

ORIGINAL ARTICLE

Exploration of the Relationship between Macrophage-Related Proteins and the Risk and Prognosis of Breast Cancer

Hong-Fang Ma¹, Qi-Na He², Yi Lu², Jun Shen²

¹ Department of Plastic Surgery, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang Province, China

² Department of Surgical Oncology, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang Province, China

SUMMARY

Background: Macrophage-related proteins play a crucial role in breast cancer. The present study explored the relationship between macrophage-related proteins and breast cancer using Mendelian randomization (MR) for genetic variations and bioinformatics methods for transcriptomics.

Methods: Genetic instruments associated with macrophage migration inhibitory factor (MIF), macrophage inflammatory protein 1 α (MIP-1 α), macrophage inflammatory protein 1 β (MIP-1 β), and granulocyte macrophage colony-stimulating factor (GM-CSF) were gathered from genome-wide association studies (GWAS). The MR analysis was conducted using R software packages 'TwoSampleMR' and 'MRPRESSO', employing MR-Egger, inverse-variance weighted (IVW), weighted median, simple mode, and MR-PRESSO algorithms. In addition, data from the UCSC Xena database provided the TCGA BRCA dataset for a 5-year overall survival analysis of MIP-1 α .

Results: IVW analysis showed a significant positive association between MIP-1 α and breast cancer incidence (OR = 1.0837, 95% CI: 1.0284 - 1.142), and the MR-PRESSO result also confirmed a causal relationship between them (OR = 1.0789, 95% CI: 1.0266 - 1.1338). There was no significant causal relationship found between MIF, MIP-1 β , GM-CSF, and breast cancer. Survival analysis revealed that CCL3 was associated with prognosis in breast cancer patients in the Cox proportional-hazard model (HR = 1.5000, 95% CI: 1.0110 - 2.2250).

Conclusions: Elevated levels of macrophage inflammatory protein 1A may increase the risk of breast cancer and lead to poorer patient outcomes.

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Correspondence:

Jun Shen
Department of Surgical Oncology
Sir Run Run Shaw Hospital
Zhejiang University School of Medicine
Hangzhou, 310016, Zhejiang Province
China
Email: shenjun0909@zju.edu.cn

Supplementary Data

Table S1. MR analysis results of macrophage-related proteins and risk of breast cancer.

Exposures	SNPs	MR info					Cochran's Q			Horizontal pleiotropy		
		Method	β	SE	OR [95% CI]	p	Q	Q_df	Q_p	Intercept	SE	p
MIF	15	MR-Egger	-0.0046	0.0381	0.9954 [0.9237 - 1.0726]	0.9053	15.9613	13	0.2512	0.0008	0.0081	0.9185
		IVW	-0.0014	0.0216	0.9986 [0.9572 - 1.0418]	0.9480	15.9747	14	0.3149	-	-	-
		Weighted median	0.0089	0.0291	1.009 [0.9531 - 1.0681]	0.7584	-	-	-	-	-	-
		Simple mode	0.0211	0.0422	1.0214 [0.9403 - 1.1094]	0.6241	-	-	-	-	-	-
		MR-PRESSO	-0.0012	0.0180	0.9988 [0.9642 - 1.0347]	0.9484	-	-	-	-	-	-
MIP-1 α	18	MR-Egger	0.0462	0.0589	1.0473 [0.9331 - 1.1755]	0.4445	22.8039	16	0.1191	0.0061	0.0094	0.5223
		IVW	0.0804	0.0267	1.0837 [1.0284 - 1.142]	0.0026	23.4138	17	0.1363	-	-	-
		Weighted median	0.0636	0.0339	1.0657 [0.9973 - 1.1388]	0.0602	-	-	-	-	-	-
		Simple mode	0.0560	0.0602	1.0576 [0.9399 - 1.1901]	0.3653	-	-	-	-	-	-
		MR-PRESSO	0.0759	0.0253	1.0789 [1.0266 - 1.1338]	0.0077	-	-	-	-	-	-
MIP-1 β	26	MR-Egger	-1.0876	1.5169	0.337 [0.0172 - 6.59]	0.4758	27.7485	24	0.2708	-0.0036	0.0060	0.5582
		IVW	0.6687	0.4640	1.9517 [0.7861 - 4.8456]	0.1495	28.1561	25	0.3007	-	-	-
		Weighted median	0.9492	0.5388	2.5835 [0.8986 - 7.4281]	0.0781	-	-	-	-	-	-
		Simple mode	1.2241	1.4875	3.4012 [0.1843 - 62.7803]	0.4134	-	-	-	-	-	-
		MR-PRESSO	0.5910	0.4627	1.8058 [0.7292 - 4.4718]	0.2057	-	-	-	-	-	-
GM-CSF	14	MR-Egger	-0.0121	0.0339	0.988 [0.9245 - 1.0558]	0.7270	10.3691	12	0.5836	0.0003	0.0106	0.9757
		IVW	-0.0112	0.0182	0.9888 [0.9541 - 1.0248]	0.5384	10.3701	13	0.6634	-	-	-
		Weighted median	-0.0038	0.0252	0.9962 [0.9483 - 1.0466]	0.8810	-	-	-	-	-	-
		Simple mode	0.0177	0.0420	1.0178 [0.9375 - 1.1051]	0.6803	-	-	-	-	-	-
		MR-PRESSO	-0.0146	0.0160	0.9855 [0.9551 - 1.0169]	0.3756	-	-	-	-	-	-