

Figure S1. Mendelian randomization effect size estimates (z scores) of genetically predicted sepsis and death on circulating cytokine levels in UK biobank and FinnGen cohort when considering cis-eQTL instruments. Black boxes indicate P-values < 0.05. The asterisks represent significance after Bonferroni correction for testing of multiple cytokines (P<0.002 (0.05/number of cytokines)). * P<0.002, # This is only one Instrumental variables estimation, so the wald ratio method is used.

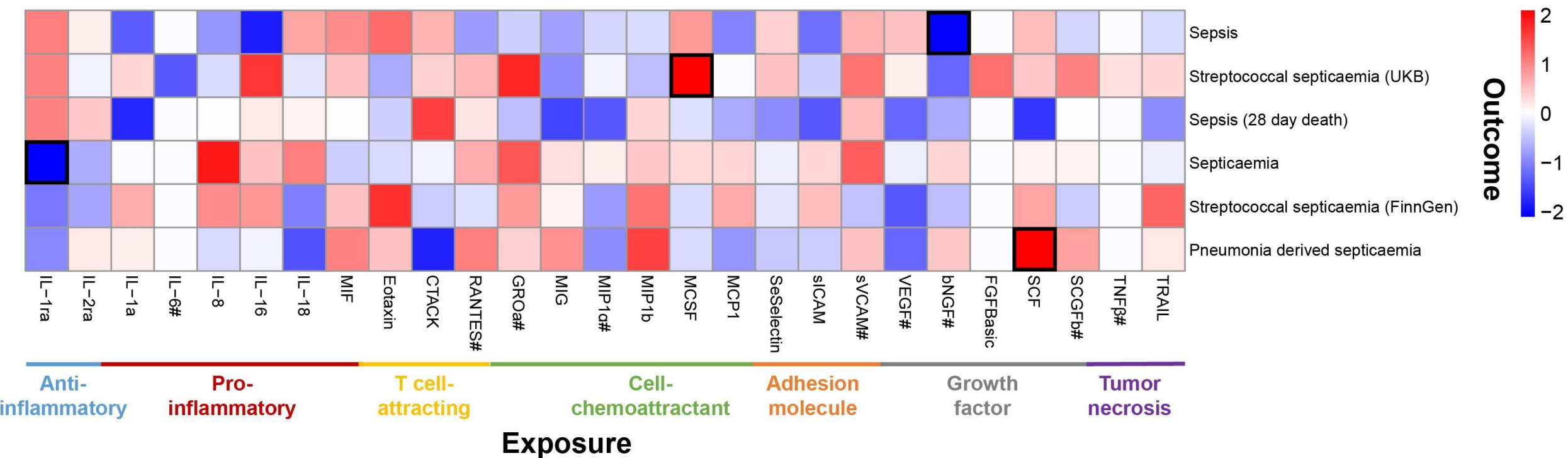


Figure S2. Scatter and leave-one-out plots showing influential outliers in the Mendelian randomization analysis of MIP1 α levels and the sepsis risk.

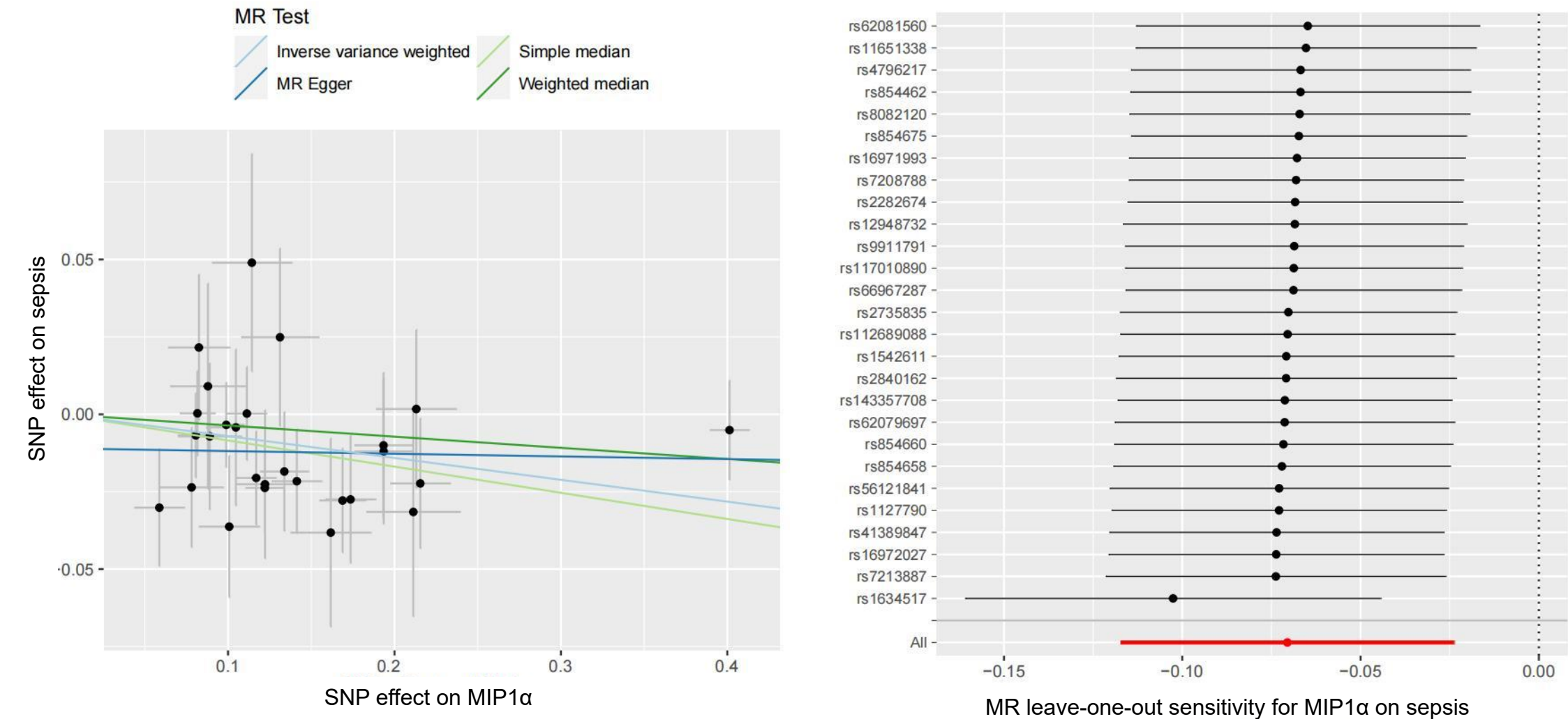


Figure S3. Scatter and leave-one-out plots showing influential outliers in the Mendelian randomization analysis of MIP1 α levels and the risk of mortality at 28 days after sepsis onset.

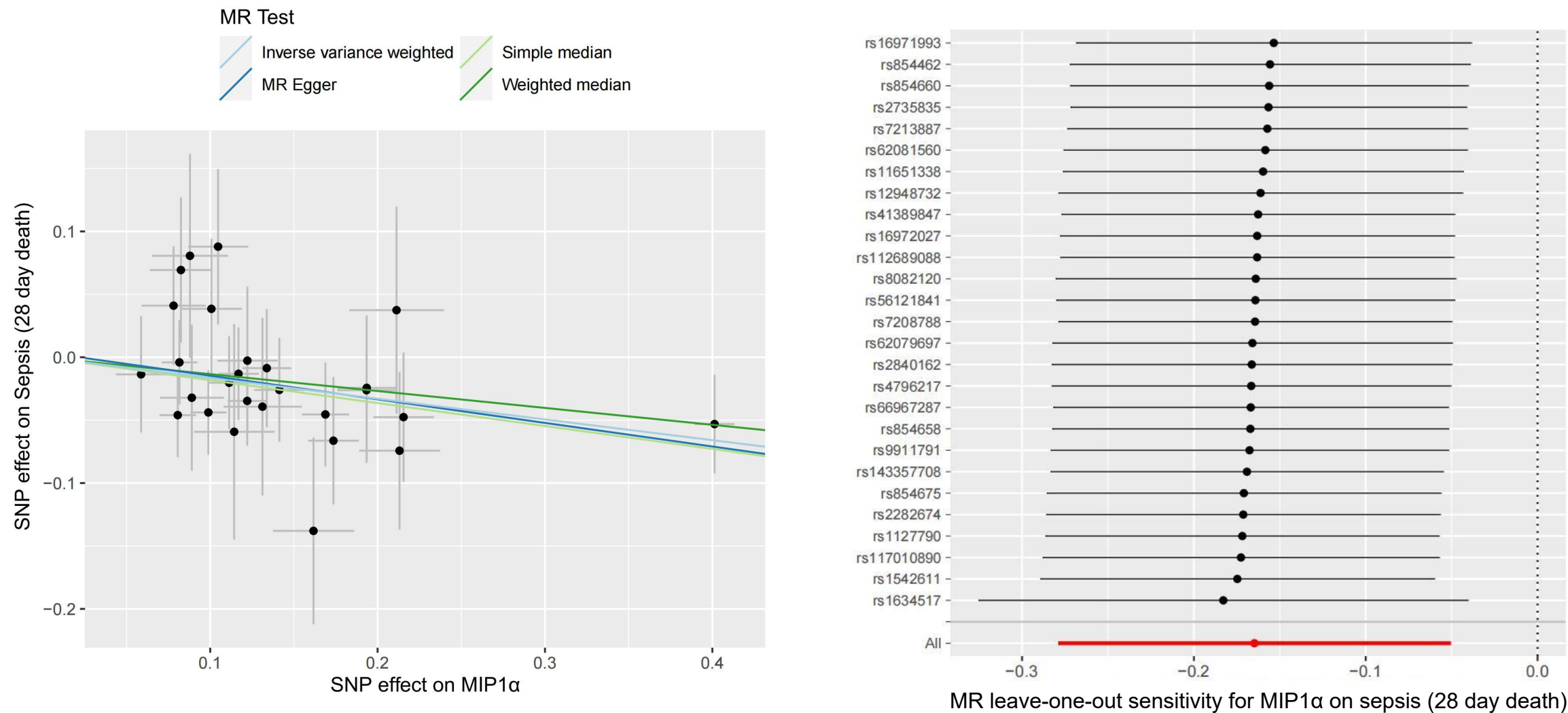
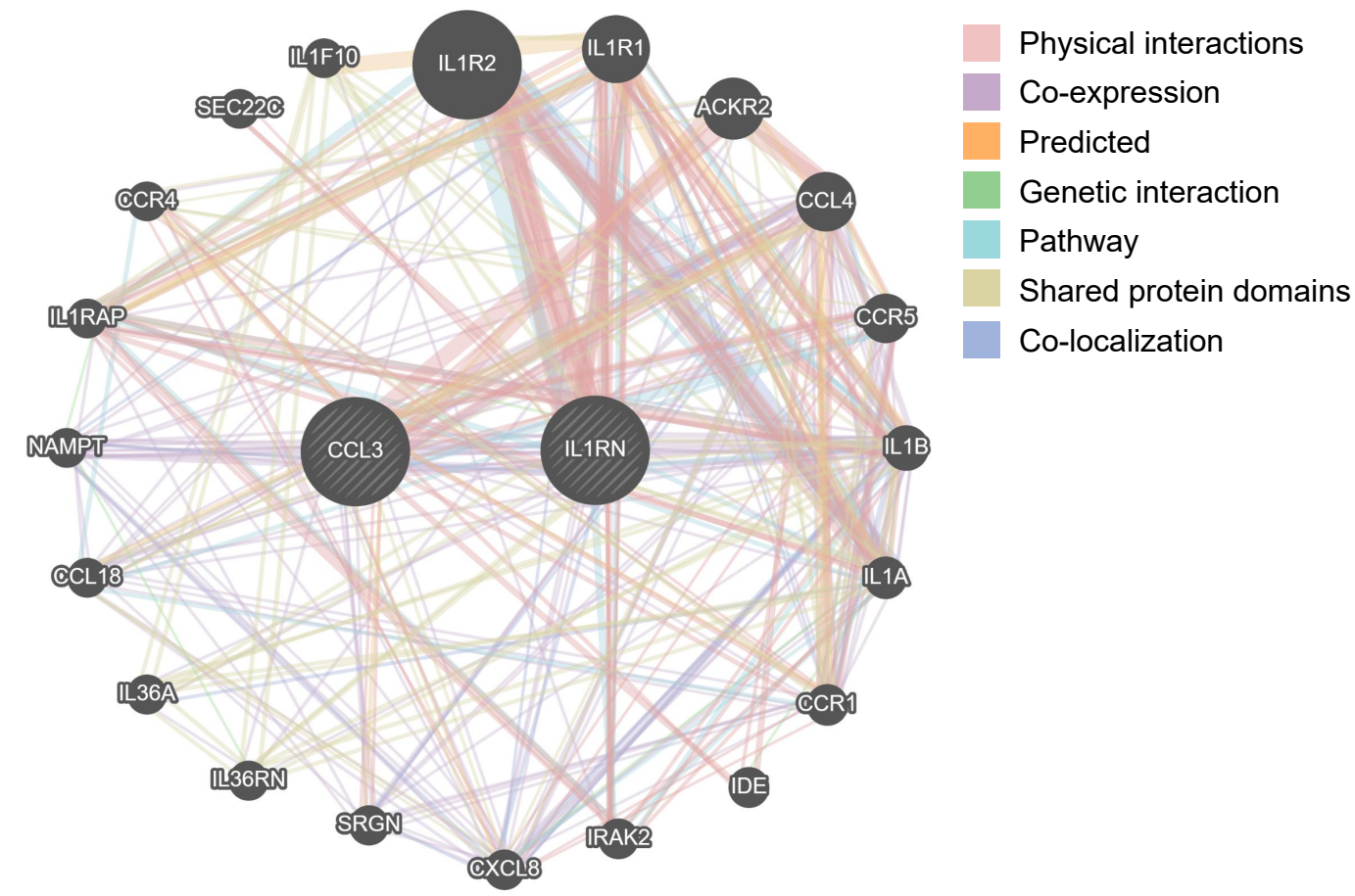


Figure S4. Gene coexpression network, pathways and GO analysis of sepsis trait-related genes (top 10 pathways). Each node is a gene, which was the selected gene in our GWAS pathway analysis. The connecting lines are drawn if the two genes have a relationship, such as co-expression, shared protein domain, physical interactions, co-localization, or pathway. The thickness of the lines represents the degree of similarity between two genes. Gene network is produced using GeneMANIA.



Function	FDR
response to interleukin-1	8.57E-14
cellular response to molecule of bacterial origin	9.67E-09
response to lipopolysaccharide	9.67E-09
cytokine receptor activity	1.11E-08
cellular response to biotic stimulus	1.91E-08
cellular response to interleukin-1	3.16E-08
cytokine binding	3.16E-08
response to molecule of bacterial origin	5.57E-08
cytokine receptor binding	1.04E-07
immune receptor activity	1.59E-07