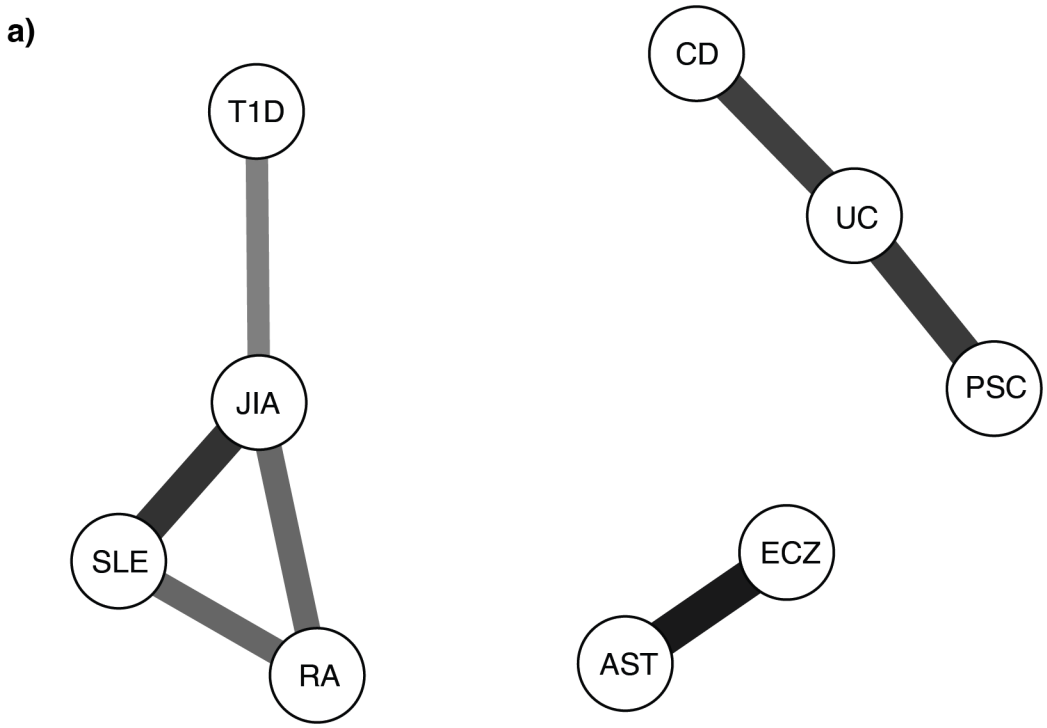
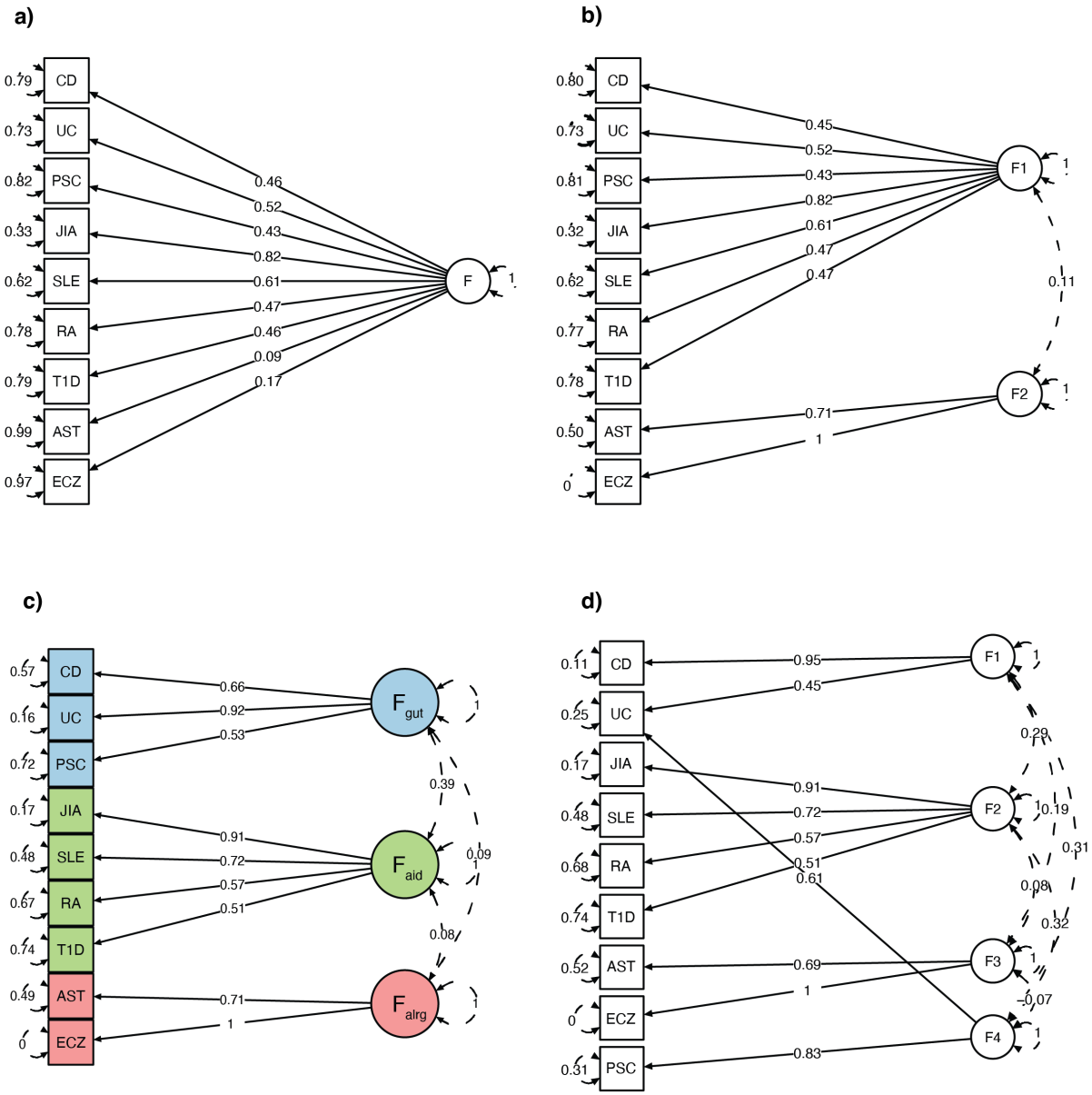
# Cross-disorder genetic analysis of immune diseases reveals distinct gene associations that converge on common pathways

# Supplementary Figures



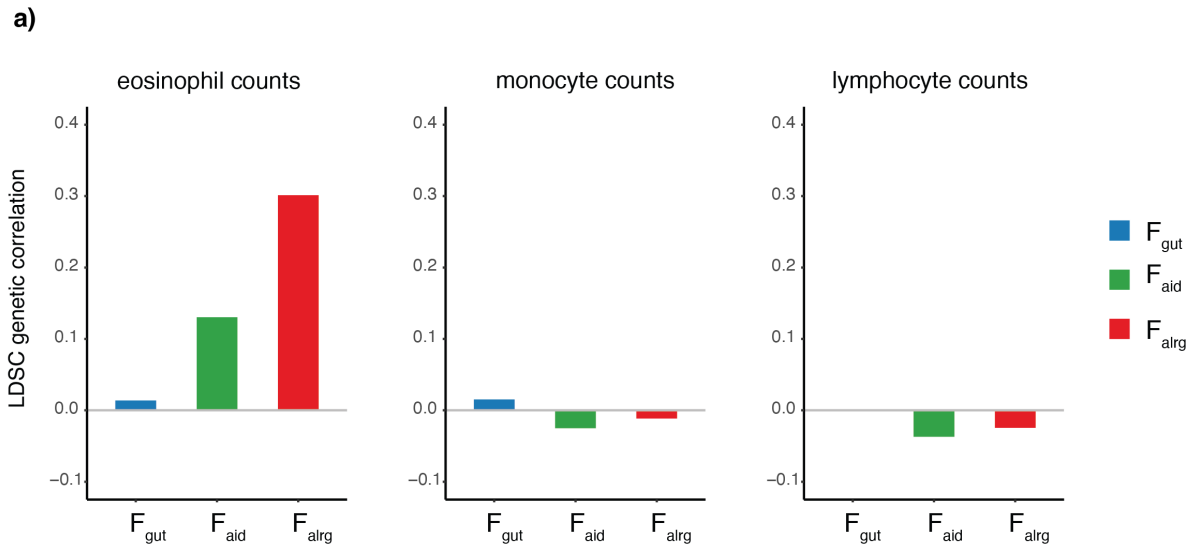

**Supplementary Figure 1. The network plot of LDSC genetic correlations among nine autoimmune diseases. a**) The grey scale and edge width represent the genetic correlation. Genetic correlations ≥ 0.4 are shown.



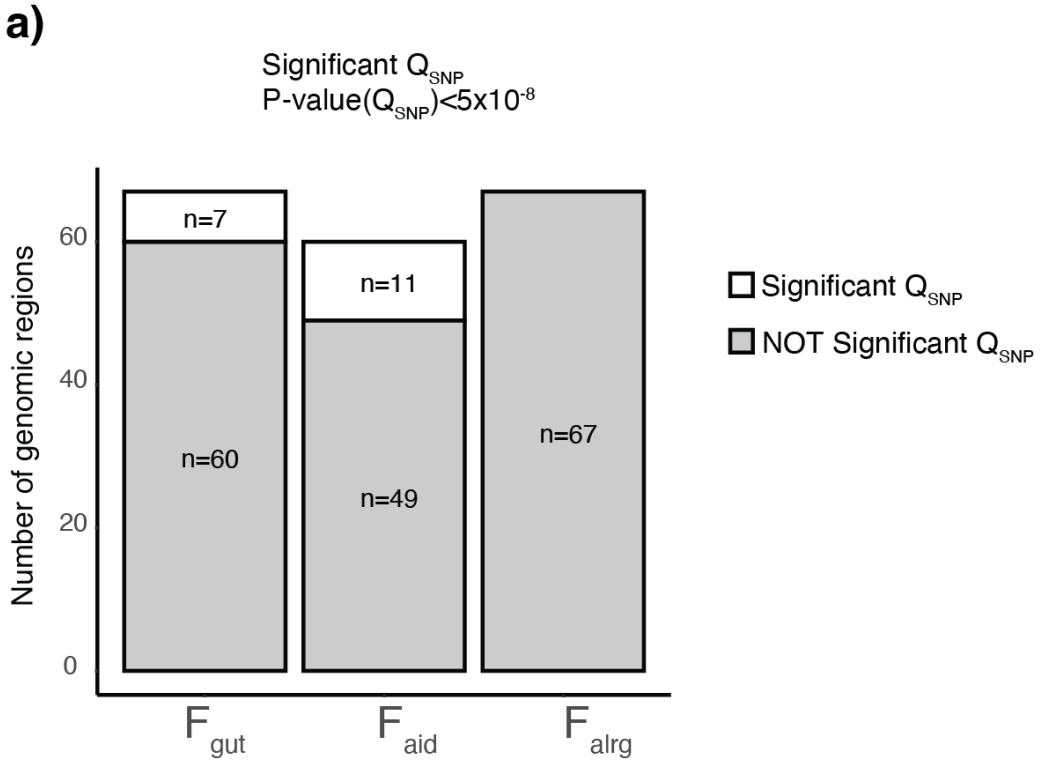

**e)**

| Model (number of factors) | $\chi^2$ | df | P-value $\chi^2$ | AIC | CFI | SRMR |
|---|---|---|---|---|---|---|
| 1 | 493.24 | 27 | 3.8E-87 | 529.24 | 0.58 | 0.16 |
| 2 | 288.02 | 26 | 5.2E-46 | 326.02 | 0.76 | 0.11 |
| 3 | 61.26 | 24 | 4.2E-05 | 103.26 | 0.97 | 0.06 |
| 4 | 32.67 | 20 | 3.7E-02 | 82.67 | 0.99 | 0.04 |

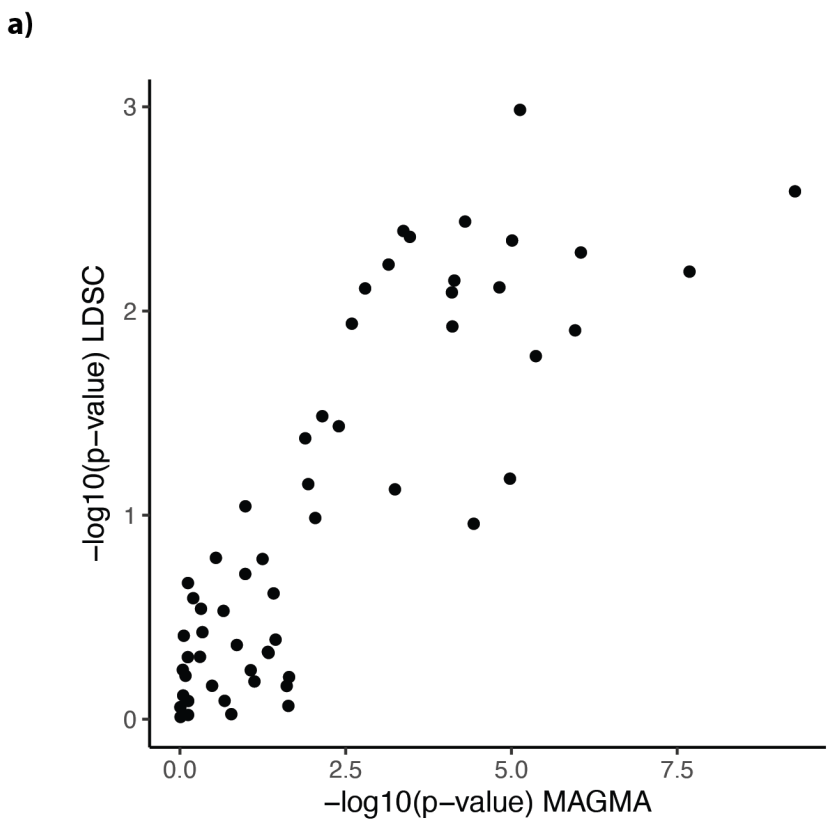
**Supplementary Figure 2. Genomic SEM model statistics. a-d**) We tested four genomic SEM models. Standardised loadings (one-headed arrows), residual variances (two-headed arrows connecting the variable with itself) and covariances (two-headed arrows connecting latent variables) are shown. **e)** Table of factor analysis fit statistics for each of the four models. df, degrees of freedom of the model. P-values were calculated from a $\chi^2$ distribution with the reported degrees of freedom (df); AIC, Akaike Information Criterion; CFI, Comparative Fit Index; SRM, Standardised Root Mean Square Residual.



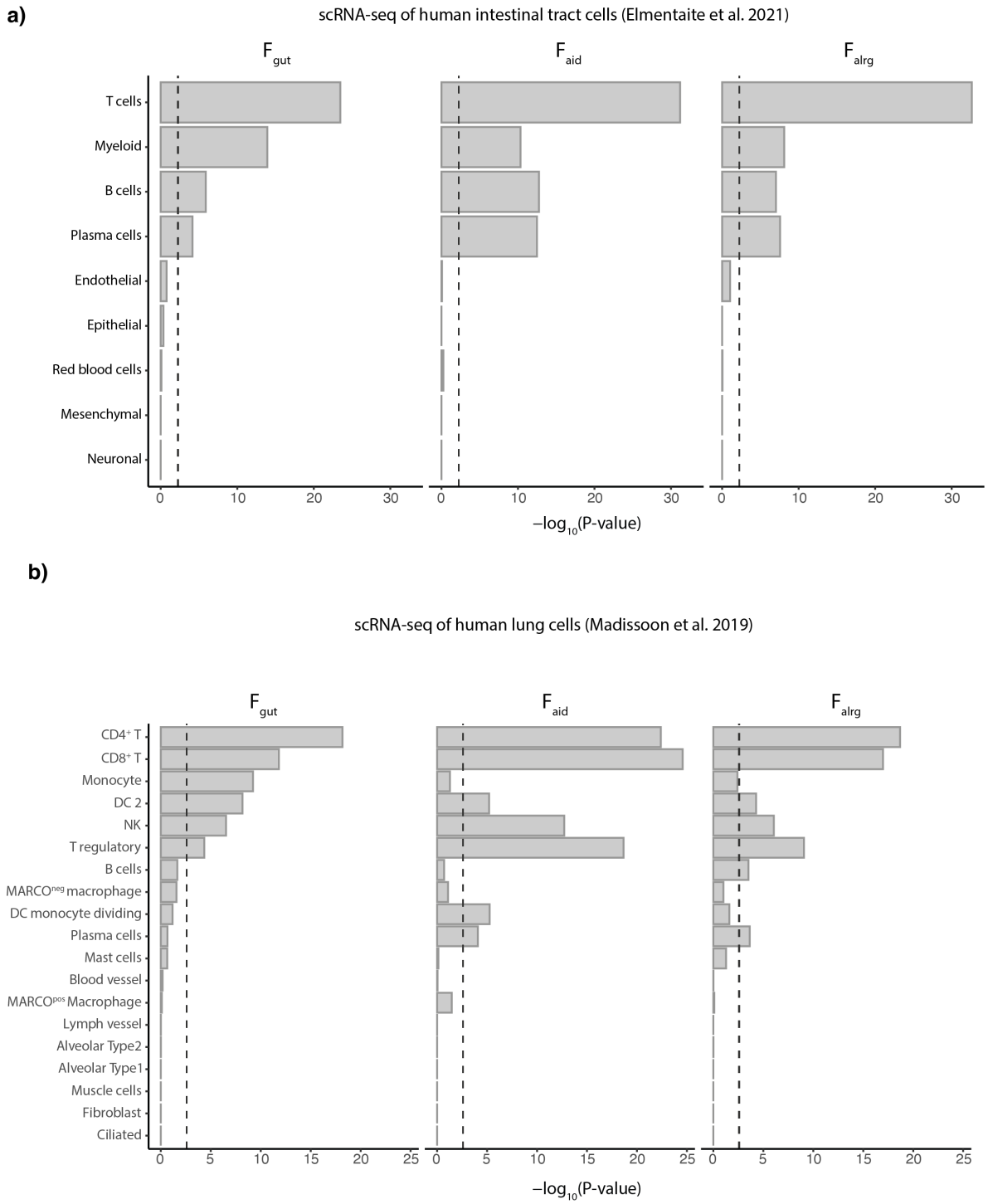

**Supplementary Figure 3. Eosinophil counts are correlated with $F_{alrg}$. a)** LDSC genetic correlations between factors and blood cell counts. Blue, green and red represent $F_{gut}$, $F_{aid}$ and $F_{alrg}$ respectively.



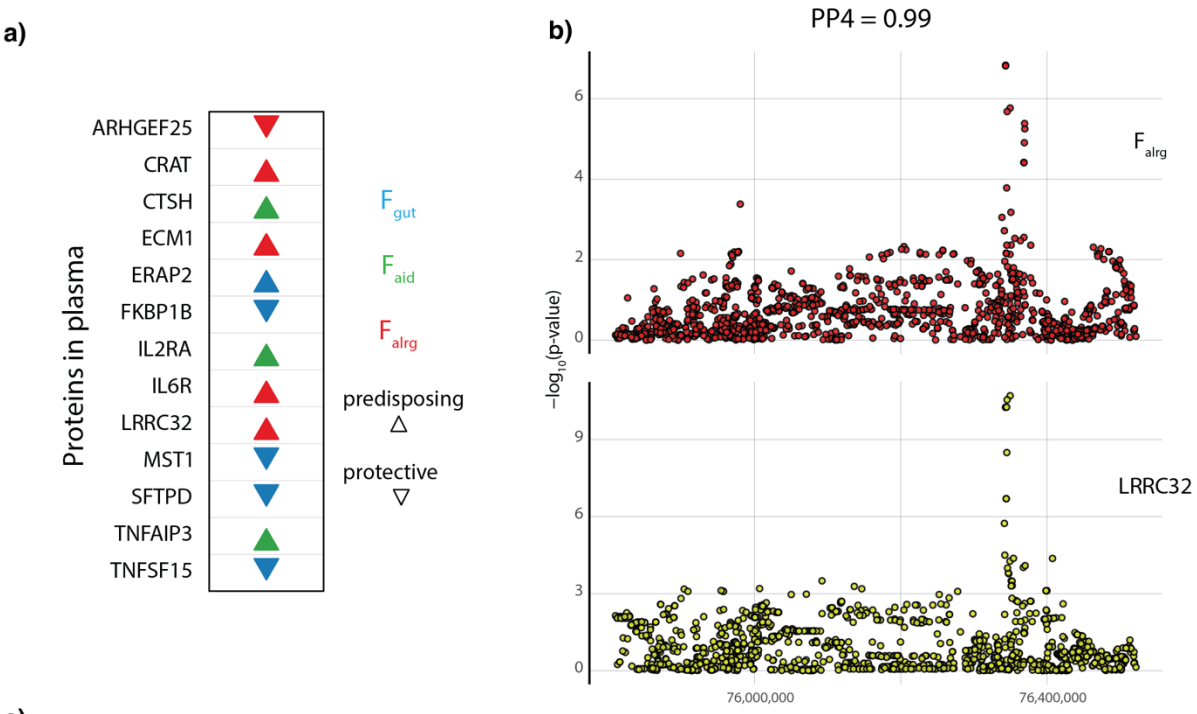

**Supplementary Figure 4. $Q_{SNP}$ statistics of factor associated loci. a)** The bar plot shows the number of lead SNPs which had a significant $Q_{SNP}$ (in white) and not significant (in grey). Genomic SEM (WLS estimation method) was used to conduct the main GWAS and to estimate the independent model for $Q_{SNP}$ calculation. P-values of $Q_{SNP}$ were calculated from a $\chi^2$ distribution with 2, 3 and 1 degrees of freedom for $F_{gut}$, $F_{aid}$ and $F_{alrg}$ respectively.




**Supplementary Figure 5. Comparison of LDSC and MAGMA enrichments. a)** Dot plot shows correlation of -$\log_{10}$(p-value) between MAGMA and LDSC outputs for OneK1K cohort**.** P-values were estimated with MAGMA and LDSC (one-sided test).




**Supplementary Figure 6. Factor-associated loci are specifically enriched in tissue immune cells. a-b**) MAGMA gene-property results of intestinal cells(**a**) and lung cells(**b**). The barplot shows -$\log_{10}$(p-value) of the enrichment. P-values were estimated with MAGMA for testing the null-hypothesis (one-sided test) that the risk variants were not enriched in the cell-types.




c)

| Protein | Drug | Type | Clinical indication | Application in immune-mediated disease | pQTL effect |
|---|---|---|---|---|---|
| *ERAP2* | tosedostat | inhibitor | cancer | - | predisposing |
| *IL2RA* | anti-TAC 90 Y-HAT | binding agent | cancer | - | predisposing |
| | aldesleukin | agonist | T1D, CD, cancer, liver disease, tuberculosis, AIDS, COVID-19 | phase I - II | predisposing |
| | basiliximab | inhibitor | immune system disease, T1D, UC, kidney disease, cancer | phase I - III | predisposing |
| | dacilizumab | inhibitor | immune system disease, T1D, MS, UC, asthma, psoriasis, HIV, cancer | phase II - III | predisposing |
| | denileukin difititox | binding agent | cancer | - | predisposing |
| | Lmb-2 | binding agent | cancer | - | predisposing |
| | camidanlumab tesirine | binding agent | cancer | - | predisposing |
| | inolimomab | antagonist | graft versus host disease | - | predisposing |
| *IL6R* | levilimab | inhibitor | RA, COVID-19 | phase II - III | predisposing |
| | sarilumab | antagonist | RA, JIA, COVID-19 | phase I - IV | predisposing |
| | satralizumab | antagonist | immune system disease | phase IV | predisposing |
| | tocilizumab | inhibitor | RA, JIA, T1D, SLE COVID-19, cancer, | phase I - IV | predisposing |
| | vobarilizumab | inhibitor | RA, SLE | phase I - II | predisposing |

**Supplementary Figure 7. Colocalization of protein QTLs. a)** Triangles pointing upwards indicate that an increase in protein level increases disease risk, while triangles point downwards indicate decrease of disease risk. Blue, green and red represent $F_{gut}$, $F_{aid}$ and $F_{alrg}$ respectively. Mendelian Randomization with Wald ratio method was used to estimate the p-value (two-sided). Only significant MR results (p-value <0.05) are shown. **b)** Locus-zoom plot representing the colocalization between the level of LRRC2 protein in plasma and $F_{alrg}$. P-values refer to the SNP p-values derived from the $F_{alrg}$ GWAS and from the p-QTL dataset. **c)** Table representing pQTLs which are known drug targets. MS, multiple sclerosis; UC, ulcerative colitis; CD, Crohn's disease; RA, rheumatoid arthritis; JIA, juvenile idiopathic arthritis; T1D, type 1 diabetes; SLE, systemic lupus erythematosus.