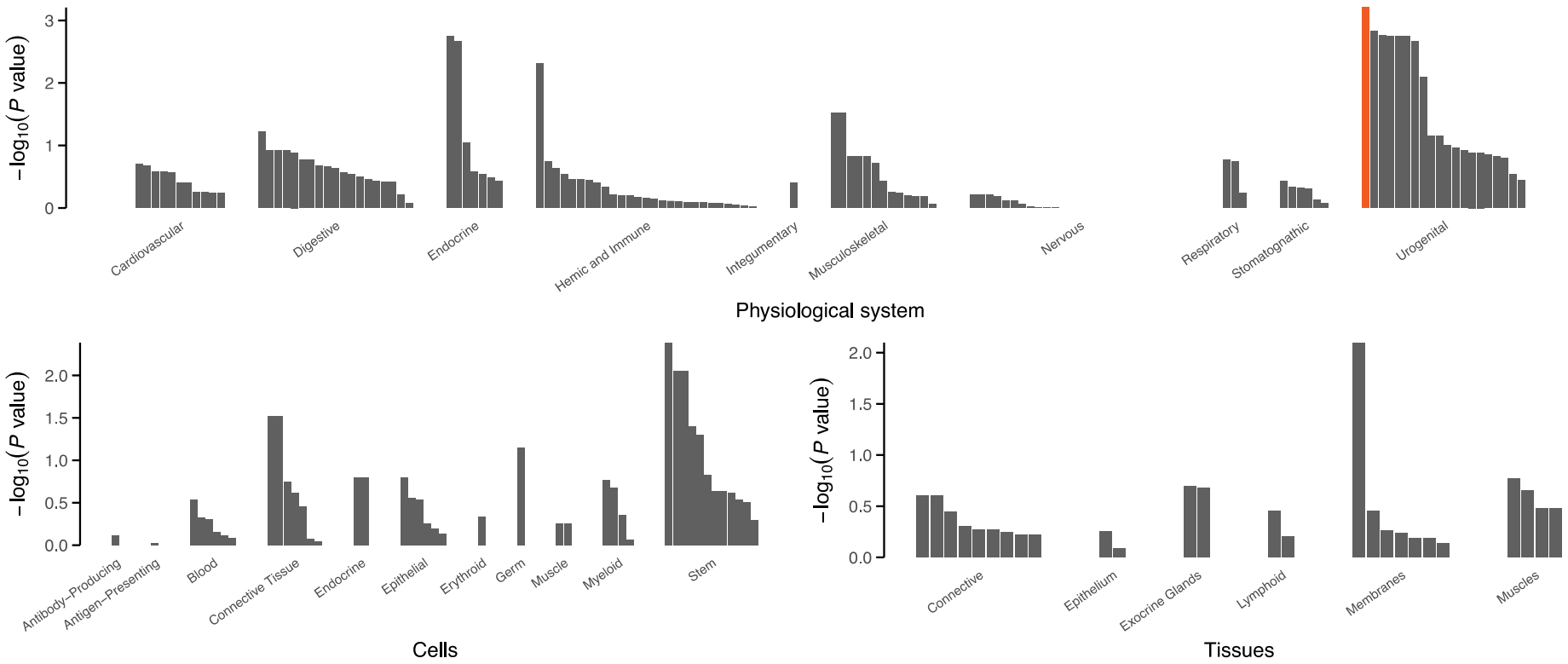
Supplementary Fig. 2 FOXO1 immunostaining. **a)** Nuclear expression of FOXO1 is 1.69-fold greater in UL compared to patient-matched myometrial samples. Percent of positive nuclei were quantified in 40 UL and 34 myometrium samples (six patients with two UL) replicated on two separate tissue microarrays. Average number of positively-stained nuclei was significantly higher in UL than myometrial tissue (t = 2.60, degrees of freedom (df) = 39, P = 0.01). **b)** Nuclear expression of FOXO1 is 2.32-fold greater in UL compared to myometrial samples. Percent of positive nuclei were quantified in 335 UL and 35 myometrium samples replicated on two separate tissue microarrays. Average number of positively-stained nuclei was significantly higher in UL than myometrial tissue (t = 7.22, df = 56, $P = 1.52 \times 10^{-9}$).



Supplementary Fig. 3 Stratification of nuclear FOXO1 expression by genotype. FOXO1 expression and genotypes were quantified and determined in a total of 109 UL. **a)** One-way analysis of variance showed a significant relationship between allelic dosage of the rs6563799 risk variant [T] and FOXO1 expression ($F = 3.2$, df = 2, $P = 0.047$). To compare mean expression of UL homozygous for the risk variant [T] against those with C/C or C/T genotypes, we performed an unpaired *t*-test ($t = 2.51$, df = 8, $P = 0.035$). **b)** One-way analysis of variance showed no significant relationship between allelic dosage of the rs7986407 risk variant [A] and FOXO1 expression ($F = 1.5$, df = 2, $P = 0.22$). To compare mean expression of UL homozygous for the risk variant against those with G/G or G/A genotypes, we performed an unpaired *t*-test ($t = 1.49$, df = 105, $P = 0.14$).



Supplementary Fig. 4 Regional association plots for five top loci in the meta-analysis across all cohorts. **a)** Chromosome 6q25.2. **b)** Chromosome 17p13.1. **c)** Chromosome 1p36.12. **d)** Chromosome 11q22.3. **e)** Chromosome 11p13. The labeled SNP represents the most significant SNP for each locus. SNP association *P*-value is shown on the y axis, while SNP position (with gene annotation) appears on the x axis. Each SNP is colored according to the strength of LD with the lead SNP. Plots were produced in LocusZoom.



Supplementary Fig. 5 Tissue enrichment analysis. Results from DEPICT-based tissue enrichment analysis of 162 independent lead SNPs identified from 5,185 SNPs with suggestive ($P < 1 \times 10^{-5}$) or significant associations ($P < 5 \times 10^{-8}$). Red indicates significant gene-set enrichment with FDR < 0.05.

Supplementary Table 1. GWAS Cohorts. Four conventional population-based cohorts and one direct-to-consumer cohort from the FibroGENE consortium were included in the genome-wide association analyses.

Cohorts	Cases[a]	Controls[a]	Total
Conventional Population-Based Cohorts	20,406	223,918	244,324
Women's Genome Health Study (WGHS)	3,375	9,465	12,840
Northern Finnish Birth Cohort (NFBC)	363	5,000	5,363
Queensland Institute of Medical Research (QIMR)	1,484	3,701	5,185
UK Biobank	15,184	205,752	220,936
Direct-to-Consumer Cohort			
23andMe	15,068	43,587	58,655
Total	35,474	267,505	302,979

[a] Cases and controls defined solely based on self-report or clinically documented history of uterine leiomyomata

Supplementary Table 2. Statistics of GWAS Cohorts. Overview of genomic inflation factor (γ_{GC}) used for adjustments and total number of SNPs analyzed in the GWA analyses.

Cohort	γ_{GC}	N_{SNP}
WGHS	1.008	8,767,907
NFBC	1.006	8,424,735
QIMR	0.998	8,279,309
UKBB	1.061	10,308,721
23andMe	1.051	9,164,495
Meta-Analysis	1.020	8,519,088

Supplementary Table 3. Results of the discovery-phase meta-analysis. Overview of peak SNPs with significant associations ($P < 5 \times 10^{-8}$) in meta-analyses of GWAS conducted in four population-based cohorts across 244,324 women of white European ancestry.

Locus	rsID	*P*	OR (95% CI)	P_{Het}	Genes of interest[a]
1p36.12[b]	rs2235529	$7.39e^{-21}$	1.14 (1.11 - 1.17)	**0.015**[d]	*WNT4, CDC42*
1q24.3	rs59760198	$2.76e^{-08}$	1.06 (1.04 - 1.08)	0.412	*DNM3*
2p25.1[b]	rs10929757	$1.19e^{-12}$	1.07 (1.05 - 1.10)	0.368	*GREB1*
3q26.2	rs2293607	$4.06e^{-08}$	1.07 (1.04 - 1.09)	0.007	*TERC*
4q12	rs4864806	$5.95e^{-14}$	1.16 (1.12 - 1.21)	0.302	*LNX1, PDGFRA*
4q13.3	rs12640488	$3.83e^{-10}$	1.06 (1.04 - 1.09)	0.087	*SULT1B1*
5p15.33	rs72709458	$6.07e^{-15}$	1.11 (1.08 - 1.13)	0.050	*TERT*
5q35.2	rs2456181	$5.62e^{-09}$	1.07 (1.05 - 1.09)	0.021	*ZNF346, UIMC1*
6q25.2[b]	rs58415480	$3.65e^{-32}$	1.18 (1.15 - 1.21)	0.204	*SYNE1, ESR1*
9p24.3	rs10815466	$5.63e^{-13}$	1.11 (1.08 - 1.14)	0.139	*ANKRD15*
10q24.3[c]	rs9419958	$1.20e^{-09}$	1.09 (1.06 - 1.12)	0.243	*OBFC1, SLK*
11p15.5[c]	rs547025	$4.78e^{-13}$	1.15 (1.11 – 1.19)	0.223	*RIC8A, BET1L*
11p14.1[b]	rs11031006	$2.91e^{-08}$	1.08 (1.05 - 1.12)	0.134	*FSHB*
11p13	rs11031731	$2.04e^{-21}$	1.14 (1.11 - 1.17)	0.136	*WT1*
11p13	rs2553772	$1.20e^{-08}$	1.06 (1.04 - 1.08)	0.206	*PDHX, CD44*
11q22.3	rs149934734	$7.05e^{-19}$	1.34 (1.26 - 1.43)	**0.035**[d]	*C11orf65, KDELC2*
12q13.11	rs9669403	$1.57e^{-09}$	1.06 (1.04 - 1.09)	0.513	*SLC38A2*
12q24.31	rs641760	$7.64e^{-09}$	1.07 (1.05 - 1.10)	0.446	*PITPNM2*
13q14.11	rs1986649	$1.07e^{-11}$	1.09 (1.06 - 1.11)	0.140	*FOXO1*
16q12.1	rs66998222	$2.29e^{-08}$	1.07 (1.05 - 1.10)	0.052	
17p13.1	rs78378222	$3.84e^{-26}$	1.64 (1.50 - 1.80)	**0.001**[d]	*SHBG, TP53*
20p12.3	rs16991615	$2.83e^{-08}$	1.12 (1.08 - 1.17)	0.963	*MCM8, TRMT6*
22q13.1[c]	rs12484776	$4.08e^{-12}$	1.09 (1.06 - 1.12)	0.437	*TNRC6B*
Xp22.2	rs181473301	$2.24e^{-11}$	1.98 (1.62 - 2.42)	< 0.001	

[a] ≤ 300 kb distant from association signal
[b] Loci previously associated with endometriosis
[c] Loci previously associated with UL
[d] Peak SNP had significant heterogeneity ($P < 0.05$), but second significant SNP in LD had non-significant heterogeneity.

Supplementary Table 4. Results from meta-analysis across all cohorts. Overview of peak SNPs with significant associations ($P < 5 \times 10^{-8}$) in meta-analyses of GWAS conducted in 302,979 women of white European ancestry.

Locus	rsID	P_{Meta}	OR (95% CI)	Genes of interest[a]
1p36.12[b]	rs7412010	2.43e^{-29}	1.13 (1.11 – 1.16)	*WNT4, CDC42*
2p23.2	**rs55819434**	**5.59e^{-09}**	**1.09 (1.06 – 1.12)**	***BABAM2***
2p25.1[b]	rs35417544	2.32e^{-19}	1.09 (1.07 – 1.10)	*GREB1*
3q26.2	rs35446936	1.03e^{-08}	1.06 (1.04 – 1.08)	*TERC*
4q12	rs62323682	4.92e^{-18}	1.15 (1.12 – 1.19)	*LNX1, PDGFRA*
4q13.3	rs12640488	4.00e^{-14}	1.06 (1.05 – 1.08)	*SULT1B1*
4q22.3	**rs4699299**	**4.72e^{-08}**	**1.05 (1.03 – 1.07)**	***PDLIM5***
5p15.33	rs72709458	4.66e^{-21}	1.10 (1.08 – 1.13)	*TERT*
5q35.2	rs2456181	1.14e^{-11}	1.06 (1.04 – 1.08)	*ZNF346, UIMC1*
6p21.31	**rs116251328**	**2.95e^{-08}**	**1.15 (1.09 – 1.21)**	***GRM4, HMGA1***
6q25.2[b]	rs58415480	1.86e^{-54}	1.19 (1.17 – 1.22)	*SYNE1, ESR1*
7q31.2	**rs2270206**	**4.64e^{-08}**	**1.06 (1.04 – 1.09)**	***WNT2***
9p24.3	rs10976689	2.37e^{-13}	1.06 (1.05 – 1.08)	*ANKRD15*
10q24.3[c]	rs9419958	1.05e^{-16}	1.10 (1.08 – 1.13)	*OBFC1, SLK*
10p11.22	**rs10508765**	**1.51e^{-10}**	**1.07 (1.05 – 1.09)**	***ZEB1, ARHGAP12***
11p15.5[c]	rs547025	1.45e^{-14}	1.13 (1.09 – 1.16)	*RIC8A, BET1L*
11p14.1[b]	rs11031006	5.65e^{-15}	1.10 (1.07 – 1.12)	*FSHB*
11p13	rs61889186	1.39e^{-25}	1.12 (1.10 – 1.15)	*WT1*
11p13	rs2785202	6.94e^{-14}	1.06 (1.05 – 1.08)	*PDHX, CD44*
11q22.3	rs149934734	1.10e^{-27}	1.33 (1.26 – 1.40)	*C11orf65, KDELC2*
12q13.11	rs2131371	1.62e^{-18}	1.08 (1.06 – 1.10)	*SLC38A2*
12q15	**rs11178393**	**3.34e^{-08}**	**1.08 (1.05 – 1.10)**	***PTPRR***
12q24.31	rs28583837	2.31e^{-08}	1.06 (1.04 – 1.08)	*PITPNM2*
13q14.11	rs117245733	5.69e^{-14}	1.31 (1.21 – 1.39)	*FOXO1*
17p13.1	rs78378222	7.11e^{-31}	1.54 (1.43 – 1.66)	*SHBG, TP53*
20p12.3	rs16991615	8.82e^{-10}	1.11 (1.07 – 1.14)	*MCM8, TRMT6*
22q13.1[c]	rs4821939	7.83e^{-16}	1.08 (1.06 – 1.10)	*TNRC6B*

Bolded loci are novel discoveries in the meta-analysis.
[a] ≤ 300 kb distant from association signal
[b] Loci previously associated with endometriosis
[c] Loci previously associated with UL

Supplementary Table 5. Independent loci identified from 5,185 SNPs with suggestive ($P < 1 \times 10^{-5}$) or significant associations ($P < 5 \times 10^{-8}$) for DEPICT analyses.

Chr	BP	SNP	*P*	NTotal	Nsig
1	22384713	rs12035094	2.03e-09	16	12
1	22436446	rs7412010	2.43e-29	312	57
1	22508922	rs2807370	6.91e-07	115	51
1	28793149	rs61748637	6.19e-06	88	36
1	59718153	rs147305679	2.40e-06	1	0
1	163924366	rs1579807	9.83e-06	136	46
1	172137119	rs672740	1.26e-07	347	82
1	242011344	rs1776180	3.76e-06	132	19
1	244314952	rs2183478	5.77e-07	7	3
1	244364293	rs12745147	8.44e-06	36	1
1	249191706	rs4335411	6.77e-08	47	9
2	11306978	rs3951242	3.04e-08	385	149
2	11575780	rs77332934	2.83e-06	3	1
2	11660955	rs77294520	5.87e-09	33	1
2	11680403	rs35417544	2.32e-19	117	0
2	12102123	rs62115045	7.17e-08	131	21
2	17942230	rs2081601	5.40e-06	132	25
2	27598097	rs4665972	6.21e-06	360	139
2	28072550	rs57309923	4.48e-06	145	142
2	28333109	rs55819434	5.59e-09	379	18
2	62782323	rs17025727	5.07e-06	27	19
2	67090367	rs17631680	9.39e-06	46	21
2	100109913	rs10186340	6.17e-07	591	24
2	135292926	rs542851	1.39e-06	267	123
2	135778708	rs7593284	1.59e-06	93	3
2	136290607	rs59605931	2.19e-07	968	22
2	173150012	rs68130068	4.17e-07	121	96
2	177770340	rs6712128	1.05e-06	359	106
2	202865534	rs12612045	1.10e-07	200	92
2	226531574	rs10933107	6.88e-06	292	161
2	239888052	rs6543539	2.91e-06	105	15
3	4716214	rs3804984	2.42e-07	23	11
3	4719426	rs4684436	1.51e-07	33	20
3	11649334	rs11712416	5.69e-07	339	106
3	24223206	rs4858583	1.09e-06	123	39
3	27331854	rs543882	1.31e-06	904	331
3	57957040	rs1658367	4.68e-06	400	129
3	128119565	rs760383	2.32e-06	575	278
3	156786437	rs10936060	2.52e-06	203	100
3	169486508	rs35446936	1.03e-08	217	100
3	183558402	rs3732581	1.29e-06	438	320
3	185490240	rs13073992	5.37e-08	109	10
4	8040251	rs114887409	4.65e-06	9	3
4	18223649	rs150497359	3.44e-06	187	145
4	31290995	rs150544012	3.62e-06	8	6
4	53858948	rs116112143	2.20e-06	71	26
4	54550174	rs62323682	4.92e-18	65	17
4	55804691	rs114726826	5.26e-06	6	3
4	70600738	rs12640488	4.00e-14	327	74
4	70700567	rs75699008	2.41e-07	31	20
4	95501166	rs4699299	4.72e-08	279	24
4	99952710	rs1037475	3.30e-06	599	328
4	103761862	rs223369	7.60e-07	896	59

Chr	BP	SNP	*P*	NTotal	Nsig
5	1267356	rs4246742	1.83e-06	46	4
5	1277577	rs33961405	1.30e-08	5	2
5	1283755	rs72709458	4.66e-21	35	0
5	1322654	rs34880677	3.21e-06	80	3
5	132436392	rs28548389	4.60e-06	419	152
5	141600807	rs72801930	5.32e-06	1	1
5	176450837	rs2456181	1.14e-11	173	25
6	31380422	rs115387084	7.39e-06	1769	1436
6	31580507	rs114075146	6.28e-06	381	241
6	34177510	rs116251328	2.95e-08	109	0
6	34181995	rs9357174	4.04e-06	375	324
6	36651284	rs3176348	6.23e-06	152	24
6	37108380	rs7741267	8.60e-06	83	14
6	70973766	rs12195966	6.44e-06	172	125
6	108944165	rs3813498	2.04e-07	193	98
6	109376118	rs11153158	3.76e-06	283	21
6	152526179	rs2763025	8.73e-08	35	4
6	152539054	rs1408461	7.29e-19	55	7
6	152562271	rs58415480	1.86e-54	113	9
6	152592680	rs75510204	1.67e-09	6	1
6	152593102	rs6904757	4.61e-16	34	2
6	152626689	rs9383984	3.74e-07	0	0
6	152629586	rs9371581	1.34e-07	27	7
6	152644111	rs7738189	2.98e-06	14	8
6	152648145	rs9371585	8.62e-10	96	22
6	152658342	rs201427355	5.59e-09	0	0
6	152872272	rs9397523	8.48e-10	141	80
6	152880372	rs148780923	5.31e-08	9	0
7	20781414	rs62453391	9.12e-06	219	52
7	33048397	rs4723230	4.80e-06	360	85
7	116913567	rs2270206	4.64e-08	110	35
7	120759424	rs2968338	1.03e-07	316	22
7	130620723	rs35908158	3.32e-06	53	3
8	30310335	rs13275869	7.03e-06	326	164
8	129518281	rs1516980	1.38e-06	333	20
9	680714	rs10815466	2.17e-12	221	63
9	720492	rs10976044	1.11e-06	11	7
9	804886	rs10976689	2.37e-13	179	70
9	827224	rs2277163	2.43e-07	56	11
9	860004	rs7021646	2.29e-07	80	33
9	876418	rs11790408	1.42e-07	89	24
9	92116564	rs11265780	3.43e-06	304	195
9	137174079	rs11185709	6.54e-06	10	7
10	21806832	rs946711	9.29e-07	402	220
10	31968783	rs10508765	1.50e-10	129	25
10	68370790	rs2394216	4.86e-07	142	32
10	90091540	rs1426619	2.12e-07	358	28
10	105659369	rs3850670	3.89e-08	259	141
10	105675946	rs9419958	1.04e-16	185	26
10	126782331	rs1152677	6.02e-06	163	53
11	218141	rs3847647	9.49e-07	234	145
11	224063	rs12222188	2.70e-10	36	6
11	232855	rs547025	1.45e-14	67	11
11	270071	rs10751644	1.99e-06	30	18
11	14242862	rs147235561	9.30e-06	43	15
11	30226528	rs11031006	5.65e-15	388	5
11	30561123	rs523639	4.37e-06	198	127
11	32359961	rs12807010	2.69e-06	29	23

Chr	BP	SNP	*P*	NTotal	Nsig
11	32367570	rs61889186	1.39e-25	460	5
11	32371215	rs932503	4.44e-13	46	13
11	32433044	rs5030233	6.68e-06	67	63
11	32441111	rs7114908	1.93e-11	119	4
11	32911258	rs4633439	6.39e-06	395	287
11	35084835	rs2785202	6.94e-14	176	10
11	108315606	rs149934734	1.10e-27	53	2
11	108359689	rs72993806	4.84e-15	185	39
11	108371924	rs79088165	2.78e-09	123	103
11	128363717	rs11604768	2.93e-06	50	24
12	46650396	rs34792811	5.59e-08	8	1
12	46796522	rs2131371	1.62e-18	447	5
12	46949205	rs12230643	2.88e-09	29	6
12	54566379	rs12827282	2.70e-06	106	49
12	66836183	rs76103439	5.88e-06	13	7
12	71150658	rs11178393	3.34e-08	76	11
12	110507991	rs148526428	6.14e-07	371	37
12	123296204	rs138062324	7.52e-06	46	38
12	123863620	rs28583837	2.31e-08	478	104
13	40300545	rs9548898	3.22e-09	236	27
13	40487456	rs9532454	2.77e-07	69	0
13	40706991	rs12872985	5.69e-06	109	24
13	40723944	rs117245733	5.68e-14	1	0
13	40736289	rs6563799	2.23e-10	106	15
13	40836913	rs17061057	2.76e-06	18	5
13	40843805	rs6563812	7.88e-09	29	2
13	41179798	rs7986407	2.02e-13	393	73
13	71715091	rs61957931	8.56e-06	90	20
14	29977679	rs1191561	7.92e-06	13	0
14	53163421	rs145576330	6.11e-06	61	39
14	93101528	rs10147131	5.98e-06	105	37
15	68213895	rs436903	6.72e-07	399	132
15	68611051	rs60103704	7.59e-06	109	22
16	51481596	rs66998222	5.05e-08	193	29
16	75158095	rs62059211	4.37e-06	114	71
17	7540735	rs7210750	1.57e-09	151	22
17	7571752	rs78378222	7.11e-31	21	0
17	27004703	rs7207976	6.34e-06	111	30
17	29250911	rs11867227	7.61e-07	132	50
17	41370074	rs34981932	4.63e-06	617	111
19	22260842	rs62110991	1.58e-06	970	82
19	22660286	rs11878410	8.58e-06	10	7
20	5948227	rs16991615	8.82e-10	39	26
20	56019801	rs8115191	2.88e-07	101	50
20	62441599	rs6062322	9.37e-06	140	74
21	24595021	rs182209255	1.85e-06	6	4
21	36445050	rs6517273	5.83e-06	90	35
22	36683555	rs9610482	3.77e-07	111	43
22	40535963	rs2179422	8.96e-07	189	43
22	40546525	rs79499264	2.12e-07	15	3
22	40659251	rs4821939	7.83e-16	504	39

Lead SNP is reported with genomic location as indicated by chromosome (**Chr**) and base-pair (**BP**), as well as the total number of genes (**NTotal**) and significant genes (**Nsig**) in associated locus.

Supplementary Table 7. RegulomeDB results. Up to 30 most significant SNPs from each of the 27 loci identified in meta-analysis of GWAS across all cohorts were considered. Listed below are all SNPs with RegulomeDB score under 3, indicating their likely involvement in gene regulation. SNPs in bold are potential eQTLs.

rsID	Chr	Base pair	Cytoband	RegulomeDB score	Interpretation	Genomic overlap
rs3820282	1	22468215	p36.12	2b	TF binding + any motif + DNase Footprint + DNase peak	Three WNT4 transcripts (intron variant)
rs79050195	1	22349386	p36.12	2b	TF binding + any motif + DNase Footprint + DNase peak	Four LINC00339 transcripts (upstream gene variant) One RP1-224A6.3 transcript (downstream gene variant)
rs12404660	1	22458794	p36.12	2b	TF binding + any motif + DNase Footprint + DNase peak	Four WNT4 transcripts (intron variant/upstream gene variant)
rs4669746	2	11682018	p25.1	2b	TF binding + any motif + DNase Footprint + DNase peak	Four GREB1 transcripts (intron variant/upstream gene variant) One MIR4429 transcript (upstream gene variant)
rs353490	5	176433063	q35.2	2b	TF binding + any motif + DNase Footprint + DNase peak	Eleven UIMC1 transcripts (intron variant)
rs114760566	6	34192036	p21.31	2b	TF binding + any motif + DNase Footprint + DNase peak	One CYCSP55 transcript (downstream gene variant)
rs12110479	6	152554396	q25.2	2b	TF binding + any motif + DNase Footprint + DNase peak	Eight SYNE1 transcripts (intron variant)
rs34800401	9	806736	p24.3	2b	TF binding + any motif + DNase Footprint + DNase peak	Regulatory region variant (CTCF binding site)
rs35469085	9	806912	p24.3	2b	TF binding + any motif + DNase Footprint + DNase peak	Regulatory region variant (CTCF binding site)
rs10815717	9	801571	p24.3	2b	TF binding + any motif + DNase Footprint + DNase peak	Regulatory region variant (promoter flanking region)
rs10115078	9	802053	p24.3	2b	TF binding + any motif + DNase Footprint + DNase peak	Regulatory region variant (promoter flanking region)
rs34379047	10	105644473	q24.33	2b	TF binding + any motif + DNase Footprint + DNase peak	Four OBFC1 transcripts (intron variant) One RP11-541N10.3 transcript (upstream gene variant)
rs498217	**11**	**249097**	**p15.5**	**1f**	**eQTL + TF binding / DNase peak**	**Fourteen PSMD13 transcripts (intron variant/upstream gene variant/ downstream gene variant)**
rs4071558	11	30344591	p14.1	2b	TF binding + any motif + DNase Footprint + DNase peak	Three ARL14EP transcripts (upstream gene variant)
rs7947350	11	30338842	p14.1	2b	TF binding + any motif + DNase Footprint + DNase peak	Intergenic variant
rs7106353	11	32351427	p13	2b	TF binding + any motif + DNase Footprint + DNase peak	One RP1-65P5.1 transcript (intron variant)
rs36034326	11	107903818	q22.3	2b	TF binding + any motif + DNase Footprint + DNase peak	Four CUL5 transcripts (intron variant)
rs11183479	12	46824164	q13.11	2b	TF binding + any motif + DNase Footprint + DNase peak	One RP11-96H19.1 transcript (intron variant)
rs3936214	12	46825812	q13.11	2b	TF binding + any motif + DNase Footprint + DNase peak	One RP11-96H19.1 transcript (intron variant)
rs11183478	12	46824066	q13.11	2b	TF binding + any motif + DNase Footprint + DNase peak	One RP11-96H19.1 transcript (intron variant)
rs1641528	**17**	**7548320**	**p13.1**	**1b**	**eQTL + TF binding + any motif + DNase Footprint + DNase peak**	**One ATP1B2 transcript (upstream gene variant)**

rs78378222	17	7571752	p13.1	2b	TF binding + any motif + DNase Footprint + DNase peak	Eighteen TP53 transcripts (3' UTR variant/intron variant/downstream gene variant)
rs4821942	22	40718100	q13.11	2c	TF binding + matched TF motif + DNase peak	Five TNRC6B transcripts (intron variant/downstream gene variant)