

## Online Supplementary Material

Xin Yun Zou, et al., Association Between Immune Cells And Endometrial Cancer: A Bidirectional Mendelian Randomization Study

**Table S1** Exploration of The Causal Effect of Immunophenotypes Onset On EC in MR analyses

<sup>1</sup>Abbreviations: CI, confidence interval; EC, endometrial cancer; MR, Mendelian randomization; OR, odds ratio; SNP, single nucleotide polymorphism.

**Supplementary Table 1** Exploration of The Causal Effect of Immunophenotypes Onset On EC in MR analyses

Immunophenotypes	<i>F</i> mean	Methods	N.SNP	OR	95% CI	OR/ <i>P</i> val	Pleiotropy/ <i>P</i> val	heterogeneity/ <i>P</i> val
Absolute count								
T cell AC								
	23.03	MR Egger	20	0.99	0.87-1.12	0.896	0.148	0.003
		Weighted median	20	0.93	0.86-1.00	0.064		
		Inverse variance weighted	20	0.92	0.85-0.99	0.020		0.001
		Simple mode	20	0.90	0.80-1.02	0.107		
		Weighted mode	20	0.92	0.85-1.01	0.087		
HLA DR+ CD4+ AC								
	25.68	MR Egger	24	0.97	0.91-1.04	0.435	0.504	0.467
		Weighted median	24	0.95	0.90-1.01	0.095		
		Inverse variance weighted	24	0.95	0.92-1.00	0.018		0.500
		Simple mode	24	0.91	0.83-1.00	0.067		
		Weighted mode	24	0.94	0.89-1.00	0.054		
CD45RA- CD28- CD8br AC								
	30.35	MR Egger	286	1.00	1.00-1.00	0.017	0.983	0.036
		Weighted median	286	1.00	1.00-1.00	0.353		
		Inverse variance weighted	286	1.00	1.00-1.00	0.004		0.039
		Simple mode	286	1.00	1.00-1.00	0.367		
		Weighted mode	286	1.00	1.00-1.00	0.312		
CD62L- monocyte AC								
	24.82	MR Egger	19	1.04	0.98-1.10	0.206	0.888	0.036
		Weighted median	19	1.04	0.98-1.10	0.157		

**Supplementary Table 1** Exploration of The Causal Effect of Immunophenotypes Onset On EC in MR analyses

		Inverse variance weighted	19	1.04	1.00-1.08	0.039		0.039
		Simple mode	19	1.09	1.00-1.20	0.069		
		Weighted mode	19	1.05	1.00-1.10	0.121		
CD33br HLA DR+ CD14dim								
AC								
	24.07	MR Egger	26	0.94	0.90-1.00	0.021	0.2093	0.995
		Weighted median	26	0.98	0.94-1.02	0.303		
		Inverse variance weighted	26	0.97	0.94-1.00	0.021		0.991
		Simple mode	26	0.98	0.92-1.05	0.541		
		Weighted mode	26	0.97	0.93-1.02	0.318		
CD33dim HLA DR+ CD11b-								
AC								
	23.97	MR Egger	28	0.98	0.95-1.00	0.118	0.958	0.694
		Weighted median	28	0.99	0.96-1.02	0.547		
		Inverse variance weighted	28	0.98	0.95-1.00	0.034		0.742
		Simple mode	28	0.94	0.88-1.00	0.076		
		Weighted mode	28	0.98	0.95-1.02	0.355		
Transitional AC								
	22.37	MR Egger	31	1.00	0.92-1.08	0.964	0.187	0.339
		Weighted median	31	0.97	0.90-1.04	0.407		
		Inverse variance weighted	31	0.95	0.91-1.00	0.049		0.299
		Simple mode	31	1.01	0.89-1.14	0.904		
		Weighted mode	31	0.99	0.91-1.08	0.796		
CD14- CD16- AC								
	26.70	MR Egger	25	1.01	1.00-1.01	0.059	0.661	0.837

**Supplementary Table 1** Exploration of The Causal Effect of Immunophenotypes Onset On EC in MR analyses

		Weighted median	25	1.01	1.00-1.01	0.072		
		Inverse variance weighted	25	1.01	1.00-1.01	0.033		0.865
		Simple mode	25	1.03	0.98-1.08	0.293		
		Weighted mode	25	1.01	1.00-1.01	0.042		
	Leukocyte AC							
	23.08	MR Egger	10	0.88	0.77-1.02	0.119	0.358	0.553
		Weighted median	10	0.93	0.86-1.00	0.083		
		Inverse variance weighted	10	0.94	0.89-1.01	0.035		0.554
		Simple mode	10	0.93	0.82-1.00	0.280		
		Weighted mode	10	0.93	0.86-1.01	0.102		
	MFI							
	BAFF-R on CD20- CD38-							
	30.18	MR Egger	17	0.93	0.88-0.98	0.011	0.43	0.55
		Weighted median	17	0.94	0.88-1.00	0.036		
		Inverse variance weighted	17	0.94	0.91-0.98	0.001		0.58
		Simple mode	17	0.91	0.82-1.00	0.080		
		Weighted mode	17	0.94	0.89-0.99	0.023		
	CD20 on IgD- CD24-							
	22.78	MR Egger	29	1.02	0.98-1.06	0.377	0.091	0.579
		Weighted median	29	1.03	0.98-1.07	0.253		
		Inverse variance weighted	29	1.04	1.01-1.07	0.005		0.464
		Simple mode	29	1.04	0.96-1.13	0.373		
		Weighted mode	29	1.02	0.98-1.06	0.323		
	CD38 on PB/PC							
	22.26	MR Egger	15	0.95	0.84-1.07	0.379	0.554	0.594

**Supplementary Table 1** Exploration of The Causal Effect of Immunophenotypes Onset On EC in MR analyses

		Weighted median	15	0.94	0.86-1.03	0.177		
		Inverse variance weighted	15	0.92	0.86-0.98	0.006		0.641
		Simple mode	15	0.96	0.84-1.09	0.506		
		Weighted mode	15	0.95	0.85-1.05	0.336		
CD45RA on TD CD8br	27.95	MR Egger	12	1.09	0.95-1.24	0.239	0.879	0.328
		Weighted median	12	1.04	0.96-1.14	0.332		
		Inverse variance weighted	12	1.08	1.01-1.50	0.019		0.408
		Simple mode	12	1.04	0.90-1.20	0.601		
		Weighted mode	12	1.02	0.89-1.17	0.778		
CD19 on PB/PC								
	21.92	MR Egger	24	1.01	0.93-1.10	0.840	0.223	0.792
		Weighted median	24	1.04	0.97-1.11	0.321		
		Inverse variance weighted	24	1.05	1.00-1.10	0.037		0.755
		Simple mode	24	1.08	0.97-1.21	0.183		
		Weighted mode	24	1.02	0.94-1.11	0.644		
CD20 on IgD+ CD38- naive								
	23.04	MR Egger	17	1.04	0.95-1.13	0.388	0.855	0.275
		Weighted median	17	1.02	0.97-1.08	0.382		
		Inverse variance weighted	17	1.05	1.00-1.09	0.028		0.335
		Simple mode	17	1.02	0.94-1.11	0.593		
		Weighted mode	17	1.02	0.97-1.08	0.436		
CD25 on memory B cell								
	33.28	MR Egger	24	1.05	0.98-1.14	0.179	0.809	0.216
		Weighted median	24	1.03	0.98-1.09	0.240		

**Supplementary Table 1** Exploration of The Causal Effect of Immunophenotypes Onset On EC in MR analyses

		Inverse variance weighted	24	1.05	1.00-1.09	0.032		0.259
		Simple mode	24	1.02	0.94-1.11	0.619		
		Weighted mode	24	1.04	0.99-1.00	0.142		
CD3 on CD28+ CD45RA- CD8br								
32.69		MR Egger	20	0.99	0.90-1.10	0.880	0.365	0.568
		Weighted median	20	0.97	0.91-1.03	0.319		
		Inverse variance weighted	20	0.95	0.91-1.00	0.028		0.575
		Simple mode	20	0.94	0.86-1.03	0.195		
		Weighted mode	20	0.96	0.91-1.02	0.250		
HVEM on TD CD8br								
21.53		MR Egger	27	0.96	0.90-1.02	0.196	0.792	0.016
		Weighted median	27	0.97	0.93-1.01	0.110		
		Inverse variance weighted	27	0.97	0.94-1.00	0.037		0.021
		Simple mode	27	0.98	0.92-1.05	0.612		
		Weighted mode	27	0.98	0.93-1.02	0.326		
CD16-CD56 on HLA DR+ NK								
25.01		MR Egger	25	0.97	0.92-1.01	0.149	0.918	0.494
		Weighted median	25	0.98	0.93-1.03	0.395		
		Inverse variance weighted	25	0.97	0.94-1.00	0.050		0.552
		Simple mode	25	0.98	0.91-1.06	0.612		
		Weighted mode	25	0.98	0.93-1.03	0.432		
CD127 on CD45RA+ CD4+								
26.47		MR Egger	22	1.08	0.98-1.18	0.128	0.428	0.849

**Supplementary Table 1** Exploration of The Causal Effect of Immunophenotypes Onset On EC in MR analyses

		Weighted median	22	1.04	0.98-1.10	0.215		
		Inverse variance weighted	22	1.04	1.00-1.09	0.050		0.857
		Simple mode	22	1.03	0.94-1.13	0.511		
		Weighted mode	22	1.02	0.94-1.11	0.609		
HLA DR on CD14- CD16+ monocyte								
	54.86	MR Egger	17	0.93	0.85-1.02	0.148	0.573	0.095
		Weighted median	17	0.93	0.88-0.98	0.005		
		Inverse variance weighted	17	0.95	0.91-1.00	0.032		0.113
		Simple mode	17	0.91	0.83-1.00	0.061		
		Weighted mode	17	0.93	0.88-0.98	0.018		
CD45 on Im MDSC								
	43.78	MR Egger	10	1.01	0.96-1.07	0.674	0.286	0.654
		Weighted median	10	1.02	0.98-1.07	0.263		
		Inverse variance weighted	10	1.04	1.01-1.07	0.023		0.611
		Simple mode	10	1.06	0.99-1.13	0.113		
		Weighted mode	10	1.03	0.99-1.07	0.220		
Morphological parameter SSC-A on myeloid DC								
	29.87	MR Egger	18	1.05	1.01-1.09	0.029	0.397	0.713
		Weighted median	18	1.03	0.98-1.08	0.292		
		Inverse variance weighted	18	1.04	1.01-1.07	0.019		0.723
		Simple mode	18	0.97	0.88-1.07	0.536		
		Weighted mode	18	1.04	1.00-1.09	0.109		
Relative count								

**Supplementary Table 1** Exploration of The Causal Effect of Immunophenotypes Onset On EC in MR analyses

IgD+ CD38br %lymphocyte

22.34	MR Egger	26	0.96	0.91-1.01	0.156	0.709	0.767
	Weighted median	26	0.96	0.91-1.02	0.183		
	Inverse variance weighted	26	0.95	0.92-1.00	0.013		0.804
	Simple mode	26	0.92	0.84-1.01	0.080		
	Weighted mode	26	0.96	0.91-1.01	0.112		

Naive-mature B  
cell %lymphocyte

21.79	MR Egger	20	0.99	0.85-1.15	0.873	0.313	0.881
	Weighted median	20	0.94	0.87-1.02	0.157		
	Inverse variance weighted	20	0.92	0.86-0.97	0.005		0.869
	Simple mode	20	0.96	0.84-1.10	0.588		
	Weighted mode	20	0.96	0.85-1.09	0.573		

Secreting Treg %CD4

31.95	MR Egger	23	1.02	0.99-1.05	0.137	0.396	0.846
	Weighted median	23	1.03	1.00-1.06	0.068		
	Inverse variance weighted	23	1.03	1.00-1.05	0.019		0.850
	Simple mode	23	1.02	0.97-1.07	0.441		
	Weighted mode	23	1.02	1.00-1.05	0.113		

CM CD4+ %T cell

21.82	MR Egger	25	1.04	0.93-1.17	0.500	0.563	0.029
	Weighted median	25	1.06	0.98-1.14	0.161		
	Inverse variance weighted	25	1.07	1.01-1.14	0.018		0.034
	Simple mode	25	1.00	0.88-1.14	0.983		
	Weighted mode	25	1.05	0.97-1.15	0.256		



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Immunophenotype	Estimate	Method	N	OR	95% CI	P	IVW	P
DP (CD4+CD8+) %leukocyte	25.96	MR Egger	23	0.88	0.78-0.99	0.052	0.474	0.344
		Weighted median	23	0.92	0.85-0.99	0.029		
		Inverse variance weighted	23	0.92	0.87-0.97	0.002		
		Simple mode	23	0.88	0.77-1.02	0.106		
		Weighted mode	23	0.93	0.83-1.04	0.194		
B cell % CD3- lymphocyte	24.48	MR Egger	28	1.03	1.00-1.06	0.027	0.496	0.967
		Weighted median	28	1.04	1.01-1.07	0.018		
		Inverse variance weighted	28	1.03	1.00-1.05	0.018		
		Simple mode	28	1.03	0.98-1.07	0.228		
		Weighted mode	28	1.03	1.01-1.05	0.020		
CD127- CD8br %T cell	21.68	MR Egger	13	0.96	0.82-1.12	0.591	0.505	0.240
		Weighted median	13	0.92	0.84-1.01	0.078		
		Inverse variance weighted	13	0.91	0.85-0.98	0.011		
		Simple mode	13	0.87	0.76-1.01	0.088		
		Weighted mode	13	0.91	0.81-1.04	0.190		
CD20- %lymphocyte	21.74	MR Egger	18	0.95	0.90-1.02	0.169	0.894	0.660
		Weighted median	18	0.96	0.90-1.03	0.299		
		Inverse variance weighted	18	0.95	0.91-0.99	0.024		
		Simple mode	18	1.01	0.91-1.12	0.890		
		Weighted mode	18	0.97	0.91-1.04	0.389		

**Supplementary Table 1** Exploration of The Causal Effect of Immunophenotypes Onset On EC in MR analyses

Immunophenotype	Estimate	Method	N	OR	95% CI	P	IVW P	MR P	
CD11c+ monocyte %monocyte	21.80	MR Egger	20	1.06	0.97-1.15	0.225	0.905	0.935	
		Weighted median	20	1.04	0.98-1.11	0.188			
		Inverse variance weighted	20	1.05	1.01-1.10	0.028			0.955
		Simple mode	20	1.00	0.89-1.12	0.960			
		Weighted mode	20	1.01	0.92-1.11	0.885			
Im MDSC %CD33dim HLA DR- CD66b-	23.70	MR Egger	21	0.95	0.90-1.00	0.048	0.277	0.978	
		Weighted median	21	0.96	0.92-1.00	0.062			
		Inverse variance weighted	21	0.97	0.94-1.00	0.045			0.968
		Simple mode	21	0.97	0.89-1.04	0.397			
		Weighted mode	21	0.95	0.90-1.01	0.093			
NK %CD3- lymphocyte	26.44	MR Egger	24	0.97	0.95-1.00	0.036	0.520	0.947	
		Weighted median	24	0.97	0.94-1.00	0.032			
		Inverse variance weighted	24	0.98	0.96-1.00	0.021			0.954
		Simple mode	24	0.96	0.92-1.01	0.107			
		Weighted mode	24	0.97	0.94-0.99	0.024			
CD39+ CD4+ %CD4+	144.56	MR Egger	23	1.01	0.93-1.01	0.834	0.170	0.810	
		Weighted median	23	0.97	0.92-1.02	0.268			
		Inverse variance weighted	23	0.96	0.92-1.00	0.028			0.742
		Simple mode	23	0.99	0.91-1.07	0.755			

**Supplementary Table 1** Exploration of The Causal Effect of Immunophenotypes Onset On EC in MR analyses

		Weighted mode	23	0.99	0.92-1.06	0.735	
CD45RA+ CD28- CD8br %T cell							
	28.68	MR Egger	177	1.00	1.00-1.00	0.099	0.944
		Weighted median	177	1.00	1.00-1.00	0.800	
		Inverse variance weighted	177	1.00	1.00-1.00	0.028	0.315
		Simple mode	177	1.00	1.00-1.00	0.965	
		Weighted mode	177	1.00	1.00-1.00	0.501	

<sup>1</sup>Abbreviations: CI, confidence interval; EC, endometrial cancer; MR, Mendelian randomization; OR, odds ratio; SNP, single nucleotide polymorphism.