Supplementary Appendix

Supplementary Methods

This appendix provides operational details that complement the main-text Methods. The main manuscript summarizes the overall study design, datasets, primary analytical framework, and key thresholds, whereas the present appendix documents panel provenance, analysis-specific decision rules, supplementary sensitivity procedures, and evidence-integration details. All analyses were performed using summary-level data only, and no individual-level genotype or phenotype data were accessed. Layer-specific SMR summaries are provided in Supplementary Table S1, MR sensitivity analyses in Supplementary Table S2, public variant-level trait lookup summaries in Supplementary Table S3, druggability and tractability assessment in Supplementary Table S4, and summary colocalization evidence across retained candidate loci, molecular layers, pQTL panels, and evaluated windows in Supplementary Table S5.

1. Molecular QTL resources

1.1 Protein QTL resources

Protein-layer analyses were based on two independent plasma pQTL resources.[1,2] The first was the deCODE plasma proteomics dataset, in which plasma protein levels measured using 4907 SomaScan aptamers were analyzed in 35,559 Icelandic participants.[1] In the present study, the deCODE4907 SMR-formatted panel was used for source-specific MR screening and protein-layer SMR, whereas protein-layer colocalization used the available deCODE summary data for each candidate, including candidate-specific dense data where applicable. In the working exposure tables used here, protein-specific sample sizes ranged from 34,530 to 35,424.

The second resource was the UK Biobank Pharma Proteomics Project (UKB-PPP), which characterized plasma proteomic profiles in 54,219 UK Biobank participants using the Olink Explore 3072 platform and covered 2923 unique proteins.[2] The EuropeanDiscovery SMR-formatted panel was used as an independent resource for source-specific MR screening, protein-layer SMR, and colocalization analyses. In the working exposure tables used here, protein-specific sample sizes ranged from 13,082 to 34,090. The use of two pQTL resources allowed protein-layer consistency to be assessed across cohorts and proteomic platforms.[1,2]

1.2 eQTL and mQTL resources

Because infertility-relevant tissue-specific QTL resources were not consistently available, transcript- and methylation-layer analyses were performed using curated eQTL and mQTL reference panels in BESD format compatible with SMR.[3,4] These panels were used for both SMR and colocalization analyses. The panel or source

identifiers and molecular feature identifiers used in each analysis are reported in Supplementary Tables S1 and S5, with molecular QTL genome builds and window-specific details provided in Supplementary Table S5. Source-panel metadata and sample-size information are summarized above and in the corresponding source publications. For each retained locus and molecular layer, candidate transcripts or probes were first screened for evaluability. Features were excluded if they lacked usable overlap with the outcome dataset, lacked the minimum summary statistics required for SMR or colocalization, or did not yield an interpretable analysis result. When multiple evaluable features were available within a locus, one representative feature was selected for downstream colocalization using a prespecified hierarchy that prioritized data completeness, usable overlap with the outcome dataset, interpretable SMR output, and then strength of association among the remaining evaluable features.

2. Source-specific Mendelian randomization

2.1 Instrument selection and harmonization

Source-specific MR screening was performed separately in the deCODE and UKB-PPP pQTL resources, using FinnGen female infertility as the sole outcome.[1,2,5] Genetic instruments were selected within each pQTL source using prespecified rules. Variants were required to satisfy a significance threshold of $P < 5 \times 10^{-8}$ in the source-specific working pQTL tables and were restricted to cis-pQTLs located within ±1 Mb of the encoded gene. Source-level linkage disequilibrium clumping had already been applied to the working exposure tables using $r^2 < 0.001$ within a 10,000-kb window based on the 1000 Genomes Phase 3 European reference panel.[6] Palindromic variants with ambiguous strand orientation were removed during harmonization. Analyses were restricted to directly overlapping harmonized variants, and no systematic proxy-substitution procedure was implemented.

2.2 Estimation and multiple testing

For proteins instrumented by a single variant, causal estimates were derived using the Wald ratio. For proteins instrumented by multiple independent variants, the primary estimator was inverse-variance weighted Mendelian randomization. Effect estimates were aligned to the exposure-increasing allele. False discovery rate correction was applied within each source-specific MR screening round using the Benjamini–Hochberg procedure.

2.3 Candidate advancement

The first-stage MR screen was intended to identify proteins eligible for multilayer follow-up rather than to establish a rank order based on MR evidence alone. Within each source-specific analysis, FDR < 0.05 was considered statistically significant. Proteins with P < 0.005 in at least one source-specific analysis were also considered eligible for downstream multilayer evaluation, including signals that did not meet the FDR threshold. The availability and completeness of the relevant molecular QTL data determined whether individual SMR and colocalization analyses were evaluable.

Source-specific MR was used as an initial screening step, and no candidate ranking or priority-tier assignment was performed at this stage. Detailed MR sensitivity results are provided in Supplementary Table S2.

3. SMR analyses across molecular layers

SMR analyses were performed using SMR version 1.4.0, with heterogeneity in dependent instruments assessed using the HEIDI test.[7] SMR was carried out across the protein, transcript, and methylation layers. For each retained locus, the purpose of multilayer SMR was to determine whether one or more molecular layers warranted formal colocalization, rather than to require concordant support across all layers. Layer-specific SMR summaries are provided in Supplementary Table S1.

3.1 Protein-layer SMR

Protein-layer SMR used pQTL summary statistics from the deCODE and UKB-PPP resources.[1,2] For each retained locus, SMR was used to test whether a genetic signal associated with the molecular trait was also associated with female infertility. HEIDI testing was used to assess whether the observed association was compatible with a shared underlying signal rather than with linkage between distinct causal variants.[7]

3.2 Transcript-layer SMR

Transcript-layer SMR was performed analogously using the curated eQTL reference panel.[3] When multiple evaluable transcripts were available within a locus, one representative feature was selected for downstream colocalization according to the prespecified feature-selection hierarchy described above.

3.3 Methylation-layer SMR

Methylation-layer SMR was performed analogously using the curated mQTL reference panel.[4] When multiple evaluable CpG probes were available within a locus, one representative probe was selected for downstream colocalization according to the same prespecified hierarchy.

3.4 SMR support categories used for manuscript display

For manuscript display, SMR results were classified using a rule-based framework based on P_{SMR} and P_{HEIDI}. Results were classified as supported when $P_{SMR} < 0.05$ and PHEIDI > 0.05, and as borderline when $P_{SMR} < 0.05$ and $0.01 < P_{HEIDI} \leq 0.05$. Results were classified as unsupported when $P_{SMR} \geq 0.05$ or when $P_{SMR} < 0.05$ but $P_{HEIDI} \leq 0.01$. Analyses were classified as not evaluable when no interpretable SMR result was available or when a nominal SMR association was obtained but the HEIDI test could not be evaluated. The distinction between supported and borderline results was retained to convey the degree of HEIDI compatibility.

4. Colocalization analyses

Colocalization summaries by gene and layer are provided in Supplementary Table S5.

4.1 Framework and priors

Colocalization analyses were implemented using the coloc R package under the coloc.abf framework, assuming a single causal variant per locus.[8] Summary statistics were formatted using beta coefficients and standard errors where available, with the outcome specified as a case-control trait and the molecular trait specified as a quantitative trait. The primary priors were $p1 = 1 \times 10^{-4}$, $p2 = 1 \times 10^{-4}$, and $p12 = 1 \times 10^{-5}$. Analyses were restricted to variants present in both the outcome and molecular QTL datasets after allele harmonization.

4.2 Locus definition, genome-build handling, and window sensitivity analyses

For transcript- and methylation-layer analyses, regional molecular QTL variants were selected using coordinates from the corresponding molecular QTL reference panel. Because the molecular QTL panels and FinnGen outcome summary statistics were not consistently represented on the same genome build, FinnGen variants were not independently selected using the molecular QTL genomic coordinates. Instead, outcome summary statistics were retrieved for the molecular QTL variants by rsID and subsequently harmonized according to effect and other alleles. The resulting colocalization inputs were therefore molecular-QTL-anchored and based on rsID- and allele-matched variants. Protein-layer locus construction followed the coordinates and variant information available in the corresponding pQTL resource.

Primary analyses generally used molecular-QTL-anchored ±1-Mb regions centered on the relevant probe, molecular QTL feature, or locus anchor. For selected gene-layer pairs, additional ±500-kb and ±250-kb regions were evaluated as window-sensitivity analyses where sufficient overlapping variants were available. The ±1-Mb result was used for primary interpretation and manuscript display where evaluable. For ABO mQTL, no evaluable molecular QTL variants were available within the standard ±1-Mb region; therefore, a probe-centered ±2-Mb fallback region was examined. Because only a limited number of usable overlapping variants remained, this analysis was interpreted cautiously. Except for this explicitly documented fallback analysis, alternative windows were not substituted into the primary display solely because they produced a higher PP.H4 value. Gene-layer pairs with unavailable molecular data, incomplete summary statistics, or insufficient usable variant overlap were classified as not evaluable. Window-specific results and effective SNP overlap are reported in Supplementary Table S5.

4.3 Posterior probability interpretation

Posterior probabilities were recorded for the standard coloc hypotheses, with particular emphasis on PP.H3 and PP.H4.[8] Manuscript-level interpretation used the following thresholds: strong colocalization was defined as PP.H4 ≥ 0.8, suggestive colocalization as 0.2 ≤ PP.H4 < 0.8, and results were classified as inconclusive when PP.H4 < 0.2. Analyses were classified as not evaluable when posterior probabilities were unavailable or when overlap, locus structure, or data completeness was insufficient to support meaningful interpretation. PP.H3 was additionally inspected to identify cases in which the molecular QTL and infertility signals were more compatible with distinct causal variants than with a shared causal variant.

4.4 Cross-layer interpretation

Colocalization results were compared across the pQTL, eQTL, and mQTL layers to characterize the predominant pattern of molecular-layer support at each locus. Candidate-level interpretation considered the relative strength, evaluability, and robustness of shared-signal support across layers rather than relying on any single colocalization result alone.

5. MR sensitivity analyses and public trait lookup

Detailed MR sensitivity outputs are provided in Supplementary Table S2, and public variant-level trait lookup summaries are provided in Supplementary Table S3.

5.1 Internal MR sensitivity analyses

Where instrument count permitted, supplementary MR sensitivity analyses were performed to evaluate the robustness of the retained associations. When only one instrumental variant was available, the sensitivity analysis was limited to a Wald-ratio re-estimate, with approximate Steiger directionality assessment where possible.[9] When two or more instrumental variants were available, inverse-variance weighted MR and weighted median estimation were performed together with heterogeneity testing. When three or more variants were available, MR-Egger regression and MR-Egger intercept testing were additionally performed. The approximate Steiger procedure was based on case-count-informed reconstruction of variance explained from beta coefficients, standard errors, and effective sample-size information. When only a single instrumental variant was available, model-based pleiotropy diagnostics were necessarily limited.

Primary MR estimates reported in the main text, Table 1, and the main figures were obtained from the prespecified source-specific screening analyses. Supplementary Table S2 reports sensitivity-model re-estimates generated in TwoSampleMR using the corresponding harmonized instrument sets. Because estimator implementation and standard-error calculation differed between the primary screening and sensitivity workflows, standard errors and P values could differ slightly even when the underlying instruments and effect estimates were unchanged.

5.2 Public variant-level trait lookup

To place retained loci in a broader phenotypic context, selected instrumental variants from each retained locus were queried in publicly available variant–trait association resources, including the GWAS Catalog and the Open Targets Genetics platform.[10,11] The lookup variant set was defined for locus-level phenotypic contextualization and was not required to match the instrument count used in an individual source-specific MR sensitivity model. Accordingly, the six RELT variants queried in the public resources differed in number from the single deCODE4907 instrument used in the RELT sensitivity analysis summarized in Supplementary Table S2. Retrieved associations were collated into a combined variant-level summary and interpreted as contextual public trait lookup rather than as a newly performed phenome-wide association analysis.

5.3 Trait-domain grouping and descriptive pleiotropy categories

Retrieved trait labels were collapsed into broad domains using deterministic keyword-based grouping rules. The principal manuscript domains were cardiometabolic, hematologic, respiratory, molecular trait, musculoskeletal, and other. These grouped annotations were summarized descriptively to compare the breadth of reported cross-trait associations across loci. Differences in the number of queried variants and database coverage were considered when interpreting apparently sparse annotation. This step was used to support pleiotropy-aware interpretation rather than to override the primary genetic evidence chain.

6. Druggability and translational prioritization

Detailed druggability and tractability evidence is provided in Supplementary Table S4.

6.1 Information sources

Target class and tractability features were summarized using UniProt, the Open Targets Platform, and curated literature where relevant.[12,13] These resources were used to characterize target class, tractable family membership, feasible therapeutic modalities, and direct target-, pathway-, or target-family-level therapeutic precedent.

6.2 Assessment dimensions

For each retained candidate, the qualitative translational assessment summarized target class, target tractability, feasible therapeutic modality, clinical precedent, and reported public-trait breadth and pleiotropy context. Clinical precedent was distinguished as direct target-level, pathway-level, or target-family-level evidence where applicable. These annotations were interpreted together with the degree of mechanistic localization across molecular layers.

6.3 Translational prioritization rubric

The final manuscript used a pragmatic three-tier prioritization framework rather than a formally validated clinical scoring system. For Figure 6, target tractability, therapeutic modality, clinical precedent, and reported public-trait breadth and pleiotropy context were each represented using an ordinal score from 0 to 3, with higher values indicating a more favorable profile for candidate prioritization. These scores were used for qualitative visualization only, did not represent statistical effect estimates or uncertainty, and were not summed into a validated composite score.

Tier assignment was based on the integrated evidence chain rather than on the ordinal scores alone. Tier 1 designation reflected relatively coherent genetic support, clearer molecular-layer localization, and a comparatively favorable translational profile. Tier 2 reflected biologically informative candidates requiring greater caution because of pleiotropy, weaker translational precedent, or a less direct mechanistic chain. Tier 3 reflected retained secondary or background signals that remained scientifically informative but did not warrant near-term target-development emphasis.

6.4 Final evidence integration

Final candidate interpretation was based on five evidence domains: source-specific MR support, cross-layer SMR support, the predominant pattern of molecular-layer support from colocalization, pleiotropy context from public trait lookup, and therapeutic tractability. Candidate-level summaries are provided across Supplementary Tables S1–S5.

7. Software and implementation provenance

MR and sensitivity analyses were implemented in R version 4.4.1 using relevant packages including TwoSampleMR version 0.7.4. Additional data retrieval, preprocessing, and result integration were performed in Python version 3.10. SMR analyses were conducted using SMR version 1.4.0, and colocalization analyses were performed using coloc version 5.2.3.

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Supplementary Tables

Supplementary Table S1. Source- and layer-specific SMR results for focal candidates and an additional screened locus against FinnGen female infertility

target	candidate_status	molecular_layer	qtl_source	molecular_feature	feature_id	p_smr	p_heidi	nsnp_heidi	support_category
IL18	focal_retained	pQTL	deCODE	IL18	NA	NA	NA	NA	Not evaluable
IL18	focal_retained	pQTL	UKB-PPP	IL18	IL18_Q14116_OID20694_v1_Inflammation.gz.Q14116.IL18	0.03805631	0.0570776	20	Supported
IL18	focal_retained	eQTL	cis-eQTLs	IL18	ENSG00000150782	0.0001402784	0.02720375	20	Borderline
IL18	focal_retained	mQTL	mqtl-multiple	IL18	cg06862136	0.001163696	0.3609398	9	Supported
RELT	focal_retained	pQTL	deCODE	RELT	14112_40	0.003605029	0.9951575	20	Supported
RELT	focal_retained	pQTL	UKB-PPP	RELT	RELT_Q969Z4_OID21142_v1_Neurology.gz.Q969Z4.RELT	0.001466952	0.6402625	20	Supported
RELT	focal_retained	eQTL	cis-eQTLs	RELT	ENSG00000054967	0.006338319	0.2342343	20	Supported
RELT	focal_retained	mQTL	mqtl-multiple	P2RY6	cg21124714	0.0001822665	0.4402559	13	Supported
ABO	focal_retained	pQTL	deCODE	ABO	9253_52	0.003124338	0.0001901986	20	Unsupported
ABO	focal_retained	pQTL	UKB-PPP	ABO	ABO_P16442_OID30675_v1_Inflammation_II.gz.P16442.ABO	0.01136591	0.08915954	20	Supported
ABO	focal_retained	eQTL	cis-eQTLs	ABO	ENSG00000175164	0.07712882	0.2992766	20	Unsupported
ABO	focal_retained	mQTL	mqtl-multiple	NUP214	cg03811519	0.9909128	NA	NA	Unsupported
PILRB	screened_not_retained	pQTL	deCODE	PILRB	NA	NA	NA	NA	Not evaluable
PILRB	screened_not_retained	pQTL	UKB-PPP	PILRB	PILRB_Q9UKJ0_OID20197_v1_Cardiometabolic.gz.Q9UKJ0.PILRB	0.5155763	0.8849022	20	Unsupported
PILRB	screened_not_retained	eQTL	cis-eQTLs	PILRB	ENSG00000121716	0.8363282	0.2812942	20	Unsupported
PILRB	screened_not_retained	mQTL	mqtl-multiple	CLDN15	cg26968039	0.001314795	0.9713888	20	Supported

Supplementary Table S2. Sensitivity-model re-estimates for retained candidate loci

Gene	Outcome	pQTL panel	nSNP	Primary method	Beta (WR)	SE (WR)	P (WR)	Beta (IVW)	SE (IVW)	P (IVW)	Beta (WM)	SE (WM)	P (WM)	Beta (Egger)	SE (Egger)	P (Egger)	Cochran Q	Q P-value	Egger intercept	Egger intercept P	Steiger direction	Steiger P
RELT	N14_FEMALEINFERT	deCODE4907	1	Wald ratio	-0.6726	0.2087	0.001271	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Exposure to outcome	5.508E-06
IL18	N14_FEMALEINFERT	UKB-PPP	3	IVW	NA	NA	NA	-0.203	0.04373	3.467E-06	-0.2051	0.04255	1.43E-06	-0.2606	0.2374	0.4703	0.14	0.9324	0.01441	0.8458	Exposure to outcome	1.621E-180
ABO	N14_FEMALEINFERT	UKB-PPP	6	IVW	NA	NA	NA	0.07968	0.02028	8.52E-05	0.08687	0.02539	0.0006217	0.07191	0.05512	0.262	5.281	0.3825	0.00299	0.8846	Exposure to outcome	<1E-300

Supplementary Table S3. Public variant-level trait lookup summaries

gene	n_variants_queried	n_public_trait_hits	n_unique_traits	domains_with_hits	top_domain	n_domain_cardiometabolic	n_domain_hematologic	n_domain_respiratory	n_domain_molecular_trait	n_domain_musculoskeletal	n_domain_other	selected_representative_traits	pleiotropy_judgement
IL18	3	1	1	musculoskeletal	musculoskeletal	0	0	0	0	1	0	Bone mineral density (rs61901459, P = 2.03×10^{-28})	Sparse public annotation
RELT	6	23	17	cardiometabolic; hematologic; other; respiratory	cardiometabolic	8	7	3	0	0	5	Lung function (FEV1/FVC) (rs113689386, P = 1.00×10^{-30}) | Bicarbonate (mean, inv-norm transformed) (rs113689386, P = 4.98×10^{-20}) | Bicarbonate (minimum, inv-norm transformed) (rs113689386, P = 2.24×10^{-18}) | Diseases of veins, lymphatic vessels and lymph nodes, not elsewhere classified (rs113689386, P = 5.80×10^{-14}) | Varicose veins (rs113689386, P = 1.52×10^{-13})	Broad pleiotropic context; interpret cautiously
ABO	6	18	15	molecular trait; cardiometabolic	molecular trait	7	0	0	11	0	0	E-selectin levels (rs176694, P < 1×10^{-300}) | Alkaline phosphatase levels (rs7033492, P < 1×10^{-300}) | Soluble Tie-1 levels (rs56302081, P = 6.00×10^{-21}) | ERN1 protein levels (rs176694, P = 3.00×10^{-17}) | CTRC protein levels (rs176694, P = 2.00×10^{-16})	Broad pleiotropic context; interpret cautiously

Supplementary Table S4. Druggability and tractability assessment for retained candidates

gene	ensembl_id	target_class	known_biology	reproductive_relevance	genetic_support	predominant_layer_pattern	direct_target_tractability	feasible_therapeutic_modality	translational_precedent	clinical_maturity	safety_or_pleiotropy_caution	target_tractability_score	therapeutic_modality_score	clinical_precedent_score	specificity_pleiotropy_score	qualitative_tractability_category	priority_tier	final_interpretation
IL18	ENSG00001507082	Secreted cytokine	Pro-inflammatory cytokine in the IL-1 superfamily; extracellular pathway biology is compatible with ligand-neutralizing or pathway-blocking biologics.	Reported in endometrial and decidual biology and implicated in implantation-related inflammatory signaling.	Strong source-specific MR evidence for female infertility, supported by multilayer SMR and strong transcript-layer shared-signal evidence from eQTL colocalization.	Transcript-predominant support	High: secreted cytokine biology is directly tractable.	Ligand-neutralizing biologic or pathway-directed intervention.	Direct IL18/IL-18BP clinical programs provide pathway-level therapeutic precedent.	Pathway-level clinical precedent.	Sparse public pleiotropy annotation; immune-pathway modulation remains the main contextual caution.	3	3	3	3	High	Tier 1	IL18 is the strongest translational candidate in the current set because the genetic support is coherent and the target class is tractable, although it should still be described as a prioritized candidate rather than a validated target.
RELT	ENSG00000054967	TNFR-family membrane receptor	Orphan TNFR-family receptor with extracellular accessibility but limited direct functional and translational characterization.	No direct reproductive program established; plausibly relevant through broader TNFR-family biology rather than a fertility-specific mechanism.	Source-specific MR evidence with multilayer SMR support; the clearest colocalization support arose from the methylation layer, with additional suggestive pQTL colocalization across both protein panels.	Methylation-predominant support	Moderate: receptor-class target with extracellular accessibility.	Antibody-accessible receptor modulation.	No direct RELT program; precedent is limited to the broader TNFR family.	Family-level rationale only.	Broader cardiometabolic and hematologic public-trait context supports caution for pleiotropy.	2	2	1	1	Moderate	Tier 2	RELT remains an exploratory but tractable candidate. Its receptor biology supports tractability, but prioritization should be tempered by the pleiotropy background and weaker target-specific translational precedent.
ABO	ENSG00001751764	Glycosyltransferase enzyme	ABO blood-group glycosyltransferase with broad systemic glycan effects and	Associations with reproductive phenotypes are indirect and inconsiste	Retained secondary MR candidate with UKB-PPP protein-layer support,	No clearly localized predominant layer	Low-to-moderate: enzyme class is tractable in principle, but the specific	Context-limited; no clearly actionable modality identified in the current context.	No direct infertility-relevant therapeutic basis identified.	No direct clinical precedent.	Broad nonspecific pleiotropic background and limited target-specific actionability argue against	1	1	0	0	Low	Tier 3	ABO should be retained only as a secondary/background candidate. The signal lacks clear mechanistic localization and

gene	ensembl_id	target_class	known_biology	reproductive_relevance	genetic_support	predominant_layer_pattern	direct_target_tractability	feasible_therapeutic_modality	translational_precedent	clinical_maturity	safety_or_pleiotropy_caution	target_tractability_score	therapeutic_modality_score	clinical_precedent_score	specificity_pleiotropy_score	qualitative_tractability_category	priority_tier	final_interpretation
			a highly pleiotropic genetic background.	nt, with no clear fertility-specific therapeutic rationale.	but inconsistent evidence across pQTL sources, no convincing transcript- or methylation-layer colocalization, and limited cross-layer convergence.		target context is not clearly actionable here.				near-term prioritization.							is not a priority for fertility-focused translational development.

Supplementary Table S5. Window-specific colocalization results across retained candidate loci and molecular layers

gene	layer	panel_or_source	molecular_feature	feature_id	molecular_qtl_build	window_radius_bp	window_role	pp_h3	pp_h4	n_harmonized_overlapping_variants	top_h4_snp	top_snp_posterior_given_h4	coloc_interpretation	displayed_in_figure4	note
IL18	pQTL	deCODE	IL18	NA	GRCh38	NA	Not evaluated	NA	NA	NA	NA	NA	Not evaluable	Yes	No genome-wide significant cis-pQTL instrument was available for an interpretable deCODE protein-layer colocalization analysis.
IL18	pQTL	UKB-PPP	IL18	IL18_Q14116_OID20694_v1_Inflammation.gz.Q14116.IL18	GRCh38	1000000	Primary	0.477216780996106	0.018898960394 6239	4292	11:112209661:C:T	0.104297667102557	Inconclusive	Yes	Primary ±1-Mb analysis.
IL18	eQTL	eQTL reference panel	IL18	ENSG00000150782	GRCh37	1000000	Primary	0.094373813806606	0.832802101825814	5268	rs11606049	0.323529847288311	Strong	Yes	Primary ±1-Mb analysis.
IL18	mQTL	mQTL reference panel	BCO2	cg01015175	GRCh37	1000000	Primary	0.202286327 30391	0.099008555427 5814	159	rs45569233	0.220682073738429	Inconclusive	Yes	Representative mQTL feature selected for colocalization from the available locus features; this probe differs from the top SMR feature summarized in Table S1.
RELT	pQTL	deCODE dense	RELT	14112_40	GRCh38	1000000	Primary	0.333677276245159	0.322158948764142	7185	rs12293998	0.082325179 4934838	Suggestive	Yes	Primary ±1-Mb analysis.
RELT	pQTL	deCODE dense	RELT	14112_40	GRCh38	250000	Sensitivity	0.242009201676462	0.366626348640584	1637	rs12293998	0.082330216 6367769	Suggestive	No	Sensitivity analysis at ±250 kb.
RELT	pQTL	UKB-PPP	RELT	RELT_Q969Z4_OID21142_v1_Neurology.gz.Q969Z4.RELT	GRCh38	1000000	Primary	0.298476100250427	0.397737028062591	7266	11:73379220:G:A	0.999317585839948	Suggestive	Yes	Primary ±1-Mb analysis.
RELT	pQTL	UKB-PPP	RELT	RELT_Q969Z4_OID21142_v1_Neurology.gz.Q969Z4.RELT	GRCh38	500000	Sensitivity	0.239755250309941	0.431029488964197	3307	11:73379220:G:A	0.999317601473037	Suggestive	No	Sensitivity analysis at ±500 kb.

gene	layer	panel_or_source	molecular_feature	feature_id	molecular_qtl_build	window_radius_bp	window_role	pp_h3	pp_h4	n_harmonized_overlapping_variants	top_h4_snp	top_snp_posterior_given_h4	coloc_interpretation	displayed_in_figure4	note
RELT	eQTL	eQTL reference panel	RELT	ENSG00000054967	GRCh37	1000000	Primary	0.387052174418561	0.125910789917509	5062	rs11235746	0.980109236 99954	Inconclusive	Yes	Primary ±1-Mb analysis.
RELT	eQTL	eQTL reference panel	RELT	ENSG00000054967	GRCh37	250000	Sensitivity	0.319495617640962	0.139788152839722	1192	rs11235746	0.980109236 99954	Inconclusive	No	Sensitivity analysis at ±250 kb.
RELT	mQTL	mQTL reference panel	P2RY6	cg21124714	GRCh37	1000000	Primary	0.040652795 8495938	0.863162025558506	77	rs11235707	0.256356555 274627	Strong	Yes	Primary ±1-Mb analysis.
RELT	mQTL	mQTL reference panel	P2RY6	cg21124714	GRCh37	500000	Sensitivity	0.040652795 8495938	0.863162025558506	77	rs11235707	0.256356555 274627	Strong	No	Sensitivity analysis at ±500 kb.
ABO	pQTL	deCODE dense	ABO	9253_52	GRCh38	1000000	Primary	0.438562894276352	0.167525182202752	10663	rs950529388	0.521250283 962765	Inconclusive	Yes	Primary ±1-Mb analysis.
ABO	pQTL	UKB-PPP	ABO	ABO_P16442_OID30675_v1_Inflammation_II.gz.P16442.ABO	GRCh38	1000000	Primary	0.321730223982097	0.212622572097336	3179	rs505922	1	Suggestive	Yes	Primary ±1-Mb analysis.
ABO	eQTL	eQTL reference panel	ABO	ENSG00000175164	GRCh37	1000000	Primary	0.370765938966719	0.027906074220 7813	7062	rs75179845	0.647800356 480657	Inconclusive	Yes	Primary ±1-Mb analysis.
ABO	mQTL	mQTL reference panel	NUP214	cg03811519	GRCh37	2000000	Fallback	3.86717593444774E-05	0.005973747987 67722	5	rs7024857	0.425414377 340027	Not evaluable	Yes	Probe-centered ±2-Mb fallback analysis with five usable overlapping variants; posterior probabilities are reported for completeness but were not considered sufficiently reliable for primary interpretation.