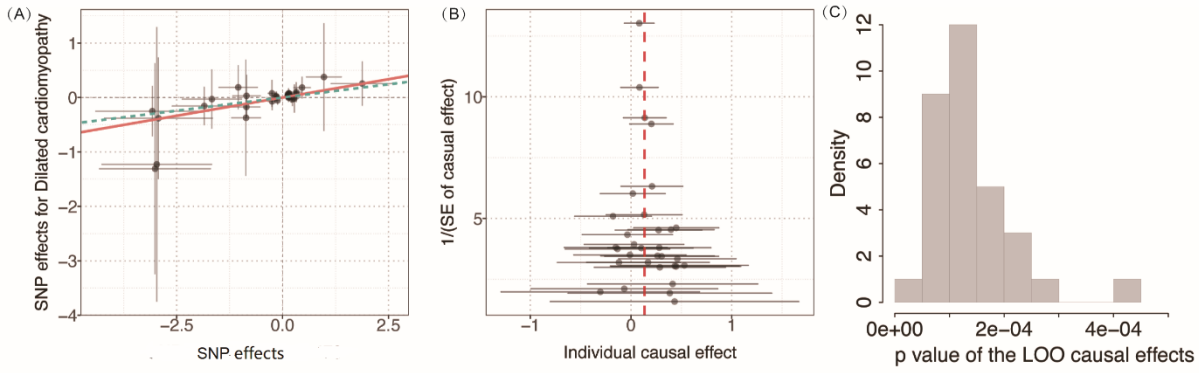
Supplementary Material

Supplementary Figure 1. Panels A–C show supplementary analyses based on inverse-variance weighted Mendelian randomization for causal inference. (A) Scatter Plot: All genetic variants cluster near the regression line, indicating consistency with the overall causal effect. The regression slope (red solid line) reflects the inverse-variance weighted estimate, while the green dashed line represents the weighted median estimate. (B) Funnel Plot: The plot is symmetrically inverted, with horizontal lines for each SNP flanking the vertical line that denotes the overall causal effect. (C) LOOCV Analysis: The leave-one-out cross-validation bar chart displays a unimodal distribution, with the peak aligning closely to the overall P-value.



Supplementary Table 1. Summary of single nucleotide polymorphisms (SNPs) selected as genetic instruments. This table outlines the specific SNPs selected as instrumental variables for the Mendelian randomization analysis, including genomic coordinates, allele frequency, and strength of association.

Accessible at: https://doi.org/10.6084/m9.figshare.29480987.v1

Supplementary Table 2. Comparative causal effects of immune cell traits on dilated cardiomyopathy and chronic heart failure (CHF): inverse-variance weighted Mendelian randomization Results. Note: No significant causal associations were observed for CHF-related outcomes.

Accessible at: https://doi.org/10.6084/m9.figshare.29480963.v1

Supplementary Table 3. Sensitivity analyses using alternative Mendelian randomization (MR) approaches for immune traits validation of causal inferences using complementary MR estimators, including weighted median and MR-Egger, for both dilated cardiomyopathy and chronic heart failure phenotypes.

Accessible at: https://doi.org/10.6084/m9.figshare.29481017.v1

Supplementary Table 4. Horizontal pleiotropy assessment using the MR-PRESSO Global test This table reports the detection of horizontal pleiotropy across immune traits and outcomes using the MR-PRESSO global test, to ensure instrument validity.

Exposure (ID)	No.	Global Residual Sum of Squares observed	Global P value	MR-PRESSO	standard error	lower limit of the 95% confidence interval	Upper limit of the 95% confidence interval	P value
90001479	32	20.55469586	0.96	0.134219451	0.027185598	0.08093568	0.187503223	2.57E-05

Supplementary Table 5. Results from reverse Mendelian randomization analysis assessing whether dilated cardiomyopathy (DCM) may causally influence immune cell traits. Note: This analysis was conducted solely for the DCM outcome.

outcome	Methods	Methods	BETA	Standard Error	Odd ratio	lower limit of the 95%CI	Upper limit of the 95%CI	P value	Heterogeneity Estimate	Heterogeneity P value
Heart_dilated_cardiomyopathy	90001479	IVW_fix	0.095758	0.126188939	1.100493129	0.859359963	1.409287353	0.447942754	2.644313782	0.103921022
Heart_dilated_cardiomyopathy	90001479	IVW_random	0.095758	0.205200201	1.100493129	0.736072526	1.645333965	0.640744363	2.644313782	0.103921022
Heart_dilated_cardiomyopathy	90001479	Egger_slope	NA	NA	NA	NA	NA	NA	NA	NA
Heart_dilated_cardiomyopathy	90001479	Egger_intercept	NA	NA	NA	NA	NA	NA	NA	NA
Heart_dilated_cardiomyopathy	90001479	weighted_mode	NA	NA	NA	NA	NA	NA	NA	NA
Heart_dilated_cardiomyopathy	90001479	weighted_Median	NA	NA	NA	NA	NA	NA	NA	NA
Heart_dilated_cardiomyopathy	90001479	DIVW	0.101274	0.150920037	1.106580027	0.823226721	1.487463082	0.502191584	NA	NA
Heart_dilated_cardiomyopathy	90001479	MR-RAPS	0.103834	0.133600952	1.109416314	0.853829432	1.441511045	0.437043549	NA	NA

Supplementary Table 6. cis-expression quantitative trait loci (cis-eQTLs) annotation of risk SNPs associated with the relative count of $CD4^+$ Treg cells. This table lists the significant cis-eQTLs identified using GTEx for risk SNPs mapped to candidate genes. These SNPs are linked to the causally implicated immune cell trait—the relative count of $CD4^+$ regulatory T cells—in our investigation of dilated cardiomyopathy.

No.	rs	Chromosome	Position	Allele	RegPotential	Conservation	Nearby Gene	Distance (bp)	Nearby Gene
1	rs10212061	22	47965613	A/G	NA	0	LOC100128946||LOC643653	-288574||-30174	LOC100128946
2	rs10905856	10	6207130	C/T	0	0.009	RBM17||PFKFB3	-8281||-77771	RBM17
3	rs11869223	17	30799826	C/G	NA	0	SLFN13	13598||59	SLFN13
4	rs12244238	10	6123245	A/G	NA	0	IL2RA	29733||21033	LOC643653
5	rs12722600	10	6094771	T/C	0	0	IL2RA	1259||49507	PFKFB3
6	rs1571025	10	6174875	A/G	0	0.001	RBM17	3862||23974	LOC100129962
7	rs219948	6	12263885	A/G	NA	0	HIVEP1	143175||9333	HIVEP1
8	rs2526941	14	72225488	T/C	0.184066	0	DPF3	19075||205074	DPF3
9	rs28445004	8	34679563	C/T	0	0.009	LOC137107||LOC100133273	-378861||-171613	LOC137107
10	rs2916808	6	30028295	C/T	NA	0	HCP5P3||HCG4P4	-3015||-2666	HCP5P3
11	rs509240	11	30525219	A/G	0.070447	0	MPPED2	136872||33397	MPPED2
12	rs56043453	17	77782879	A/T	NA	NA	SLC16A3	3297||7779	SLC16A3
13	rs57379327	5	102721501	C/T	NA	NA	C5orf30||LOC100129962	-79241||-72621	C5orf30

14	rs61907712	11	127666352	C/G	NA	NA		LOC387820||ETS1	-349434||-167518	LOC387820
15	rs62055610	17	5581595	C/T	NA	NA		LOC100128284||WSCD1	-6483||-333063	LOC100128284
16	rs62626343	10	6168380	C/G	NA	NA		IL2RA||RBM17	-24102||-2633	WSCD1
17	rs7078614	10	6115837	G/T		0	0	IL2RA	22325||28441	LOC100133273
18	rs7742676	6	42462544	C/T		0	0	TRERF1	158702||65217	TRERF1
19	rs7910656	10	6167436	C/T	NA		0	IL2RA||RBM17	-23158||-3577	IL2RA
20	rs971864	6	164517677	C/T		0	0.002	LOC728275	253191||160900	LOC728275 ETS1 HCG4P4

Supplementary Table 7. Functional enrichment of candidate genes mapped from dilated cardiomyopathy -associated single nucleotide polymorphisms (SNPs) via Gene Ontology (GO) and Kyoto Encyclopaedia of Genes and Genomes (KEGG) pathway analysis. Enriched biological processes, molecular functions, cellular components, and signaling pathways are reported, highlighting immune-related and cardiovascular-relevant functional categories.

Accessible at: https://doi.org/10.6084/m9.figshare.29481038.v1