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ORIGINAL ARTICLE

Clinical and Translational Research

Bibliometric analysis of phosphoglycerate kinase 1 expression in breast cancer and its distinct upregulation in triple-negative breast cancer

Jing-Yu Chen, Jian-Di Li, Rong-Quan He, Zhi-Guang Huang, Gang Chen, Wen Zou

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Abstract

BACKGROUND
Phosphoglycerate kinase 1 (PGK1) has been identified as a possible biomarker for breast cancer (BC) and may play a role in the development and advancement of triple-negative BC (TNBC).

AIM
To explore the PGK1 and BC research status and PGK1 expression and mechanism differences among TNBC, non-TNBC, and normal breast tissue.

METHODS
PGK1 and BC related literature was downloaded from Web of Science Core Collection Core Collection. Publication counts, key-word frequency, cooperation networks, and theme trends were analyzed. Normal breast, TNBC, and non-TNBC mRNA data were gathered, and differentially expressed genes obtained. Area under the summary receiver operating characteristic curves, sensitivity and specificity of PGK1 expression were determined. Kaplan Meier revealed PGK1's prognostic implication. PGK1 co-expressed genes were explored, and Gene Ontology, Kyoto Encyclopedia of Genes and Genomes, and Disease Ontology applied. Protein-protein interaction networks were constructed. Hub genes identified.

RESULTS
PGK1 and BC related publications have surged since 2020, with China leading the way. The most frequent keyword was "Expression". Collaborative networks were found among co-citations, countries, institutions, and authors. PGK1 expression

and BC progression were research hotspots, and PGK1 expression and BC survival were research frontiers. In 16 TNBC *vs* non-cancerous breast and 15 TNBC *vs* non-TNBC datasets, PGK1 mRNA levels were higher in 1159 TNBC than 1205 non-cancerous breast cases [standardized mean differences (SMD): 0.85, 95% confidence interval (95%CI): 0.54-1.16, I^2 = 86%, P < 0.001]. PGK1 expression was higher in 1520 TNBC than 7072 non-TNBC cases (SMD: 0.25, 95%CI: 0.03-0.47, I^2 = 91%, P = 0.02). Recurrence free survival was lower in PGK1-high-expression than PGK1-low-expression group (hazard ratio: 1.282, P = 0.023). PGK1 co-expressed genes were concentrated in ATP metabolic process, HIF-1 signaling, and glycolysis/gluconeogenesis pathways.

CONCLUSION

PGK1 expression is a research hotspot and frontier direction in the BC field. PGK1 may play a strong role in promoting cancer in TNBC by mediating metabolism and HIF-1 signaling pathways.

Key Words: Phosphoglycerate kinase 1; Breast cancer; Triple-negative breast cancer; Bibliometric analysis; Computational pathology

Core Tip: The expression of phosphoglycerate kinase 1 (PGK1) in breast cancer (BC) was shown to be both a research hotspot and frontier of BC research. PGK1 mRNA levels were significantly higher in triple-negative BC (TNBC) than in non-cancerous breast tissue. Within the population with BC, PGK1 mRNA expression levels were distinctly upregulated in TNBC compared with non-TNBC. Recurrence-free survival was markedly lower in the PGK1-high-expression than the PGK1-low-expression group. PGK1 has a significant role in promoting TNBC through metabolism and HIF-1 signaling pathways.

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INTRODUCTION

Breast cancer (BC) has become the most frequent malignancy to affect females. Based on the 2024 statistics from the American Cancer Society, BC accounted for 32.0% of the estimated new cases of female cancer, and the incidence of female BC has been said to exhibit a 0.6% annual growth rate[1]. Obtaining the best prognosis for BC patients is mainly dependent on early BC detection and intervention[2-8]. Thus, it is necessary that we explore more accurate BC biomarkers to improve methods for early, accurate identification and treatment to reduce mortality from BC[9-18].

BC is classified according to the presence or absence of the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER-2). BC that does not express these receptors is classified as triple-negative BC (TNBC)[19-21], and this subtype accounts for approximately 12%-20% of all BC cases[22]. Compared with non-TNBC, TNBC has its own clinical characteristics: It is more common in younger women (< 50 years old), and it has higher degree of invasiveness, higher recurrence rate, shorter recurrence time, lower survival rate, and more *BRCA1/2* gene mutations[23-27]. TNBC patients do not benefit from endocrine therapy, unlike ER/PR-positive cases, or from targeted therapy, as used for HER-2-positive cases[23-29]. The mechanisms of TNBC occurrence and development have been investigated by some researchers. Studies have found gene mutations, DNA repair defects, and non-coding RNA to be involved in the carcinogenic, proliferative, and invasive processes of TNBC. The Notch, Wnt/β-catenin, and Hedgehog signaling pathways have also been reported to be important contributors to incidences of TNBC[30-32]. Nevertheless, there are different opinions on the key mechanisms of TNBC[33,34], and many molecular events believed to be related to TNBC need more scientific attention.

Phosphoglycerate kinase 1 (PGK1) is a core enzymes of the glycolysis pathway[35], being involved in a reversible reaction that produces ATP during glycolysis[36], and plays a pivotal part in balancing energy production, redox, and biosynthesis[37]. The phenomenon of PGK1 overexpression has been observed in a variety of malignant tumors, *e.g.*, hepatocellular carcinoma[38], non-small cell lung cancer[39], and pancreatic ductal adenocarcinoma[40]. The presence of higher PGK1 levels in BC tissue had been linked to a worse prognosis, and this trend is mirrored in TNBC[35,41-46]. This suggests that PGK1 could serve as a promising biomarker for BC and may play a role in the initiation and progression of TNBC.

In this research, we concentrated on employing bibliometric analysis to gain insights into the current status and future directions of PGK1 and BC studies, with a focus on comparing the expression levels and underlying mechanisms of PGK1 in BC *vs* normal breast tissue, as well as in TNBC *vs* non-TNBC, through computational pathology and various methods of high-throughput data mining.

MATERIALS AND METHODS

PGK1 and BC bibliometric analysis

Bibliometric analysis data sources: The Web of Science Core Collection (WOS) was used to search the scientific literature related to PGK1 and BC with the following search formula: ("PGK1" OR "phosphoglycerate kinase 1" OR "HEL-S-68p" OR "MIG10" OR "PGKA") AND ("breast" OR "mammary" OR "nipple") AND ("cancer" OR "tumor" OR "carcinoma" OR "neoplasm" OR "neoplasia" OR "malignancy" OR "malignant"). WOS was searched until September 3, 2022. The inclusion and exclusion criteria were as follows: (1) Including BC and PGK1 related studies, and excluding studies unrelated to PGK1; (2) Including English literature in WOS, and excluding literature in other languages (such as German, Spanish, *etc.*); (3) Including original research and review articles, and excluding comments, letters, and conference abstracts; and (4) Excluding retracted articles. The total number of papers irrelevant to BC and PGK1 was 39, as shown in Figure 1.

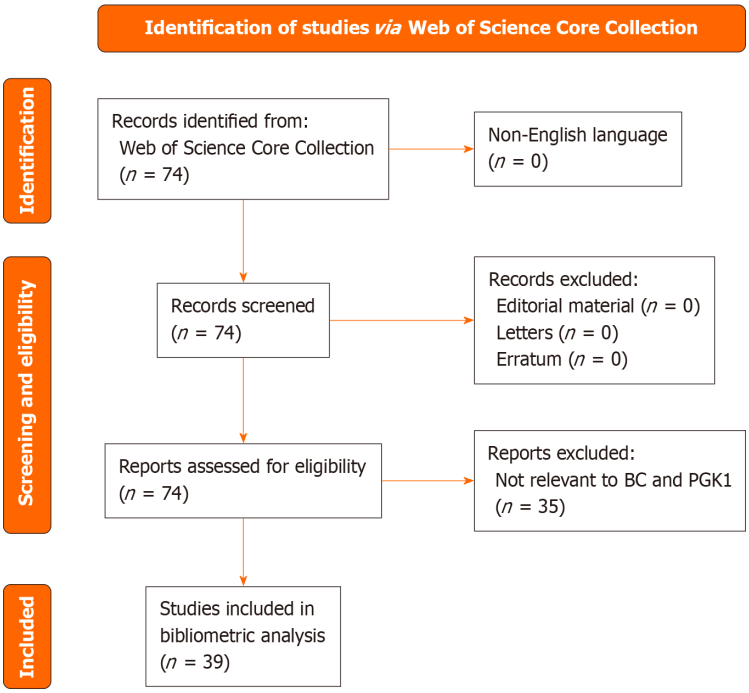

Figure 1 PRISMA flow diagram of the data screening procedure used in the current study. BC: Breast cancer; PGK1: Phosphoglycerate kinase 1.

Data processing methods: The Bibliometrix program in R language was employed to retrieve document data, draw the annual scientific publication curve and geographic distribution map of the corresponding authors; and making a word cloud, thematic plot, and trending topics. VOSviewer (version 1.6.18) was used to analyze the key word co-occurrence plot of the included BC- and PGK1-related literature. Using the leading Eigen clustering algorithm, cooperative networks of co-cited references, cooperative countries, university institutions, and authors were constructed.

Computational pathology associated with PGK1 in TNBC and non-TNBC

Transcriptome data for PGK1 mRNA levels in TNBC: The mRNA expression data for PGK1 in TNBC tissue were downloaded from the GEO, TCGA/GTEx, Metabric, ArrayExpress, and SRA databases. The first search term used was "breast cancer." The pathological parameters of ER/PR/HER-2-negative patients were collected, including pathological diagnosis, molecular subtypes, and relevant follow-up data such as overall survival (OS), distant-metastasis-free survival (DMFS), and relapse-free survival (RFS). The search term was then changed to "triple-negative breast cancer" to collect relevant datasets relating to TNBC. The pathological parameters of each patient were also collected. The inclusion principles for transcriptome data of TNBC were as follows: (1) Primary TNBC tissue; and (2) Sample size ≥ 6. The following data sets were removed: (1) Animal and cell line data; (2) Relapse and metastatic TNBC; and (3) Duplicated samples. The molecular diagnosis of TNBC was provided by Pam50 molecular typing of the data sets. Data sets that provided ER/PR/HER-2 status without molecular typing were included if all were negative, otherwise they were excluded. A PRISMA flow diagram of data set filtering is presented in Figure 2.

Data integration: Expression data from data sets obtained using the same platform were combined after removing batch effects using the limma-voom and sva packages. Global BC data sets were used to pinpoint upregulated genes in TNBC tissue (*i.e.*, TNBC tissue *vs* non-cancerous breast tissue, and TNBC *vs* non-TN BC tissue). The criteria were [standardized mean differences (SMD)] > 0 and $P < 0.05$.

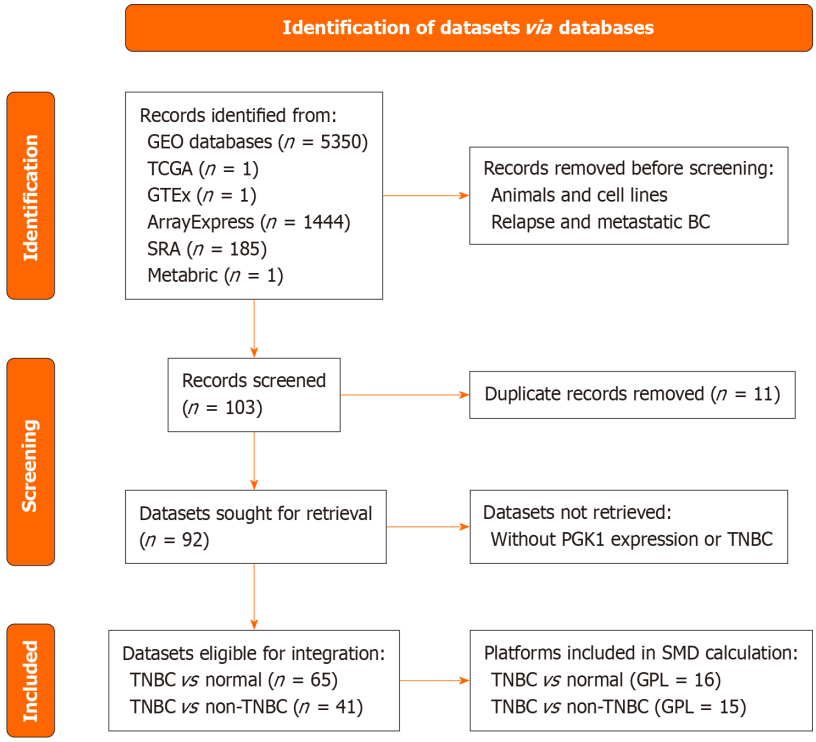

Figure 2 PRISMA flow diagram of the screening procedure used for triple-negative breast cancer data sets including phosphoglycerate kinase 1 expression. BC: Breast cancer; PGK1: Phosphoglycerate kinase 1; TNBC: Triple-negative breast cancer; SMD: Standardized mean differences.

Protein levels of PGK1 in The Human Protein Atlas: The Human Protein Atlas (THPA) (https://www.proteinatlas.org/) is one of the largest human protein maps in the world and includes immunohistochemical results from tissue chips. This research initially examined variations in the location and intensity of PGK1 protein expression between normal breast cells and BC cells with the assistance of the THPA database.

Prognostic analysis of PGK1 in TNBC patients: TNBC patients were grouped using median PGK1 expression. TNBC samples were assigned to a PGK1-overexpression group and PGK1-underexpression group, according to the ideal cutoff point, using survminer v0.4.9 and ggplot2 v3.3.6 packages. Kaplan-Meier analysis was used to filter for candidate prognostic factors in TNBC patients. The hazard ratios (HRs) for PGK1 expression in the different TNBC cohorts were integrated using the meta v4.18.2 package.

Prospective mechanisms of PGK1's effect in TNBC: Genes co-expressed with PGK1 were identified in TNBC tissue samples. The criteria for the co-expressed genes were as follows: (1) Pearson $r \geq 0.3$; and (2) $P < 0.05$. The intersections of overexpressed genes in TNBC *vs* non-TNBC and genes co-expressed with PGK1 were taken for further signaling pathway exploration. Analyses of Gene Ontology (GO), Kyoto Encyclopedia of Genes and Genomes (KEGG), and Disease Ontology (DO) were accomplished with Clusterprofiler v4.4.2 to investigate the potential function of PGK1 in TNBC. STRING v11.5 was used to construct protein-protein interaction (PPI) networks. Cytoscape v3.9.0 was used to identify hub genes.

Statistical analysis

A Wilcoxon test was applied to evaluate the differential expression of PGK1 in the BC subgroups (*i.e.*, BC *vs* non-cancerous breast tissue, TNBC *vs* non-cancerous breast tissue, and TNBC *vs* non-TNBC). Violin plots and receiver operating characteristic curves (ROCs) were drawn. Statistical analysis results with $P < 0.05$ were regarded as being significant.

RESULTS

PGK1 and BC bibliometric analysis results

Analysis of the published literature: Although the number of studies on PGK1 in BC was small, the annual number of PGK1 and BC publications has shown an upward trend since 2005 (Figure 3A). The numbers of articles published in 2020 and 2021 (8 and 9, respectively) were significantly increased from previous years, indicating that the interest of researchers in the link between PGK1 and BC had gradually increased.

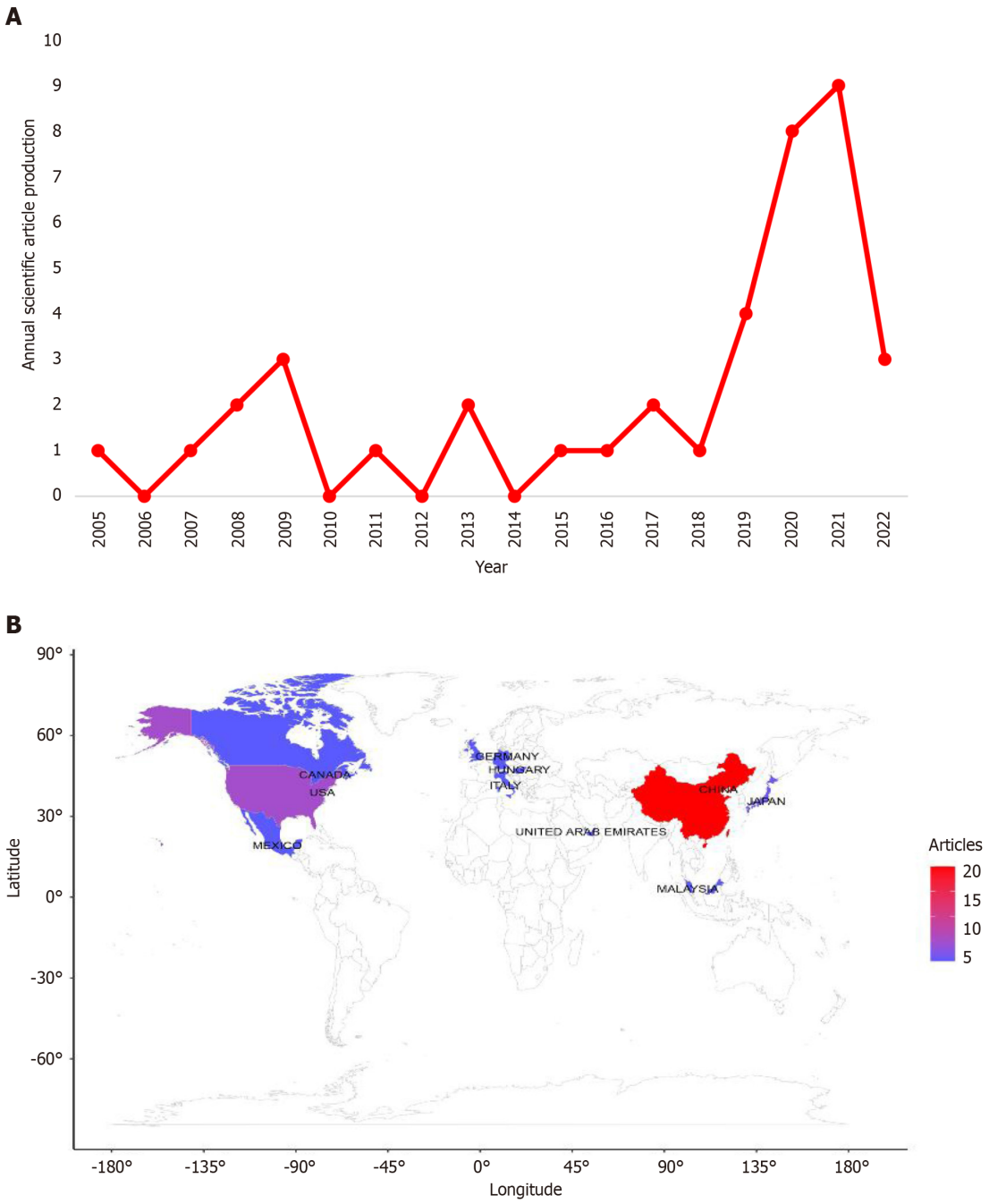

Figure 3 Global scientific research on phosphoglycerate kinase 1 and breast cancer. A: Annual scientific production. Abscissa is the year, and ordinate is number of articles; B: Geographic distribution of corresponding authors. The more articles, the redder the area on the map. Horizontal and vertical coordinates represent longitude and latitude, respectively.

Furthermore, national and regional analysis of the literature suggested that the authors of PGK1-related BC studies were from 15 countries, with 20 articles from China, 5 from the United States, and 2 from Japan, as shown in Figure 3B. A total of 33 journals have published literature on this topic. The four journals with the highest number of articles appear in Table 1.

Key word analysis: The key words with the highest frequency, as defined by the author and added to WOS, appear in Table 2. Figure 4A shows a word cloud, and Figure 4B shows a key word co-occurrence plot. The term "expression" emerged as the most prevalent key word and served as a pivotal hub in the key word co-occurrence relationship, underscoring its significance in studies linking PGK1 and BC. Other key words with a high-frequency of co-occurrence relationships included "progression", "gene", and "survival", showing these have been the focus of BC research. Key words closely related to PGK1 co-occurrence included "survival", "progression", "invasion", and "glycolysis".

Analysis of cooperation network: To complete the cooperative network analysis, first, a co-citation network (Figure 5A) was visualized. Three co-citation clusters were formed with Grandjean G, Ahmad SS, and Warburg O as the core authors, among which Sun S had the highest number of co-citations and was at the center of the co-citation network. Second, data

Table 1 Journals with the most published articles

Journal	Number
Journal of Proteome Research	3
Scientific Reports	3
Frontiers in Cell and Developmental Biology	2
Journal of Translational Medicine	2

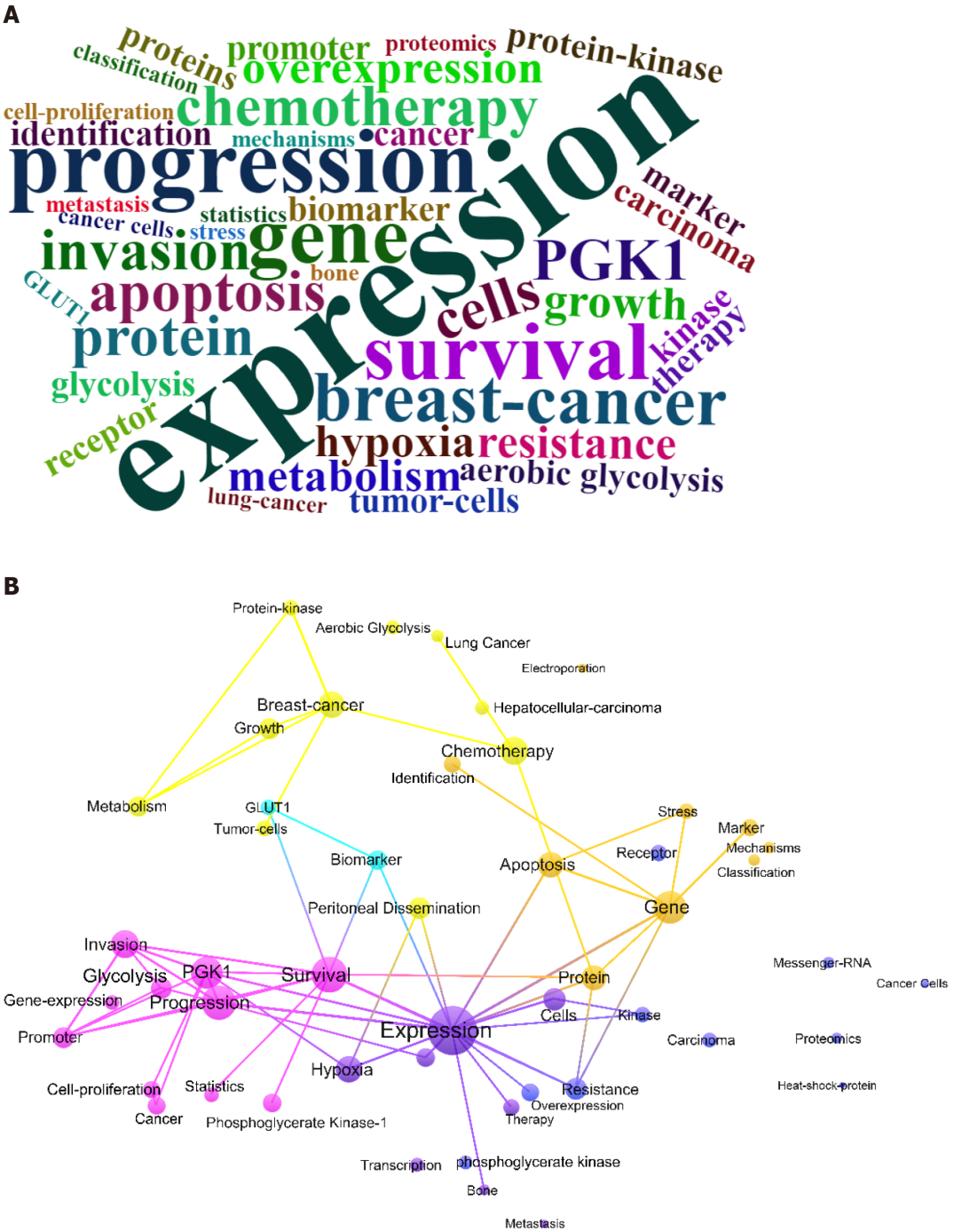

Figure 4 Key words. A: Word cloud of key words. Word frequency was counted according to the Web of Science key words for each document. The word cloud plot is randomly colored. A larger font size indicates a higher frequency; B: Key word co-occurrence plot for breast cancer and phosphoglycerate kinase 1 research. Web of Science key words were clustered using VOSviewer algorithm. Different colors represent different clusters. Font size positively correlates with total co-occurrent numbers. Edges indicate co-occurrence relationships.

Table 2 Key words with the highest frequency

Key word	Frequency
Expression	13
Progression	8
Gene	7
Survival	7
Breast cancer	6

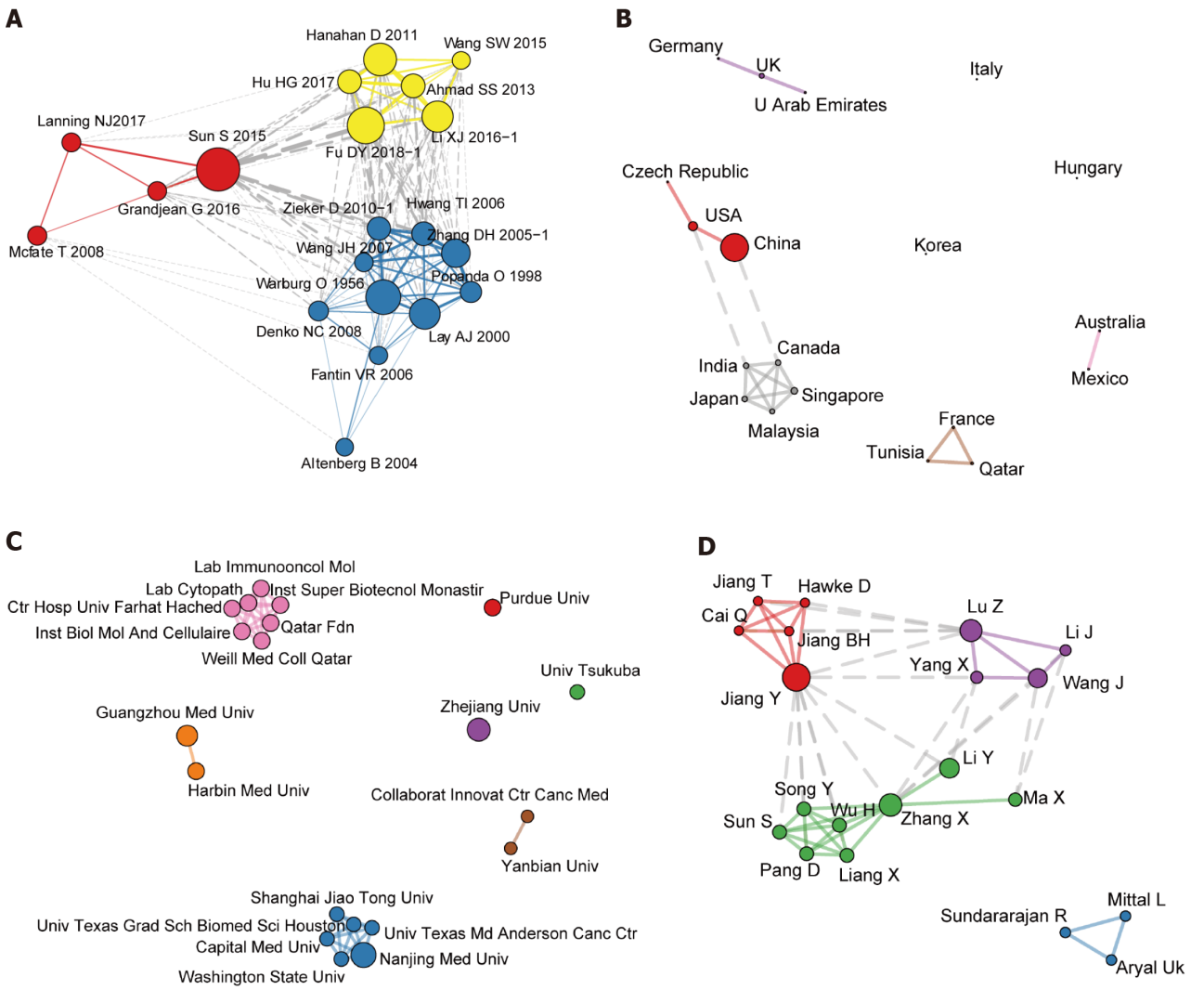

Figure 5 Cooperation network analysis for research on breast cancer and phosphoglycerate kinase 1. A: Co-citation network; B: Collaborations among countries; C: University collaborations; D: Author collaborations. The co-cited documents and cooperating countries, universities, and authors were clustered using a "leading Eigen" algorithm. Different colors represent different clusters. Node size is positively correlated with the degree of connectivity of each node in the network. Edges indicate a co-citation or collaborative relationship.

on collaborations between countries were calculated, as shown in Figure 5B. The country that published the most papers was China, while working collaboratively with the United States. A network of cooperation was formed by Canada, India, Japan, Malaysia, and Singapore. France, Tunisia, and Qatar were also involved in cooperations.

Regarding university collaborations (Figure 5C), a number of Chinese and American academic institutions, including Shanghai Jiao Tong University, Capital Medical University, Washington State University, Nanjing Medical University, and the University of Texas MD Anderson Cancer Center, had established tight-knit collaborative networks. Another partnership cluster consisted of Laboratory Immunooncol Molecular, Institut Supérieur de Biotechnologie de Monastir, Qatar Foundation, *etc*. However, as a whole, university research institutions did not form close cooperative relationships.

Author collaborations also led to the formation of different cooperation clusters (Figure 5D). Jiang Y had the largest node area, indicating that he had the highest degree of connectivity in the author cooperation network.

Citation analysis: The most relevant authors and the H-indexes of authors are shown in Tables 3 and 4, respectively. The authors with the highest number of publications and H-indexes were Jiang Y and Zhang X. In the most cited documents (Table 5), Zhang *et al*[44] showed that PGK1 was overexpressed in tissues and cell lines with receptor tyrosine kinase ErbB2 (HER-2/NEU)-positivity, particularly HER-2/NEU1-positive BC in which PGK1 exhibited even higher levels of expression. Its expression was related to the state of the HER-2/NEU signal pathway. Shashni *et al*[47] believed that the generation of ATP in the cytoplasm and mitochondria decreased with the downregulation of PGK1, which initiated cell apoptosis and inhibited tumor metabolism. Qian *et al*[48] reported that PGK1 was overexpressed in an invasive ductal carcinoma of the breast. The most cited sources can provide research directions for scientific and technological efforts in the BC- and PGK1-related fields (Table 6)[48].

Table 3 Most relevant authors in breast cancer and phosphoglycerate kinase 1 literature

Authors	Number of articles	Articles fractionalized
Zhang X	5	0.84
Jiang Y	5	0.47
Wang J	4	0.73
Li Y	4	0.59
Aryal UK	3	0.62
Mittal L	3	0.62
Sundararajan R	3	0.62
Lu Z	3	0.28
Liang Y	2	0.50
Ye T	2	0.50

Table 4 Top authors by H-index in breast cancer and phosphoglycerate kinase 1 literature

Authors	H-index	G-index	M-index	Total citations	Number of publications	Publication year
Jiang Y	3	4	0.375	256	4	2015
Zhang X	3	4	0.375	79	4	2015
Wang J	3	4	0.250	35	4	2011
Aryal UK	3	3	0.750	42	3	2019
Mittal L	3	3	0.750	42	3	2019
Sundararajan R	3	3	0.750	42	3	2019
Li Y	2	3	0.500	53	3	2019
Camarillo IG	2	2	0.667	27	2	2020
Liang Y	2	2	0.667	15	2	2020
Ye T	2	2	0.667	15	2	2020

Thematic analysis: In the thematic plot, the horizontal axis shows a higher degree of importance from left to right, and the vertical axis displays a better degree of development from bottom to top. PGK1 and BC research topics that have attracted the most attention are "expression", "gene", "apoptosis", "survival", "invasion", and "protein" as shown in Figure 6A.

The trends among topics demonstrated once again that the key words with the highest attention since 2005 have been "expression", "progress", "survival", and "gene", *etc*. According to this trend, new hot topics in PGK1 and BC in the last two years have been "survival", "protein", "invasion", and "biomarkers", *etc*. (Figure 6B).

Computational pathology results relating to PGK1 expression in TNBC and non-TNBC

mRNA expression levels of PGK1 in TNBC tissue: In a preliminary investigation, 31 high-throughput data sets from 7543 BC tissue samples were compared with 1685 non-cancerous breast tissue samples, and our analysis revealed the

Table 5 Most cited documents in breast cancer and phosphoglycerate kinase 1 literature

Ref.	Journal	DOI	Local citations	Global citations
Zhang *et al*[44], 2005	*Mol Cell Proteomics*	10.1074/mcp.M400221-MCP200	9	244
Shashni *et al*[47], 2013	*J Drug Target*	10.3109/1061186X.2012.736998	4	33
Qian *et al*[48], 2017	*Mol Cell*	10.1016/j.molcel.2017.01.027	3	133
Kabbage *et al*[53], 2008	*J Biomed Biotechnol*	10.1155/2008/564127	2	25
Fu *et al*[35], 2018	*Life Sci*	10.1016/j.lfs.2020.117863	2	11

Table 6 Most cited sources of breast cancer and phosphoglycerate kinase 1 research

Sources	Number of articles
Cancer Research	96
Journal of Biological Chemistry	65
Proceedings of the National Academy of Sciences of the United States of America	38
Clinical Cancer Research	36
Cell	35

definitive overexpression of PGK1 in BC, with an SMD of 0.76 and area under the curve (AUC) of 0.8525 for the summary ROC (sROC) (Figures 7 and 8). Tables 7 and 8 showed the included data sets for TNBC *vs* non-cancerous breast tissue, and TNBC *vs* non-TNBC tissue, respectively. Upon analyzing 16 data sets comprising 1159 cases of TNBC and 1205 cases of non-cancerous breast tissue, a clear upregulation of PGK1 mRNA expression in TNBC was observed compared to non-cancerous tissue (Figure 9A), with an SMD of 0.85 and 95% confidence interval (95%CI) of 0.54-1.16, as shown in Figure 10A. More importantly, we compared PGK1 expression across 1520 cases of TNBC and 7072 cases of non-TNBC for the first time and found that TNBC exhibited higher PGK1 mRNA expression than non-TNBC tissue in 9 out of the 15 datasets analyzed (Figure 9B). As Figure 10B shows, the comparative difference in expression was obvious (SMD: 0.25, 95%CI: 0.03-0.47).

Table 7 Included data sets for triple-negative breast cancer tissue *vs* non-cancerous breast tissue

ID	Series			
GPL1390	GSE10885-GPL1390, GSE10886, GSE10893-GPL1390		GSE1992-GPL1390, GSE2607-GPL1390, GSE6128	
GPL13607	GSE59246		GSE70951-GPL13607	
GPL17077	GSE57297		GSE80754	
GPL17586	GSE115144	GSE73540	GSE76250	GSE134359
GPL570	GSE20711	GSE50567	GSE22544	GSE146558
	GSE45827	GSE61304	GSE25407	GSE103865
	GSE65194	GSE42568	GSE26910	GSE153796
	GSE29431	GSE5764	GSE54002	GSE135565
	GSE7904	GSE10780	GSE71053	GSE7307
	GSE31448	GSE10810	GSE147472	GSE3744
	GSE29044	GSE21422	GSE140494	
GPL6244	GSE36295	GSE61724		GSE118432
	GSE86374	GSE37751		GSE81838
GPL6848	GSE26304		GSE18672	
GPL8269	GSE22384-GPL8269		GSE41119	
GPL887	GSE10885-GPL887		GSE24124	

	GSE2607-GPL887		GSE9309	
GPL96	GSE15852	GSE5364	GSE158309	GSE6883-GPL96
GSE29174				
GSE41970-GPL16299				
GSE50428				
GSE64790				
GSE92252				
TCGA_TNBC				

TNBC: Triple-negative breast cancer.

Table 8 Included data sets for triple-negative breast cancer tissue vs non- triple-negative breast cancer tissue

ID	Series				
GPL1390	GSE10885-GPL1390				
GPL13607	GSE59246				
GPL17077	GSE57297				
GPL17586	GSE115144				
GPL570	GSE20711	GSE29044	GSE10810	GSE54002	GSE103865
	GSE45827	GSE50567	GSE21422	GSE71053	GSE153796
	GSE65194	GSE61304	GSE22544	GSE147472	GSE135565
	GSE29431	GSE42568	GSE25407	GSE140494	GSE7307
	GSE7904	GSE5764	GSE26910	GSE146558	GSE3744
	GSE31448	GSE10780			
GPL6244	GSE36295				
GPL6848	GSE26304				
GPL8269	GSE22384-GPL8269				
GPL887	GSE10885-GPL887				
GPL96	GSE15852				
GSE148425					
GSE29174					
GSE50428					
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TCGA TNBC-nonTNBC					

TNBC: Triple-negative breast cancer.

The overexpression of PGK1 mRNA had an excellent ability to distinguish TNBC from non-cancerous breast tissue (AUC of sROC = 0.8578, sensitivity = 0.7637, and specificity = 0.8240, Figure 11A and Figure 10C). In Figure 12, the 13 ROC charts of TNBC *vs* non-cancerous breast tissue indicated that six data sets yielded an AUC of more than 0.7. Figure 11B showed that PGK1's ability to discern TNBC from non-TNBC tissue was moderate (AUC of sROC = 0.688, sensitivity = 0.7571, and specificity = 0.4754; Figure 10D, Figures 13-15).

Protein expression level of PGK1 in BC tissue: The THPA database showed that, in glandular epithelial cells of non-cancerous breast tissue and tumor cells, PGK1 was expressed in nuclear and cytoplasmic membranes. BC tumor cells showed diffuse but strong expression of PGK1 (Figure 16). However, owing to the restricted number of cases available in the public database, it was not feasible to conduct statistical analyses. In the future, we will increase the number of cases included and continue to verify the clinical significance of PGK1 protein expression.

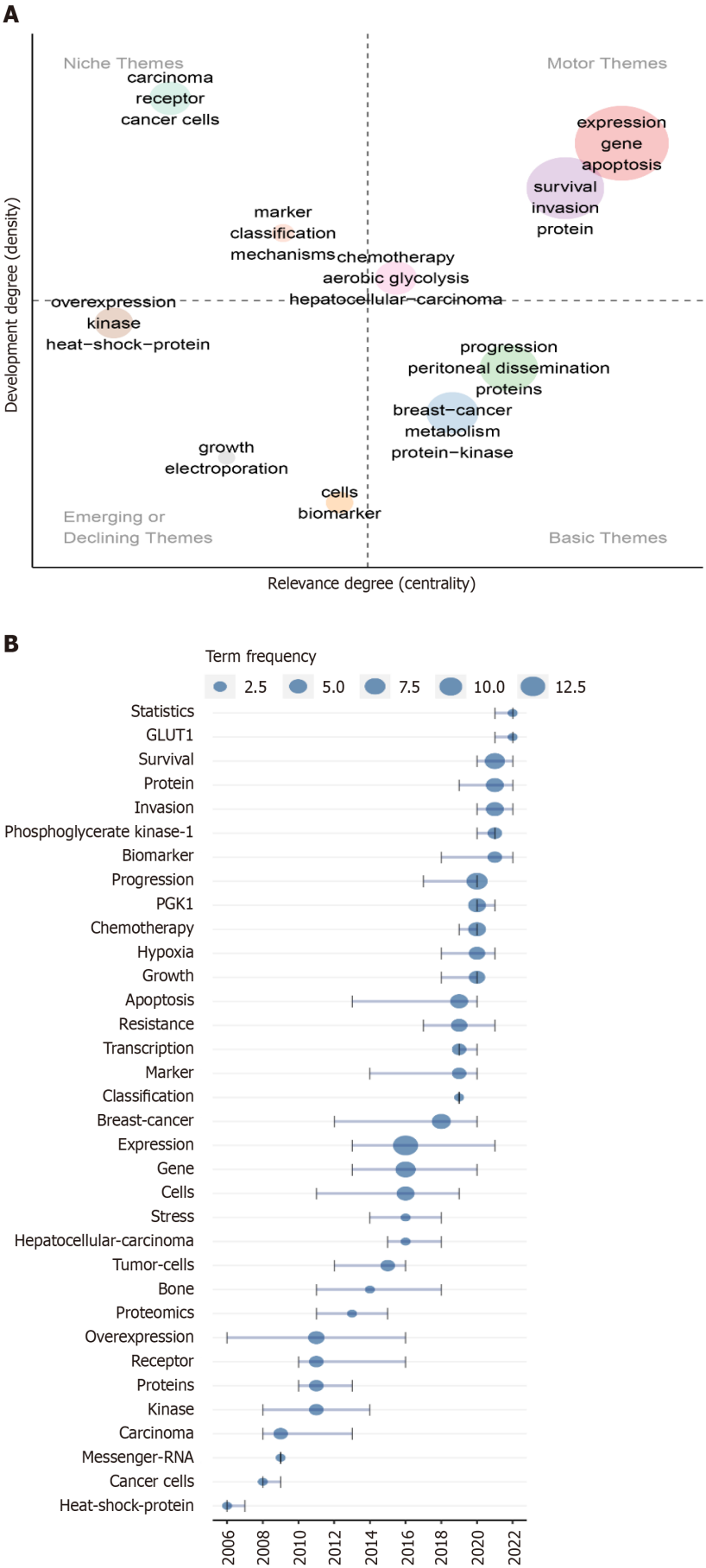


Figure 6 Thematic plot of research on breast cancer and phosphoglycerate kinase 1 and trends in topics related to breast cancer and

phosphoglycerate kinase 1 research. A: Using Web of Science key words, various research themes were detected *via* co-occurrence analysis and walktrap clustering analysis. Different colors represent different themes. Density represents the connection strength of basic knowledge units within a single topic. A larger topic density value indicates greater topic maturity. Centrality represents the strength of the connection between a topic and other topics. A higher centrality value of a topic suggests a strong interconnection with other topics, placing the topic at the heart of the research landscape. According to the density and centripetal degree values, the rectangular coordinate system was divided into four quadrants. The first quadrant contains core themes of high maturity; the second quadrant has isolated themes of high maturity, and the third quadrant contains new themes or themes that are about to disappear. The fourth quadrant encompasses basic themes of low maturity that may become research hotspots or future research trends; B: Topic trends were detected using co-word analysis. For each topic, the quartiles of publication year were calculated. The horizontal axis represents the first and third quantile years. Each node refers to the median publication year of each term. The larger the node, the more frequent the term.

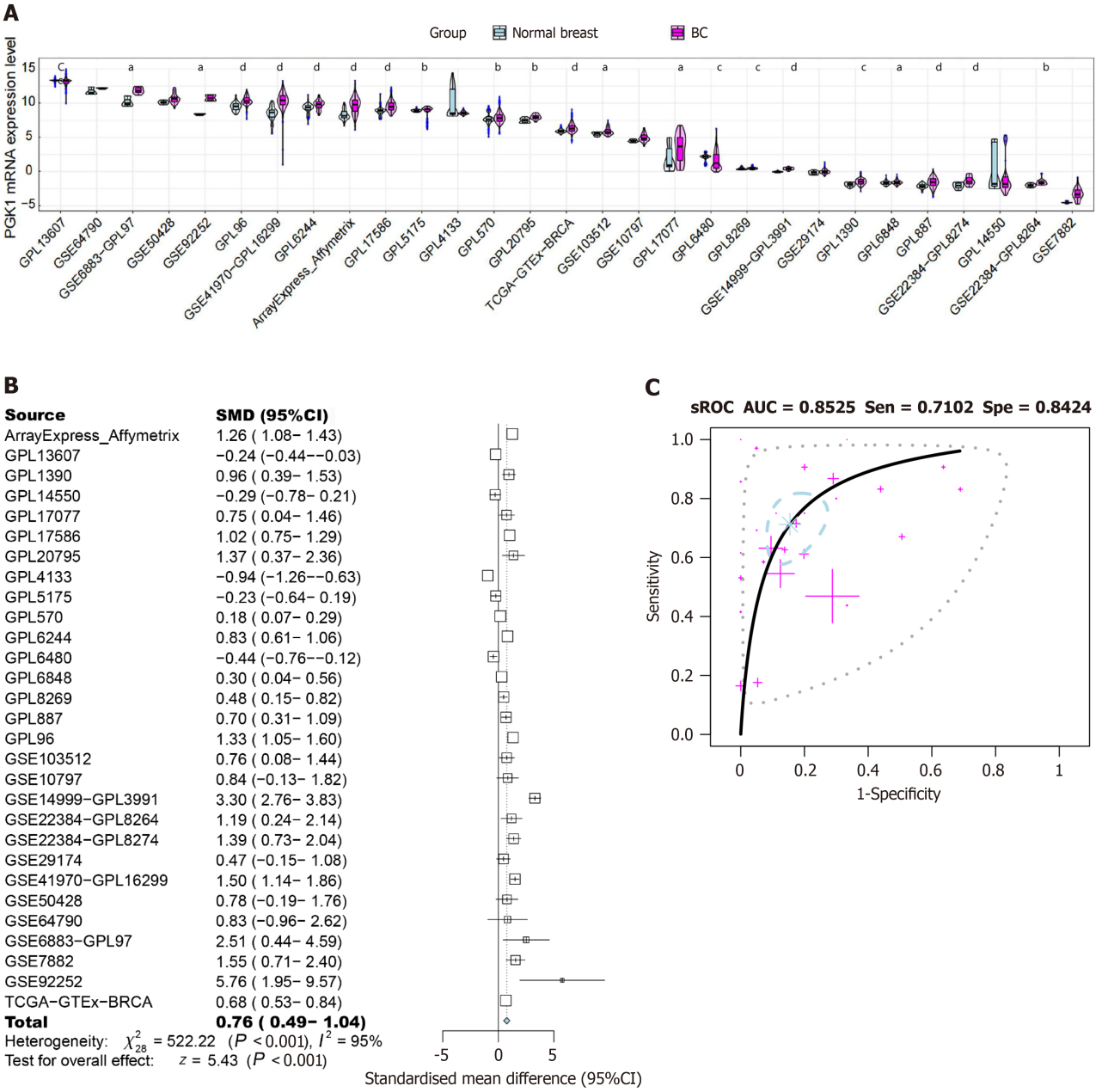


Figure 7 Expression levels of phosphoglycerate kinase 1 in breast cancer tissue *vs* normal breast tissue. A: mRNA expression level; B: Standardized mean differences; C: Summary receiver operating characteristic curves. ^aP < 0.05; ^bP < 0.01; ^cP < 0.001; ^dP < 0.0001. BC: Breast cancer; sROC: Summary receiver operating characteristic curve; AUC: Area under the curve; Sen: Sensitivity; Spe: Specificity; SMD: Standardized mean difference; 95%CI: 95% confidence interval.

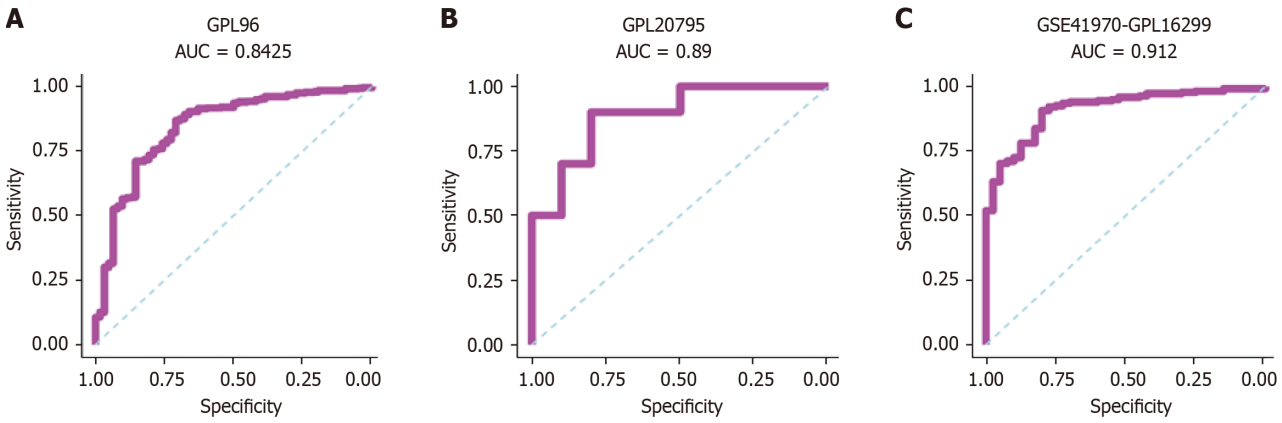


Figure 8 Receiver operating characteristic curves. A-C: Receiver operating characteristic curves of phosphoglycerate kinase 1 expression in breast cancer tissue *vs* normal breast tissue. AUC: Area under the curve.

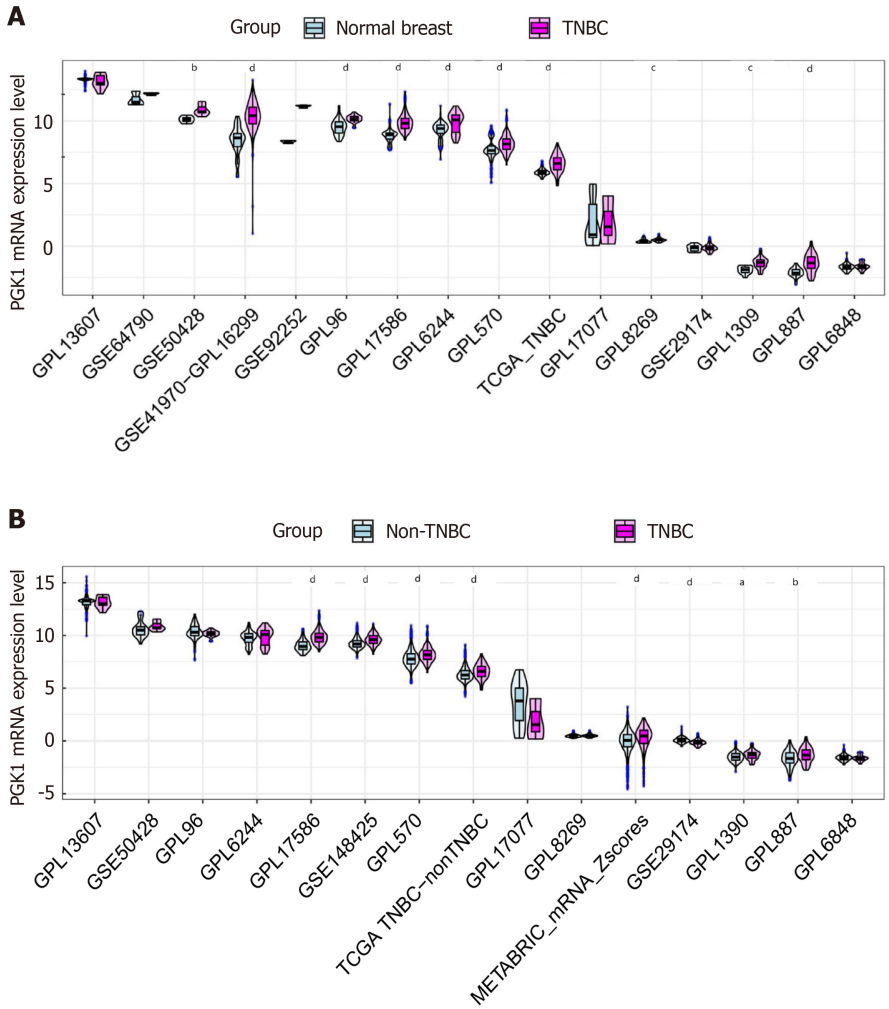


Figure 9 mRNA expression level of phosphoglycerate kinase 1 in triple-negative breast cancer. A: Triple-negative breast cancer (TNBC) tissue *vs* normal breast tissue; B: TNBC tissue *vs* non-TNBC tissue. TNBC: Triple-negative breast cancer. $^{a}P < 0.05$; $^{b}P < 0.01$; $^{c}P < 0.001$; $^{d}P < 0.0001$.

Prognostic value of PGK1 in TNBC patients: Compared with the PGK1-low-expression group, the PGK1-high-expression group had a substantially shorter RFS time (HR: 1.282, $P = 0.023$). Similar trends were observed for OS and DMFS, indicating that higher expression of PGK1 is detrimental to the prognosis of TNBC, as shown in Figure 17.

Potential functional mechanisms of PGK1 in TNBC: GO enrichment analysis demonstrated that genes co-expressed with PGK1 participate in biological processes that include "generation of precursor metabolites and energy", "ATP metabolic process", and "ATP metabolic process" (Figure 18A). Simultaneously, the co-expressed genes were notably

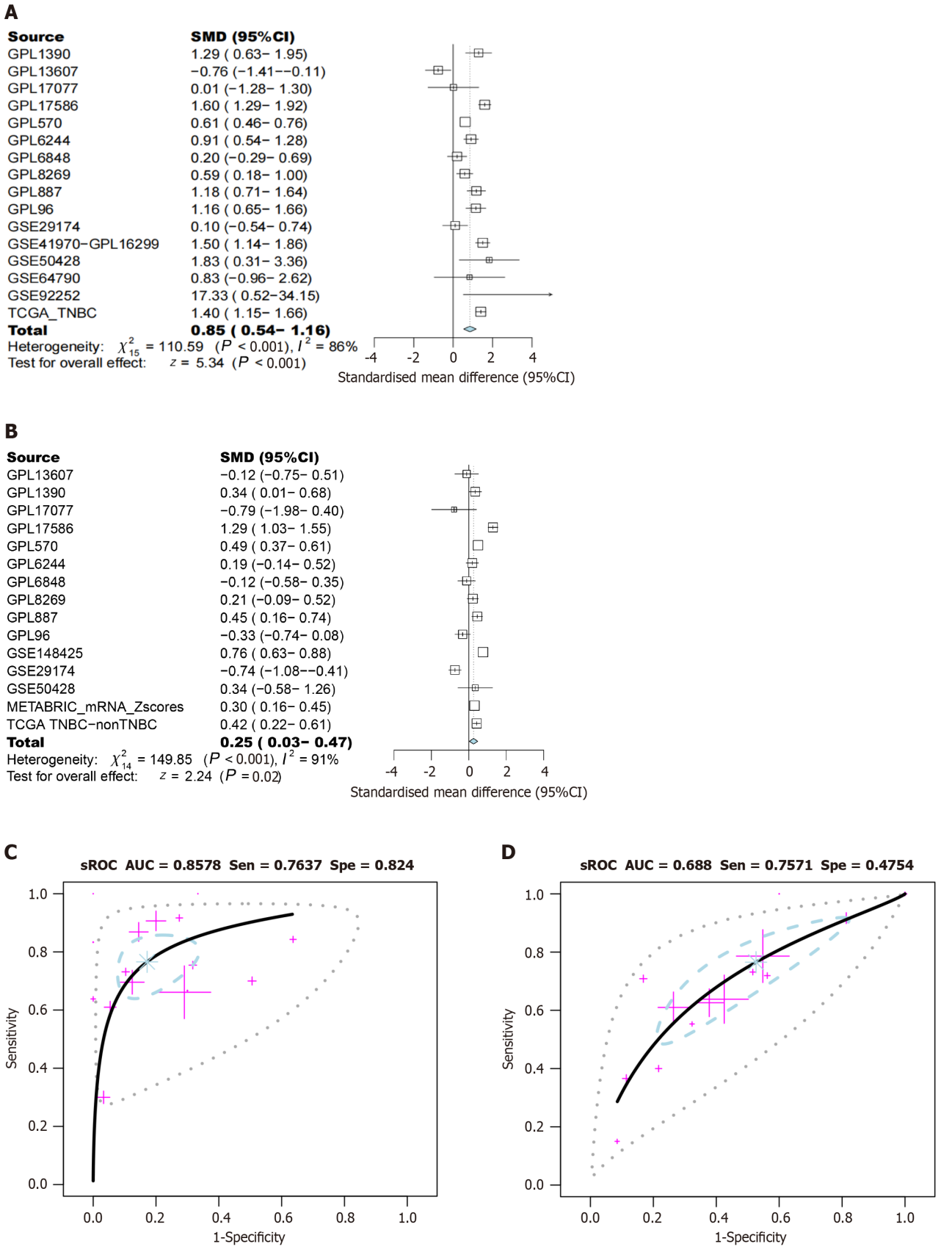


Figure 10 Comprehensive expression levels of phosphoglycerate kinase 1 in triple-negative breast cancer. A and C: Triple-negative breast cancer (TNBC) tissue *vs* normal breast tissue; B and D: TNBC tissue *vs* non-TNBC tissue. SMD: Standardized mean difference; 95%CI: 95% confidence interval; sROC: Summary receiver operating characteristic curve; AUC: Area under the curve; Sen: Sensitivity; Spe: Specificity.

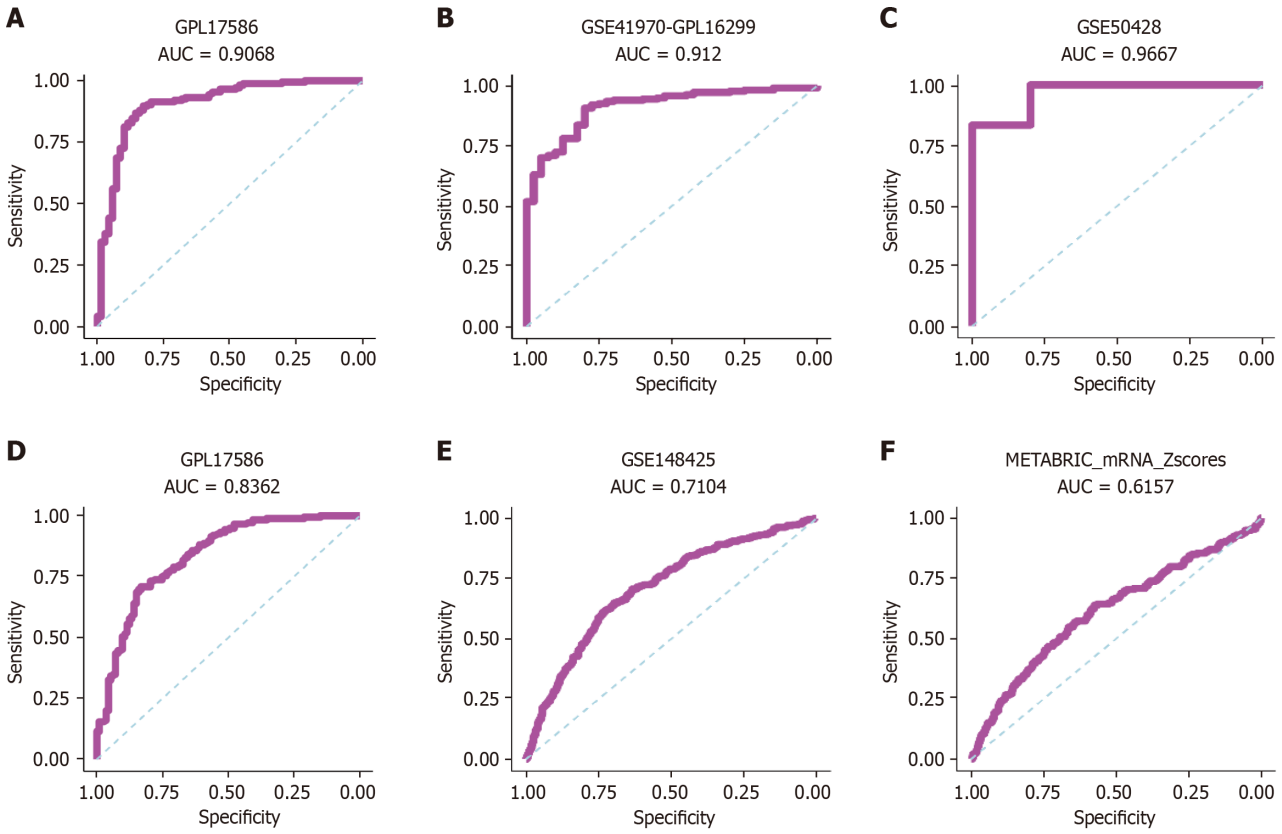


Figure 11 Receiver operating characteristic curves for phosphoglycerate kinase 1 expression in triple-negative breast cancer. A: Triple-negative breast cancer (TNBC) tissue *vs* normal breast tissue; B: TNBC tissue *vs* non-TNBC tissue. AUC: Area under the curve.

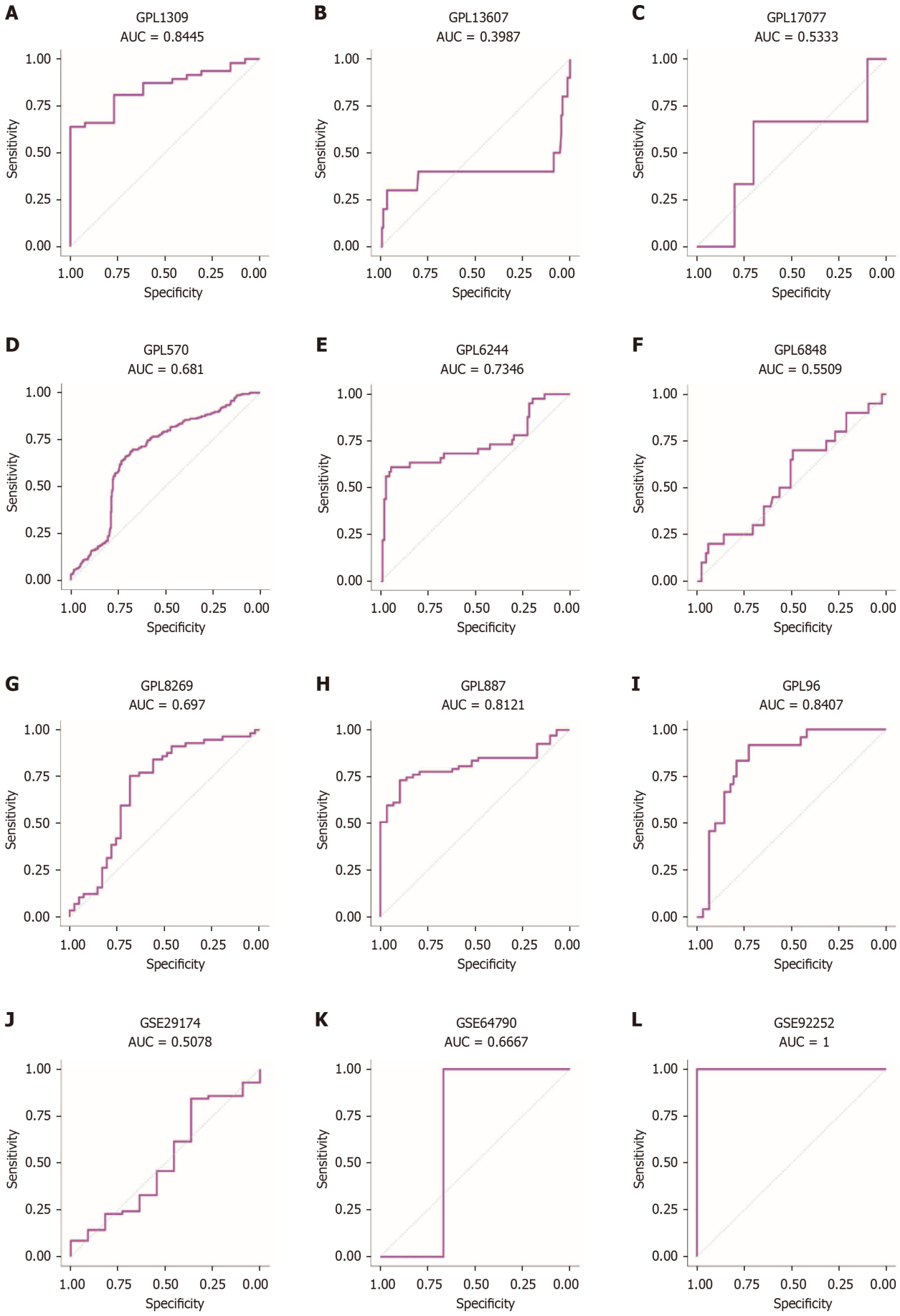
enriched in the following KEGG pathways: "Carbon metabolism", "Proteasome", "HIF-1 signaling pathway", "Central carbon metabolism in cancer", "Cell cycle", "Glycolysis/Gluconeogenesis", and "Pentose phosphate pathway", shown in Figure 18B. DO enrichment analysis showed that BC was the disease most correlated with PGK1 (Figure 18C). The major pathways relevant to the genes co-expressed with PGK1 suggest that PGK1 is closely related to metabolism and HIF-1 signaling.

The PPI network revealed 10 co-expressed genes closely related to PGK1, and TPI1 was a key gene among these 10 genes (Figure 19). The intersections of highly expressed genes between TNBC *vs* non-TNBC and genes co-expressed with PGK1 in TNBC (occurrence frequency ≥ 4) were shown in Figure 20.

DISCUSSION

There are few research documents on PGK1 and TNBC. Therefore, in this study, we concentrated on exploring the scientific knowledge gathered on BC and PGK1 in the literature in WOS with bibliometric methods to reveal the foci of recent research and suggest future research directions.

This investigation found that the total volume of PGK1 and BC related literature had been relatively small since 2005, but the number of annual publications had increased significantly from 2020, reflecting a growing interest among researchers in this area. More relevant articles came out of China than any other country. The Chinese researchers Jiang Y and Zhang X ranked first and second in terms of the number of publications and H-index. China had been an international leader in PGK1 research in BC. Different aggregations were formed among co-citations, countries, universities, and authors in the cooperation network. Although several close regional cooperative relationships had formed, some countries and institutions had not joined a cooperation cluster, and cooperation among cluster groups was also less interconnection. A lack of comprehensive collaboration might hinder communication and progress across the entire research domain. Key word analysis demonstrated that researchers were most concerned about the expression of PGK1 in BC and its link with BC progression. In the top three most cited papers, Zhang *et al*[44] and Qian *et al*[48] reported PGK1 overexpression separately in HER-2/NEU1-positive BC and invasive breast ductal carcinoma, and Shashni *et al*[47] believed that ATP generation and cancer metabolism could be affected by PGK1 downregulation. The journals with the most articles were the Journal of Proteome Research and Scientific Reports, and Cancer Research was the most cited journal. Overall, hot topics in PGK1 and BC were "expression" and "progression". BC survival, invasion, and PGK1 proteins were several new areas of attention in this field that have emerged in the past two years.


A
GPL1309
AUC = 0.8445
B
GPL13607
AUC = 0.3987
C
GPL17077
AUC = 0.5333
D
GPL570
AUC = 0.681
E
GPL6244
AUC = 0.7346
F
GPL6848
AUC = 0.5509
G
GPL8269
AUC = 0.697
H
GPL887
AUC = 0.8121
I
GPL96
AUC = 0.8407
J
GSE29174
AUC = 0.5078
K
GSE64790
AUC = 0.6667
L
GSE92252
AUC = 1
Sensitivity
Specificity
1.00
0.75
0.50
0.25
0.00

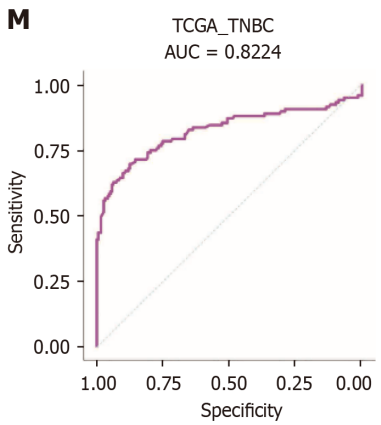


Figure 12 Receiver operating characteristic curves. A-M: Receiver operating characteristic curves for phosphoglycerate kinase 1 expression in triple-negative breast cancer *vs* normal breast tissue. AUC: Area under the curve.

This research gathered 31 high-throughput datasets on BC tissue (7543 cases) and non-cancerous breast tissue (1685 cases) and confirmed that PGK1 exhibited a markedly higher expression state in BC (SMD: 0.76; AUC of sROC = 0.8525), which was consistent with the results reported in previous items of literature. Li *et al*[42] compared 112 non-cancerous tissues and 1096 BC tissues and found that BC had stronger PGK1 expression than non-cancerous breast tissue. Similarly, Shao *et al*[49] found a rise in PGK1 mRNA levels in 145 BC tissues, which that contrasted with those of 69 non-cancerous tissues, and PGK1 mRNA was inversely correlated with the OS of BC. He *et al*[50] also compared 1066 BC and 112 non-cancerous samples and reached a conclusion in line with the above reports. Moreover, the expression level of PGK1 protein was shown to be increased in BC tissues compared with non-cancerous tissues.

The expression of PGK1 also depends on the type of BC[51]. Our study, for the first time, revealed that PGK1 expression was increased in TNBC and surpassed the levels found in both normal breast tissue and non-TNBC. Furthermore, genes co-expressed with PGK1 had been shown to be enriched in "generation of precursor metabolites and energy", "ATP metabolic process", and "response to hypoxia". In KEGG pathways analysis, they were enriched in the pathways of "proteasome", "HIF-1 signaling", and "glycolysis/gluconeogenesis".

It was discovered that the mRNA expression levels of 1159 TNBC tissue cases were noticeably higher than those of 1205 non-cancerous breast tissue cases in 16 high-throughput data sets, with an SMD of 0.85 and integrated AUC of 0.8578. This indicated that the increase in PGK1 mRNA might influence the occurrence of BC, including TNBC.

More crucially, this study also found that PGK1 might play different roles in promoting TNBC and non-TNBC. When compared with non-TNBC, TNBC samples showed much higher expression of PGK1, with the SMD of 15 data sets (including 1520 cases of TNBC and 7072 cases of non-TNBC) being 0.25, and the integrated AUC being 0.688. Previously, PGK1 was reported to be associated with the status of HER-2/ER. PGK1 expression in HER-2-positive patients (37 out of 88 cases) and ER-positive patients (70 out of 167 cases) was upregulated compared with that in the HER-2-negative group (74 out of 254 cases) and ER-negative group (66 out of 234 cases)[43]. One study also mentioned that, compared with the HER-2-positive group (19 cases), the TNBC group's (15 cases) mRNA and protein levels of PGK1 were down-regulated [52]. These findings suggested that PGK1 expression was down-regulated in BC with ER/HER-2 negative status and TNBC. Through an analysis of large data sets combining global gene chip and RNA-seq data from multi-center studies (1520 cases of TNBC and 7072 cases of non-TNBC), it was finally concluded that, though PGK1 in TNBC had both high and low expression, PGK1 showed an overall trend of increased expression in TNBC.

The prognostic analysis showed that increased PGK1 expression was closely associated with a shorter RFS in TNBC cases, and a similar pattern was observed for OS, indicating that high PGK1 expression was detrimental to the survival prognosis of TNBC patients. Therefore, we concluded that PGK1 was overexpressed in TNBC compared to normal breast tissue and non-TNBC, and that its upregulation correlated with more adverse prognoses in patients with TNBC, implying a potential role for PGK1 in tumor progression.

In this study, GO and KEGG enrichment analyses demonstrated that genes co-expressed with PGK1 were related to glycolysis, hypoxia, and HIF-1 pathways, which was reflected in previous findings in the literature. PGK1 had been shown to not only be a crucial glycolytic enzyme in ATP generation during glycolysis but also to act as a protein kinase to suppress pyruvate metabolism in the mitochondria and enhance the glycolysis of tumor cells[53].

Obviously, the metabolism of BC cells, including TNBC cells, undergoes changes. Under aerobic conditions, normal cells obtain energy by oxidative phosphorylation (OXPHOS) in the mitochondria. In hypoxia, cells acquire energy *via* the metabolic pathway of glycolysis rather than mitochondrial processes that consume oxygen[54]. Despite the availability of sufficient oxygen, malignant tumor cells continue to fulfill their metabolic demands through the glycolytic mode rather than OXPHOS, and this phenomenon is referred to aerobic glycolysis or the Warburg effect[55,56]. The generation of tumor stromal blood vessels lags behind growth rate of tumor cells, and oxygen delivery is unable to keep up with the rapid growth and proliferation of tumor cells, putting tumor cells in a continuous hypoxic microenvironment, with interrupted mitochondrial OXPHOS and a shift in energy metabolism to aerobic glycolysis[57]. Tumor cells that utilize glycolysis would then have a survival advantage in a rapidly proliferating hypoxic environments[58]. In studies, TNBC tissue displays higher glucose uptake and lactic acid (glycolytic product) secretion, and more dependence on glycolysis

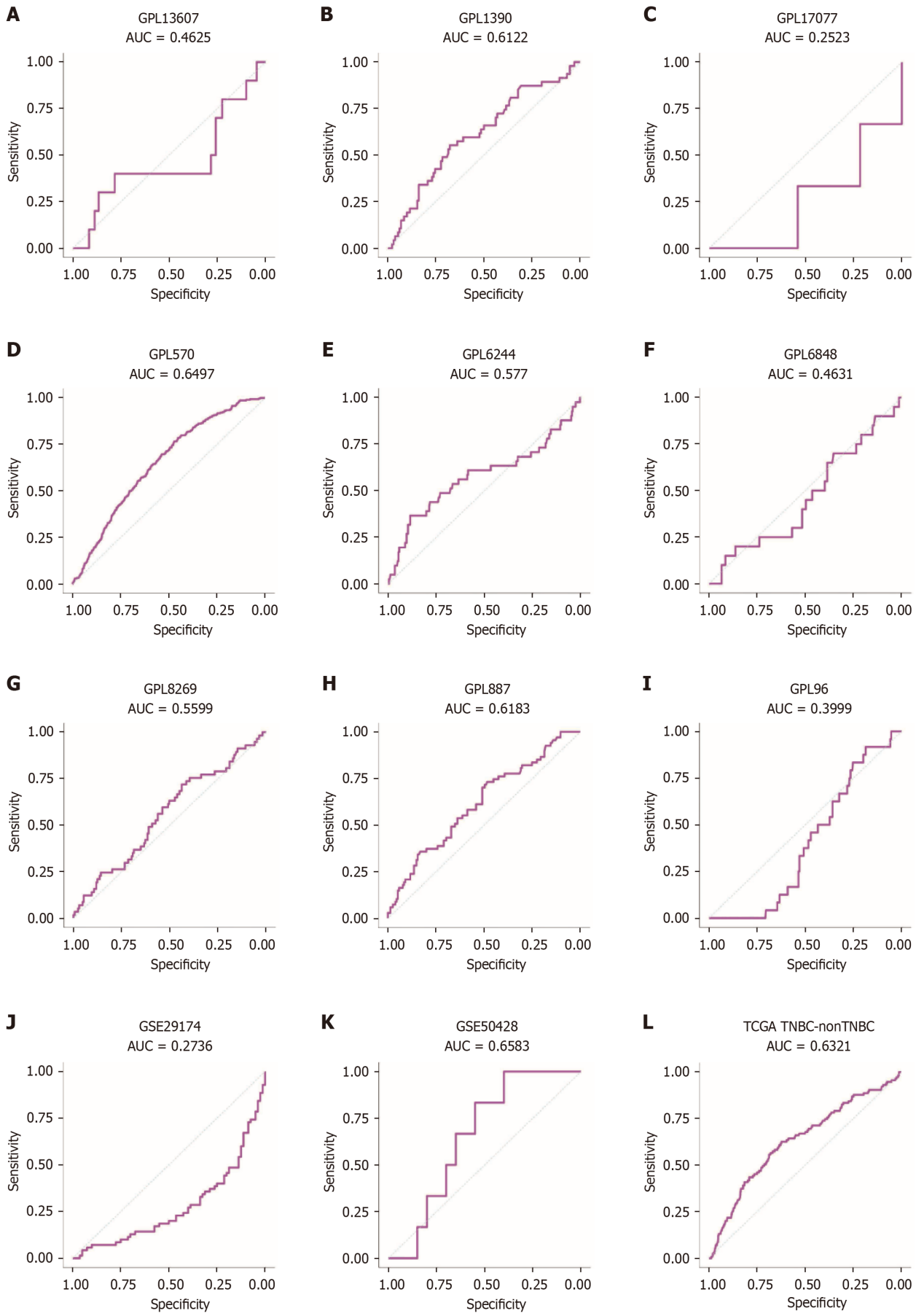


Figure 13 Receiver operating characteristic curves. A-L: Receiver operating characteristic curves for phosphoglycerate kinase 1 expression in triple-negative breast cancer *vs* non-triple-negative breast cancers. AUC: Area under the curve.

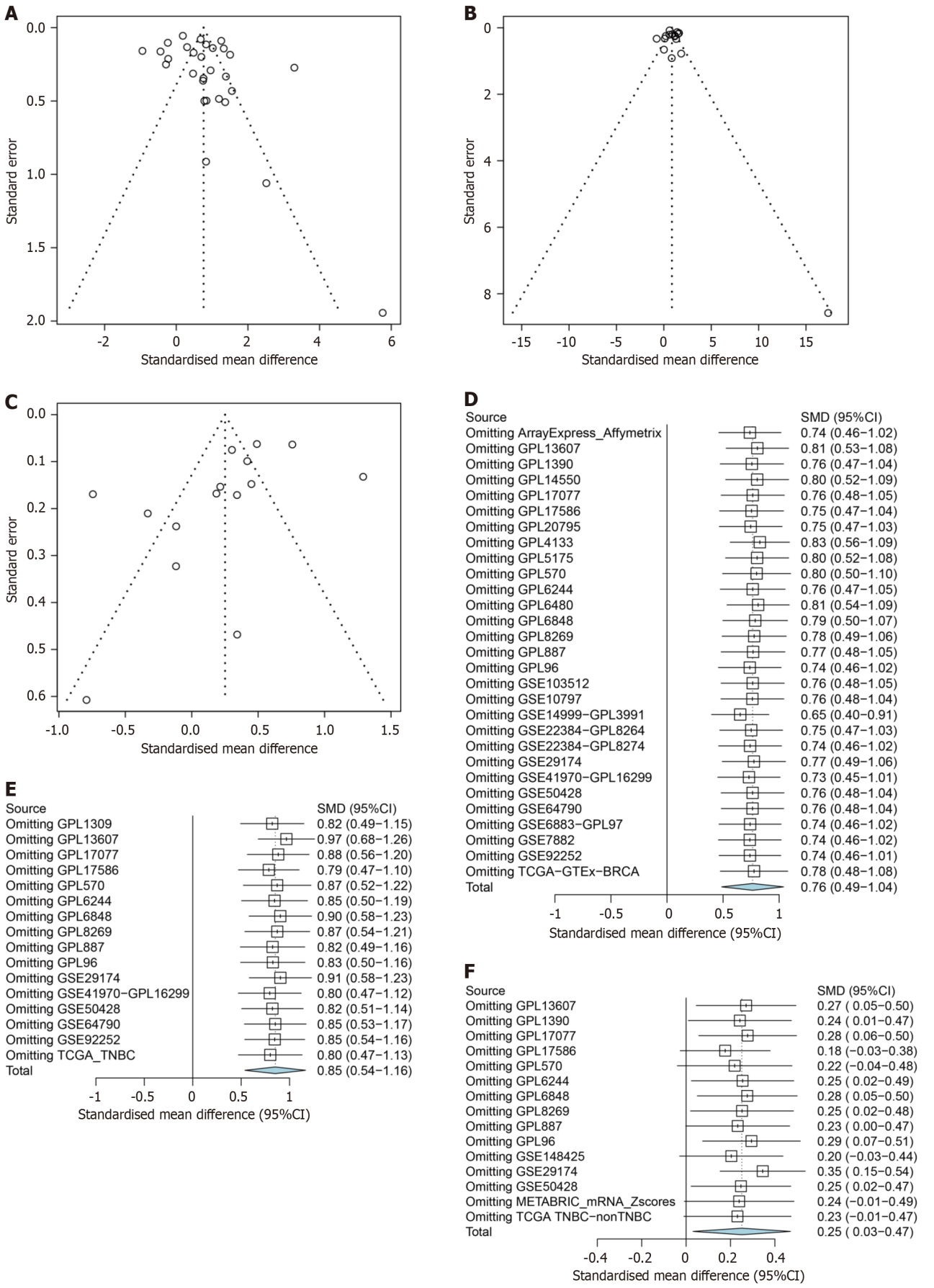
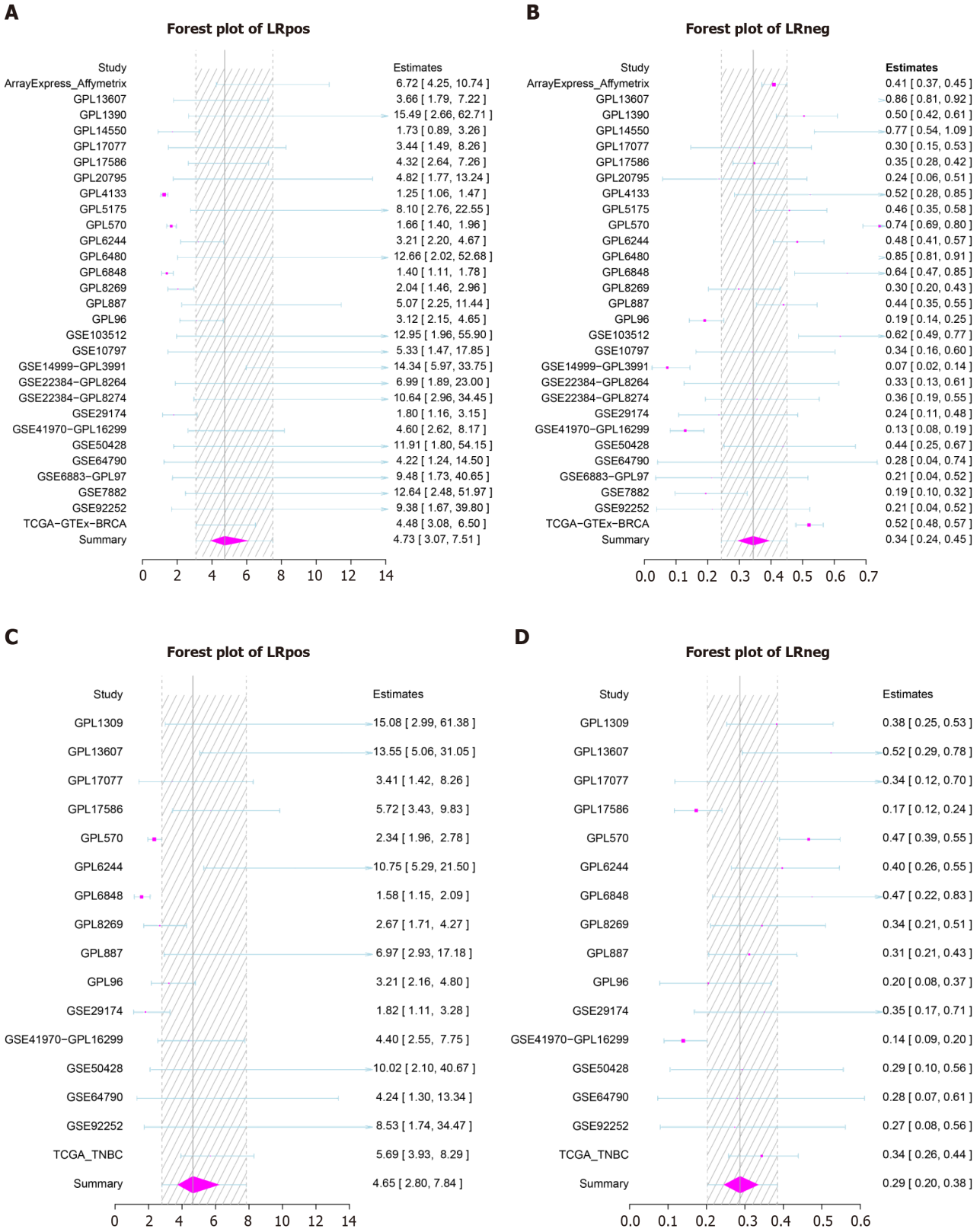


Figure 14 Funnel plots and forest plots for phosphoglycerate kinase 1 expression in breast cancer. A-C: Publication bias detection based on breast cancer (BC) *vs* normal breast tissue, triple-negative BC (TNBC) *vs* normal breast tissue, and TNBC *vs* non-TNBC tissue; D-F: Sensitivity analysis based on BC *vs* normal breast tissue, TNBC *vs* normal breast tissue, and TNBC *vs* non-TNBC tissue.


A
Forest plot of LRpos
Study
Estimates
ArrayExpress_Affymetrix 6.72 [4.25, 10.74]
GPL13607 3.66 [1.79, 7.22]
GPL1390 15.49 [2.66, 62.71]
GPL14550 1.73 [0.89, 3.26]
GPL17077 3.44 [1.49, 8.26]
GPL17586 4.32 [2.64, 7.26]
GPL20795 4.82 [1.77, 13.24]
GPL4133 1.25 [1.06, 1.47]
GPL5175 8.10 [2.76, 22.55]
GPL570 1.66 [1.40, 1.96]
GPL6244 3.21 [2.20, 4.67]
GPL6480 12.66 [2.02, 52.68]
GPL6848 1.40 [1.11, 1.78]
GPL8269 2.04 [1.46, 2.96]
GPL887 5.07 [2.25, 11.44]
GPL96 3.12 [2.15, 4.65]
GSE103512 12.95 [1.96, 55.90]
GSE10797 5.33 [1.47, 17.85]
GSE14999-GPL3991 14.34 [5.97, 33.75]
GSE22384-GPL8264 6.99 [1.89, 23.00]
GSE22384-GPL8274 10.64 [2.96, 34.45]
GSE29174 1.80 [1.16, 3.15]
GSE41970-GPL16299 4.60 [2.62, 8.17]
GSE50428 11.91 [1.80, 54.15]
GSE64790 4.22 [1.24, 14.50]
GSE6883-GPL97 9.48 [1.73, 40.65]
GSE7882 12.64 [2.48, 51.97]
GSE92252 9.38 [1.67, 39.80]
TCGA-GTEx-BRCA 4.48 [3.08, 6.50]
Summary 4.73 [3.07, 7.51]
0 2 4 6 8 10 12 14
B
Forest plot of LRneg
Study
Estimates
ArrayExpress_Affymetrix 0.41 [0.37, 0.45]
GPL13607 0.86 [0.81, 0.92]
GPL1390 0.50 [0.42, 0.61]
GPL14550 0.77 [0.54, 1.09]
GPL17077 0.30 [0.15, 0.53]
GPL17586 0.35 [0.28, 0.42]
GPL20795 0.24 [0.06, 0.51]
GPL4133 0.52 [0.28, 0.85]
GPL5175 0.46 [0.35, 0.58]
GPL570 0.74 [0.69, 0.80]
GPL6244 0.48 [0.41, 0.57]
GPL6480 0.85 [0.81, 0.91]
GPL6848 0.64 [0.47, 0.85]
GPL8269 0.30 [0.20, 0.43]
GPL887 0.44 [0.35, 0.55]
GPL96 0.19 [0.14, 0.25]
GSE103512 0.62 [0.49, 0.77]
GSE10797 0.34 [0.16, 0.60]
GSE14999-GPL3991 0.07 [0.02, 0.14]
GSE22384-GPL8264 0.33 [0.13, 0.61]
GSE22384-GPL8274 0.36 [0.19, 0.55]
GSE29174 0.24 [0.11, 0.48]
GSE41970-GPL16299 0.13 [0.08, 0.19]
GSE50428 0.44 [0.25, 0.67]
GSE64790 0.28 [0.04, 0.74]
GSE6883-GPL97 0.21 [0.04, 0.52]
GSE7882 0.19 [0.10, 0.32]
GSE92252 0.21 [0.04, 0.52]
TCGA-GTEx-BRCA 0.52 [0.48, 0.57]
Summary 0.34 [0.24, 0.45]
0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7
C
Forest plot of LRpos
Study
Estimates
GPL1309 15.08 [2.99, 61.38]
GPL13607 13.55 [5.06, 31.05]
GPL17077 3.41 [1.42, 8.26]
GPL17586 5.72 [3.43, 9.83]
GPL570 2.34 [1.96, 2.78]
GPL6244 10.75 [5.29, 21.50]
GPL6848 1.58 [1.15, 2.09]
GPL8269 2.67 [1.71, 4.27]
GPL887 6.97 [2.93, 17.18]
GPL96 3.21 [2.16, 4.80]
GSE29174 1.82 [1.11, 3.28]
GSE41970-GPL16299 4.40 [2.55, 7.75]
GSE50428 10.02 [2.10, 40.67]
GSE64790 4.24 [1.30, 13.34]
GSE92252 8.53 [1.74, 34.47]
TCGA_TNBC 5.69 [3.93, 8.29]
Summary 4.65 [2.80, 7.84]
0 2 4 6 8 10 12 14
D
Forest plot of LRneg
Study
Estimates
GPL1309 0.38 [0.25, 0.53]
GPL13607 0.52 [0.29, 0.78]
GPL17077 0.34 [0.12, 0.70]
GPL17586 0.17 [0.12, 0.24]
GPL570 0.47 [0.39, 0.55]
GPL6244 0.40 [0.26, 0.55]
GPL6848 0.47 [0.22, 0.83]
GPL8269 0.34 [0.21, 0.51]
GPL887 0.31 [0.21, 0.43]
GPL96 0.20 [0.08, 0.37]
GSE29174 0.35 [0.17, 0.71]
GSE41970-GPL16299 0.14 [0.09, 0.20]
GSE50428 0.29 [0.10, 0.56]
GSE64790 0.28 [0.07, 0.61]
GSE92252 0.27 [0.08, 0.56]
TCGA_TNBC 0.34 [0.26, 0.44]
Summary 0.29 [0.20, 0.38]
0.0 0.1 0.2 0.3 0.4 0.5 0.6

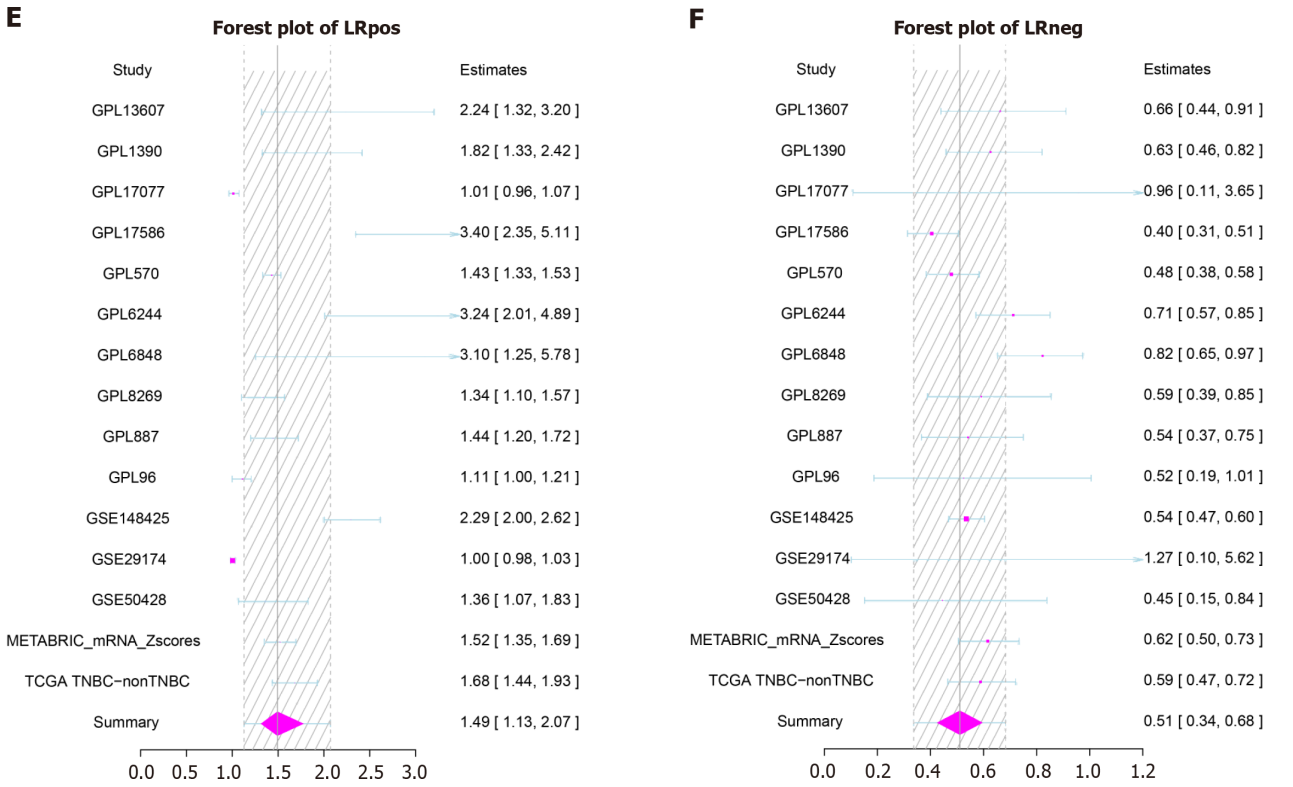


Figure 15 Forest plots of positive likelihood ratio (LRpos) and negative likelihood ratio (LRneg) for phosphoglycerate kinase 1 expression based on different groups. A and B: Breast cancer (BC) *vs* normal breast tissue; C and D: Triple-negative BC (TNBC) *vs* normal breast tissue; E and F: TNBC *vs* non-TNBC tissue.

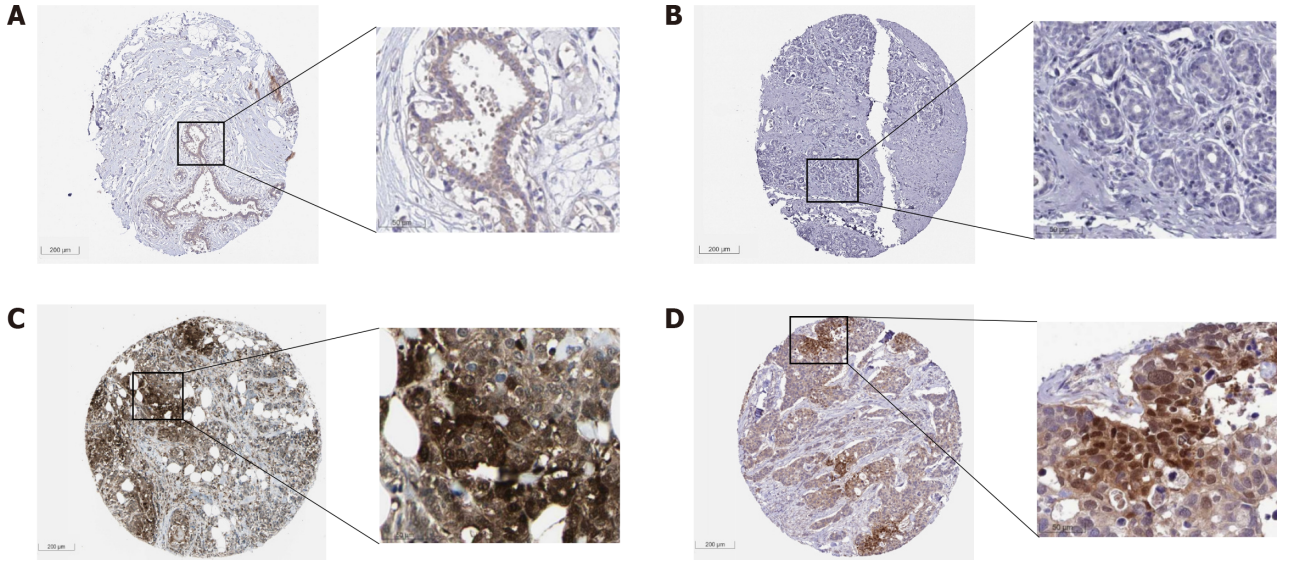


Figure 16 Immunohistochemistry staining from the Human Protein Atlas showing low or no expression of phosphoglycerate kinase 1 in normal breast tissue cells, and high expression in breast cancer cells. A: HPA045385, female, age 45, breast (T-04000), normal tissue, NOS (M-00100), Patient ID: 3544 (low or no expression). (1) Adipocytes. Staining: Not detected; Intensity: Weak; Quantity: < 25%; Location: cytoplasmic/membranous; (2) Glandular cells. Staining: Low; Intensity: Weak; Quantity: > 75%; Location: cytoplasmic/membranous; and (3) Myoepithelial cells. Staining: Low; Intensity: Weak; Quantity: > 75%; Location: Cytoplasmic/membranous; B: HPA073644, female, age 43, breast (T-04000), skin (T-01000), normal tissue, NOS (M-00100), Patient ID: 2104 (low or no expression). Adipocytes, glandular cells, and myoepithelial cells. Staining: Not detected; Intensity: Negative; Quantity: None; C: CAB010065, female, age 59, breast (T-04000), lobular carcinoma (M-85203), Patient ID: 2805 (high expression). (1) Tumor cells. Staining: High; Intensity: Strong; Quantity: 75%-25%; Location: Cytoplasmic/membranous nuclear; D: HPA045385, female, age 83, breast (T-04000), duct carcinoma (M-85003), Patient ID: 2160 (high expression). (1) Tumor cells. Staining: High. Intensity: Strong. Quantity: 75%-25%. Location: Cytoplasmic/membranous nuclear. These immunohistochemical protein expression figures were from the Human Protein Atlas (THPA) database [71].

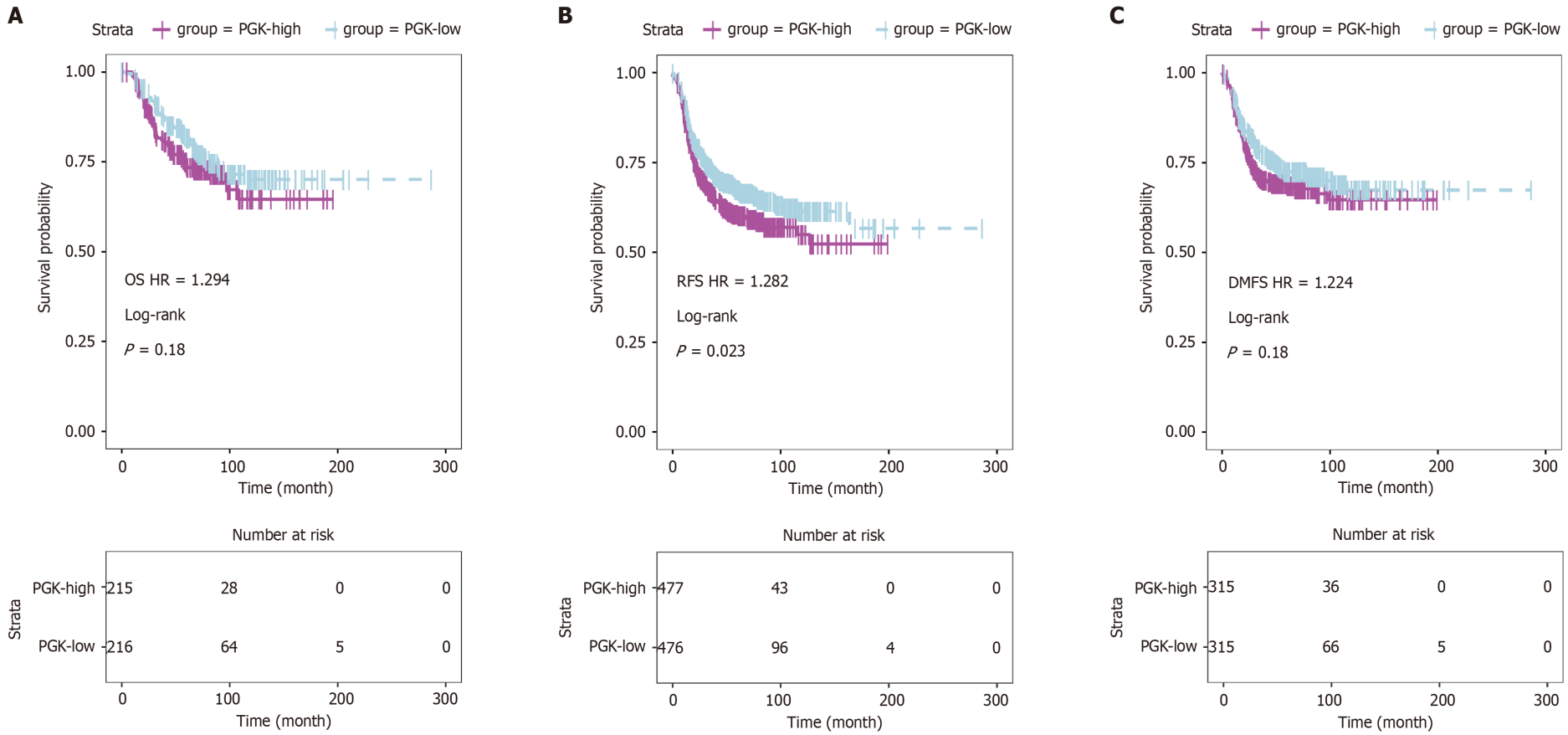


Figure 17 Kaplan-Meier curves for association between phosphoglycerate kinase 1 expression of triple-negative breast cancer patients. A: Overall survival; B: Recurrence-free survival; C: Distant metastasis free survival. OS: Overall survival; RFS: Recurrence-free survival; DMFS: Distant metastasis free survival; HR: Hazard ratio.

than other BC subtypes[59]. PGK1, as the initial rate-limiting enzyme of the cellular glycolytic pathway to ATP synthesis, directly supplies energy for cellular activities, while the other reaction product, 3-PG, is oxidized by one-carbon metabolism. This is probably the reason why PGK1 is more significant than other glycolysis enzymes in contributing to the Warburg effect in tumors[56,60,61]. Several glycolytic enzyme genes, including *PGK1*, were reported to be upregulated by HIF-1 induction under a hypoxic microenvironment, providing a molecular basis for the Warburg effect in tumor cells[57,62]. In this way, processes, including cell growth, metastasis, drug resistance, and immune evasion, are regulated *via* the Warburg effect. The high levels of PGK1 in cancerous tissues could potentiate the Warburg effect, thereby influencing the progression and prognosis of both BC and TNBC.

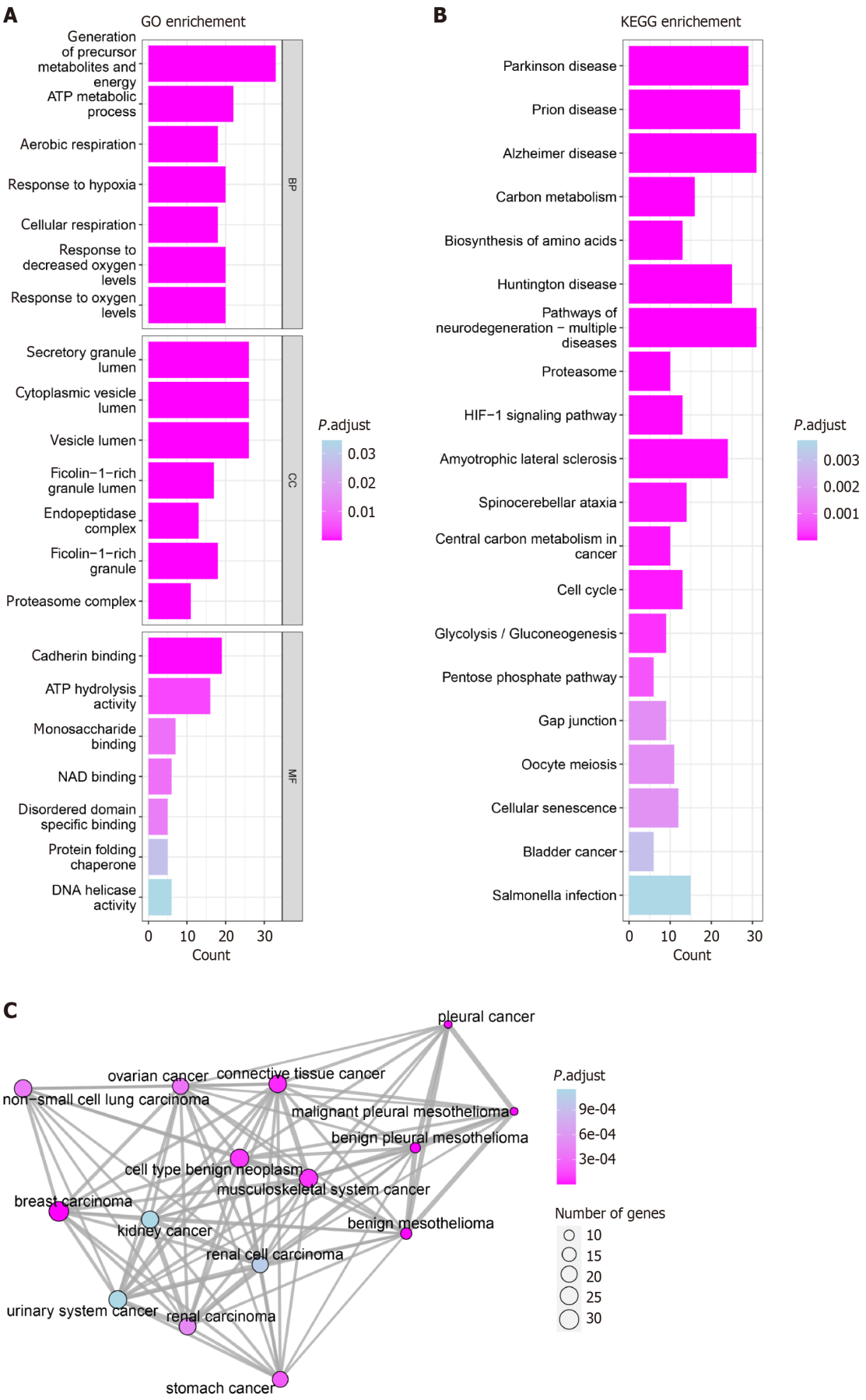


Figure 18 Pathway and disease enrichment analysis annotation. A: Gene Ontology enrichment; B: Kyoto Encyclopedia of Genes and Genomes enrichment. Columnar length represents the number of gene enrichments; the longer the column, the more gene enrichment. Color indicates the size of the *P* value;

the darker the color, the smaller the *P* value; C: Disease Ontology enrichment. The area of each circle represents the number of genes; the larger the circle, the more genes are involved. The color of each circle represents the *P* value; the darker the color, the smaller the *P* value. GO: Gene Ontology enrichment; KEGG: Kyoto Encyclopedia of Genes and Genomes.

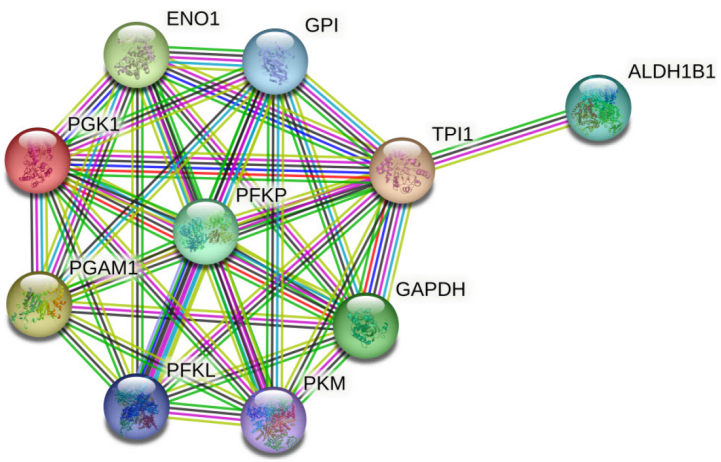


Figure 19 Protein-protein interaction network analysis of phosphoglycerate kinase 1 related genes.

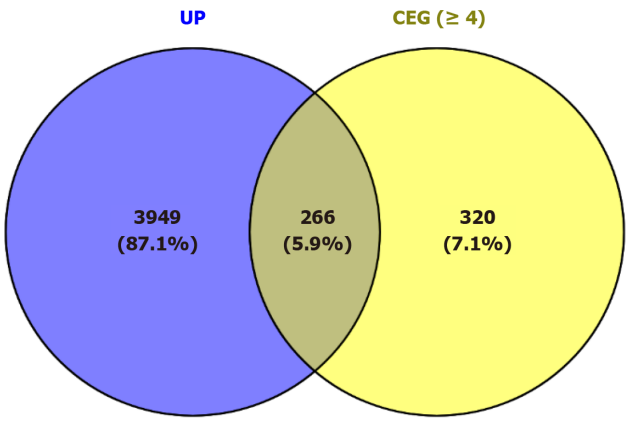


Figure 20 Intersection of triple-negative breast cancer *vs* non-triple-negative breast cancer gene overexpression and positively phosphoglycerate kinase 1 correlated gene co-expression in triple-negative breast cancer (occurrence ≥ 4). UP: Upregulated gene; CEG: Co-expressed gene.

The HIF-1/PGK1 pathway is one of the most prominent pathways in cancer cells[63]. PGK1 has been identified as a target gene of HIF-1[64] and is capable of establishing a positive-feedback loop with HIF-1[45]. HIF-1 can detect hypoxia within the tumor microenvironment, increase the expression of glucose transporters, activate genes involved in cancer glycolysis metabolism, and drive glucose toward glycolysis in cancerous cells, the latter of which is a pivotal regulatory step in the metabolic shift of tumor cells from oxidative phosphorylation to glycolysis[65-67]. Under hypoxia stress, protein receptor activation, or carcinogenic gene mutation expression, about 12% of cytoplasmic PGK1 is translocated by the accumulated HIF-1 to mitochondria, where PGK1 contributes to protein kinase activity. Pyruvate is diverted from the mitochondria into the cytoplasm to produce lactic acid, inhibiting the mitochondrial tricarboxylic acid cycle and enhancing glycolysis to support the energy and metabolite requirements of cancerous cells[64,68]. Additionally, HIF-1α expression is correlated with an ER-negative status[69]. The expression of HIF-1 was shown to be upregulated in TNBC and associated with a poorer prognosis, and it also affected the level of PGK1[66]. Regarding TNBC treatments, Sun *et al* [70] found that PGK1 expression inhibition increased the sensitivity of TNBC to paclitaxel treatment. Therefore, as PGK1 is a latent biomarker for different therapy options for TNBC, inhibiting its expression might represent a new therapeutic strategy.

CONCLUSION

Research into PGK1, a potential biomarker in BC, has made great advancements recently. PGK1 expression levels in

TNBC are subject to regulation by upstream HIF-1 and are evidently upregulated compared to those in non-TNBC and non-cancerous breast tissue. PGK1 has been shown to enhance glycolysis in TNBC. Therefore, we believe that PGK1 provides a valuable marker for predicting the disease progression of TNBC. How to inhibit the occurrence and progress of TNBC through PGK1 needs further in-depth studies. There were some limitations to our study. Our bibliometric analysis was accomplished with a single data base, and specific BC histological classifications were not assigned to the cases in the non-TNBC group.

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FOOTNOTES

Author contributions: He RQ, Huang ZG, Chen G, and Zou W designed the paper; Chen JY and Li JD performed literature and dataset screening, conducted bibliometric statistics, and carried out all computational analyses, including mRNA and protein expression, prognosis and signaling pathways; Chen JY, Li JD, Huang ZG, and Zou W constructed the figures and tables; Chen JY and Li JD wrote the draft; He RQ, Huang ZG, Chen G, and Zou W corrected the draft; and all authors have read and approved the final manuscript.

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REFERENCES

1 **Siegel RL**, Giaquinto AN, Jemal A. Cancer statistics, 2024. *CA Cancer J Clin* 2024; **74**: 12-49 [PMID: 38230766 DOI: 10.3322/caac.21820]
2 **Wang X**, Wang C, Guan J, Chen B, Xu L, Chen C. Progress of Breast Cancer basic research in China. *Int J Biol Sci* 2021; **17**: 2069-2079 [PMID: 34131406 DOI: 10.7150/ijbs.60631]
3 **Brahimetaj R**, Willekens I, Massart A, Forsyth R, Cornelis J, Mey J, Jansen B. Improved automated early detection of breast cancer based on high resolution 3D micro-CT microcalcification images. *BMC Cancer* 2022; **22**: 162 [PMID: 35148703 DOI: 10.1186/s12885-021-09133-4]
4 **Schliemann D**, Hoe WMK, Mohan D, Allotey P, Reidpath DD, Tan MM, Taib NAM, Donnelly M, Su TT. Challenges and opportunities for breast cancer early detection among rural dwelling women in Segamat District, Malaysia: A qualitative study. *PLoS One* 2022; **17**: e0267308 [PMID: 35594267 DOI: 10.1371/journal.pone.0267308]
5 **Barbirou M**, Miller AA, Gafni E, Mezlini A, Zidi A, Boley N, Tonellato PJ. Evaluation of cfDNA as an early detection assay for dense tissue breast cancer. *Sci Rep* 2022; **12**: 8458 [PMID: 35589867 DOI: 10.1038/s41598-022-12457-1]
6 **Jones MA**, Islam W, Faiz R, Chen X, Zheng B. Applying artificial intelligence technology to assist with breast cancer diagnosis and prognosis prediction. *Front Oncol* 2022; **12**: 980793 [PMID: 36119479 DOI: 10.3389/fonc.2022.980793]
7 **Din NMU**, Dar RA, Rasool M, Assad A. Breast cancer detection using deep learning: Datasets, methods, and challenges ahead. *Comput Biol Med* 2022; **149**: 106073 [PMID: 36103745 DOI: 10.1016/j.compbiomed.2022.106073]
8 **Wu M**, Yuan K, Lyu S, Li Y. Screening potential immune signatures for early-stage basal-like/triple-negative breast cancer. *World J Surg Oncol* 2022; **20**: 214 [PMID: 35751103 DOI: 10.1186/s12957-022-02683-2]
9 **Sun L**, Qi M, Cui X, Song Q. The Clinical Application of Combined Ultrasound, Mammography, and Tumor Markers in Screening Breast Cancer among High-Risk Women. *Comput Math Methods Med* 2022; **2022**: 4074628 [PMID: 35872933 DOI: 10.1155/2022/4074628]
10 **Zhang DX**, Dang XTT, Vu LT, Lim CMH, Yeo EYM, Lam BWS, Leong SM, Omar N, Putti TC, Yeh YC, Ma V, Luo JY, Cho WC, Chen G, Lee VKM, Grimson A, Le MTN. αvβ1 integrin is enriched in extracellular vesicles of metastatic breast cancer cells: A mechanism mediated by galectin-3. *J Extracell Vesicles* 2022; **11**: e12234 [PMID: 35923105 DOI: 10.1002/jev2.12234]
11 **Ebeid SA**, Abd El Moneim NA, El-Benhawy SA, Ramadan R, Ismail SE. Znhit1 and HIF-2α are correlated with cancer stem cell markers in breast cancer patients. *Sci Rep* 2022; **12**: 13918 [PMID: 35978075 DOI: 10.1038/s41598-022-18133-8]

12 **Cedano-Prieto DM**, Bergez-Hernandez F, Leal-Leon EA, Garcia-Magallanes N, Luque-Ortega F, Picos-Cardenas V, Guerrero-Arambula E, Gutierrez-Zepeda B, Romo-Martinez E, Arambula-Meraz E. Altered Expression of Survivin Variants S-2B and S-WT in Breast Cancer Is Related to Adipokine Expression. *J Oncol* 2022; **2022**: 7398444 [PMID: 35342410 DOI: 10.1155/2022/7398444]

13 **Peng W**, Li JD, Zeng JJ, Zou XP, Tang D, Tang W, Rong MH, Li Y, Dai WB, Tang ZQ, Feng ZB, Chen G. Clinical value and potential mechanisms of COL8A1 upregulation in breast cancer: a comprehensive analysis. *Cancer Cell Int* 2020; **20**: 392 [PMID: 32818022 DOI: 10.1186/s12935-020-01465-8]

14 **Li JD**, Chen G, Wu M, Huang Y, Tang W. Downregulation of CDC14B in 5218 breast cancer patients: A novel prognosticator for triple-negative breast cancer. *Math Biosci Eng* 2020; **17**: 8152-8181 [PMID: 33378938 DOI: 10.3934/mbe.2020414]

15 **Cloud AS**, Vargheese AM, Gunewardena S, Shimak RM, Ganeshkumar S, Kumaraswamy E, Jensen RA, Chennathukuzhi VM. Loss of REST in breast cancer promotes tumor progression through estrogen sensitization, MMP24 and CEMIP overexpression. *BMC Cancer* 2022; **22**: 180 [PMID: 35177031 DOI: 10.1186/s12885-022-09280-2]

16 **Tang W**, Li GS, Li JD, Pan WY, Shi Q, Xiong DD, Mo CH, Zeng JJ, Chen G, Feng ZB, Huang SN, Rong MH. The role of upregulated miR-375 expression in breast cancer: An *in vitro* and in silico study. *Pathol Res Pract* 2020; **216**: 152754 [PMID: 31787478 DOI: 10.1016/j.prp.2019.152754]

17 **Thomas CE**, Dahl L, Byström S, Chen Y, Uhlén M, Mälarstig A, Czene K, Hall P, Schwenk JM, Gabrielson M. Circulating proteins reveal prior use of menopausal hormonal therapy and increased risk of breast cancer. *Transl Oncol* 2022; **17**: 101339 [PMID: 35033985 DOI: 10.1016/j.tranon.2022.101339]

18 **Lee YJ**, Kim Y, Choi BB, Kim JR, Ko HM, Suh KH, Lee JS. The blood level of thioredoxin 1 as a supporting biomarker in the detection of breast cancer. *BMC Cancer* 2022; **22**: 12 [PMID: 34979986 DOI: 10.1186/s12885-021-09055-1]

19 **Lu B**, Natarajan E, Balaji Raghavendran HR, Markandan UD. Molecular Classification, Treatment, and Genetic Biomarkers in Triple-Negative Breast Cancer: A Review. *Technol Cancer Res Treat* 2023; **22**: 15330338221145246 [PMID: 36601658 DOI: 10.1177/15330338221145246]

20 **Yang Y**, Zhang L, Tian W, Li Y, Qin Q, Mao Y, Liu X, Hong J, Hu L, Zeng Q, Zhang Q, Zhao H. Prognosis prediction and risk factors for triple-negative breast cancer patients with brain metastasis: A population-based study. *Cancer Med* 2023; **12**: 7951-7961 [PMID: 36629093 DOI: 10.1002/cam4.5575]

21 **Deng H**, Wang L, Wang N, Zhang K, Zhao Y, Qiu P, Qi X, Zhang D, Xu F, Liu J. Neoadjuvant checkpoint blockade in combination with Chemotherapy in patients with tripe-negative breast cancer: exploratory analysis of real-world, multicenter data. *BMC Cancer* 2023; **23**: 29 [PMID: 36611131 DOI: 10.1186/s12885-023-10515-z]

22 **Wang Q**, Xu M, Sun Y, Chen J, Chen C, Qian C, Chen Y, Cao L, Xu Q, Du X, Yang W. Gene Expression Profiling for Diagnosis of Triple-Negative Breast Cancer: A Multicenter, Retrospective Cohort Study. *Front Oncol* 2019; **9**: 354 [PMID: 31134153 DOI: 10.3389/fonc.2019.00354]

23 **Lin C**, Cui J, Peng Z, Qian K, Wu R, Cheng Y, Yin W. Efficacy of platinum-based and non-platinum-based drugs on triple-negative breast cancer: meta-analysis. *Eur J Med Res* 2022; **27**: 201 [PMID: 36242046 DOI: 10.1186/s40001-022-00839-0]

24 **Li Y**, Zhang H, Merkher Y, Chen L, Liu N, Leonov S, Chen Y. Recent advances in therapeutic strategies for triple-negative breast cancer. *J Hematol Oncol* 2022; **15**: 121 [PMID: 36038913 DOI: 10.1186/s13045-022-01341-0]

25 **Bakherad H**, Ghasemi F, Hosseindokht M, Zare H. Nanobodies; new molecular instruments with special specifications for targeting, diagnosis and treatment of triple-negative breast cancer. *Cancer Cell Int* 2022; **22**: 245 [PMID: 35933373 DOI: 10.1186/s12935-022-02665-0]

26 **Yin J**, Zhu C, Wang G, Gu J. Treatment for Triple-Negative Breast Cancer: An Umbrella Review of Meta-Analyses. *Int J Gen Med* 2022; **15**: 5901-5914 [PMID: 35795302 DOI: 10.2147/IJGM.S370351]

27 **Sun H**, Xu J, Dai S, Ma Y, Sun T. Breast cancer brain metastasis: Current evidence and future directions. *Cancer Med* 2023; **12**: 1007-1024 [PMID: 35822637 DOI: 10.1002/cam4.5021]

28 **Swain SM**, Shastry M, Hamilton E. Targeting HER2-positive breast cancer: advances and future directions. *Nat Rev Drug Discov* 2023; **22**: 101-126 [PMID: 36344672 DOI: 10.1038/s41573-022-00579-0]

29 **Yang R**, Li Y, Wang H, Qin T, Yin X, Ma X. Therapeutic progress and challenges for triple negative breast cancer: targeted therapy and immunotherapy. *Mol Biomed* 2022; **3**: 8 [PMID: 35243562 DOI: 10.1186/s43556-022-00071-6]

30 **Chai Y**, Chen Y, Zhang D, Wei Y, Li Z, Li Q, Xu B. Homologous Recombination Deficiency (HRD) and BRCA 1/2 Gene Mutation for Predicting the Effect of Platinum-Based Neoadjuvant Chemotherapy of Early-Stage Triple-Negative Breast Cancer (TNBC): A Systematic Review and Meta-Analysis. *J Pers Med* 2022; **12** [PMID: 35207810 DOI: 10.3390/jpm12020323]

31 **Alghazali MW**, Al-Hetty HRAK, Ali ZMM, Saleh MM, Suleiman AA, Jalil AT. Non-coding RNAs, another side of immune regulation during triple-negative breast cancer. *Pathol Res Pract* 2022; **239**: 154132 [PMID: 36183439 DOI: 10.1016/j.prp.2022.154132]

32 **Hua Z**, White J, Zhou J. Cancer stem cells in TNBC. *Semin Cancer Biol* 2022; **82**: 26-34 [PMID: 34147641 DOI: 10.1016/j.semcancer.2021.06.015]

33 **Su YH**, Wu YZ, Ann DK, Chen JL, Kuo CY. Obesity promotes radioresistance through SERPINE1-mediated aggressiveness and DNA repair of triple-negative breast cancer. *Cell Death Dis* 2023; **14**: 53 [PMID: 36681663 DOI: 10.1038/s41419-023-05576-8]

34 **See SHC**, Smith SH, Finkelman BS, LaBoy C, Novo JE, Siziopikou KP, Blanco LZ Jr. The role of PRAME and NY-ESO-1 as potential therapeutic and prognostic biomarkers in triple-negative breast carcinomas. *Pathol Res Pract* 2023; **241**: 154299 [PMID: 36603407 DOI: 10.1016/j.prp.2022.154299]

35 **Fu D**, He C, Wei J, Zhang Z, Luo Y, Tan H, Ren C. PGK1 is a Potential Survival Biomarker and Invasion Promoter by Regulating the HIF-1α-Mediated Epithelial-Mesenchymal Transition Process in Breast Cancer. *Cell Physiol Biochem* 2018; **51**: 2434-2444 [PMID: 30537744 DOI: 10.1159/000495900]

36 **Chu Z**, Huo N, Zhu X, Liu H, Cong R, Ma L, Kang X, Xue C, Li J, Li Q, You H, Zhang Q, Xu X. FOXO3A-induced LINC00926 suppresses breast tumor growth and metastasis through inhibition of PGK1-mediated Warburg effect. *Mol Ther* 2021; **29**: 2737-2753 [PMID: 33940159 DOI: 10.1016/j.ymthe.2021.04.036]

37 **Nie H**, Ju H, Fan J, Shi X, Cheng Y, Cang X, Zheng Z, Duan X, Yi W. O-GlcNAcylation of PGK1 coordinates glycolysis and TCA cycle to promote tumor growth. *Nat Commun* 2020; **11**: 36 [PMID: 31911580 DOI: 10.1038/s41467-019-13601-8]

38 **Yi J**, Luo X, Huang W, Yang W, Qi Y, He J, Xie H. PGK1 is a potential biomarker for early diagnosis and prognosis of hepatocellular carcinoma. *Oncol Lett* 2024; **27**: 109 [PMID: 38304170 DOI: 10.3892/ol.2024.14242]

39 **Tian T**, Leng Y, Tang B, Dong X, Ren Q, Liang J, Liu T, Liu Y, Feng W, Liu S, Zhou Y, Zhao H, Shen L. The oncogenic role and regulatory mechanism of PGK1 in human non-small cell lung cancer. *Biol Direct* 2024; **19**: 1 [PMID: 38163864 DOI: 10.1186/s13062-023-00448-9]

40 **Hwang TL**, Liang Y, Chien KY, Yu JS. Overexpression and elevated serum levels of phosphoglycerate kinase 1 in pancreatic ductal

adenocarcinoma. *Proteomics* 2006; **6**: 2259-2272 [PMID: 16493704 DOI: 10.1002/pmic.200500345]

41 **Pei S**, Zhang P, Yang L, Kang Y, Chen H, Zhao S, Dai Y, Zheng M, Xia Y, Xie H. Exploring the role of sphingolipid-related genes in clinical outcomes of breast cancer. *Front Immunol* 2023; **14**: 1116839 [PMID: 36860848 DOI: 10.3389/fimmu.2023.1116839]

42 **Li W**, Xu M, Li Y, Huang Z, Zhou J, Zhao Q, Le K, Dong F, Wan C, Yi P. Comprehensive analysis of the association between tumor glycolysis and immune/inflammation function in breast cancer. *J Transl Med* 2020; **18**: 92 [PMID: 32070368 DOI: 10.1186/s12967-020-02267-2]

43 **Sun S**, Liang X, Zhang X, Liu T, Shi Q, Song Y, Jiang Y, Wu H, Jiang Y, Lu X, Pang D. Phosphoglycerate kinase-1 is a predictor of poor survival and a novel prognostic biomarker of chemoresistance to paclitaxel treatment in breast cancer. *Br J Cancer* 2015; **112**: 1332-1339 [PMID: 25867275 DOI: 10.1038/bjc.2015.114]

44 **Zhang D**, Tai LK, Wong LL, Chiu LL, Sethi SK, Koay ES. Proteomic study reveals that proteins involved in metabolic and detoxification pathways are highly expressed in HER-2/neu-positive breast cancer. *Mol Cell Proteomics* 2005; **4**: 1686-1696 [PMID: 16048908 DOI: 10.1074/mcp.M400221-MCP200]

45 **Yang H**, Geng YH, Wang P, Zhou YT, Yang H, Huo YF, Zhang HQ, Li Y, He HY, Tian XX, Fang WG. Extracellular ATP promotes breast cancer invasion and epithelial-mesenchymal transition *via* hypoxia-inducible factor 2α signaling. *Cancer Sci* 2019; **110**: 2456-2470 [PMID: 31148343 DOI: 10.1111/cas.14086]

46 **Vishnubalaji R**, Alajez NM. Single-Cell Transcriptome Analysis Revealed Heterogeneity and Identified Novel Therapeutic Targets for Breast Cancer Subtypes. *Cells* 2023; **12** [PMID: 37190091 DOI: 10.3390/cells12081182]

47 **Shashni B**, Sakharkar KR, Nagasaki Y, Sakharkar MK. Glycolytic enzymes PGK1 and PKM2 as novel transcriptional targets of PPARγ in breast cancer pathophysiology. *J Drug Target* 2013; **21**: 161-174 [PMID: 23130662 DOI: 10.3109/1061186X.2012.736998]

48 **Qian X**, Li X, Lu Z. Protein kinase activity of the glycolytic enzyme PGK1 regulates autophagy to promote tumorigenesis. *Autophagy* 2017; **13**: 1246-1247 [PMID: 28486006 DOI: 10.1080/15548627.2017.1313945]

49 **Shao F**, Yang X, Wang W, Wang J, Guo W, Feng X, Shi S, Xue Q, Gao S, Gao Y, Lu Z, He J. Associations of PGK1 promoter hypomethylation and PGK1-mediated PDHK1 phosphorylation with cancer stage and prognosis: a TCGA pan-cancer analysis. *Cancer Commun (Lond)* 2019; **39**: 54 [PMID: 31578148 DOI: 10.1186/s40880-019-0401-9]

50 **He M**, Hu C, Deng J, Ji H, Tian W. Identification of a novel glycolysis-related signature to predict the prognosis of patients with breast cancer. *World J Surg Oncol* 2021; **19**: 294 [PMID: 34600547 DOI: 10.1186/s12957-021-02409-w]

51 **Li Y**, Wang S, Zhang X, Yang R, Wei X, Yan R, Jiang Y, Shen W. Expression Characteristics and Significant Prognostic Values of PGK1 in Breast Cancer. *Front Mol Biosci* 2021; **8**: 695420 [PMID: 34291087 DOI: 10.3389/fmolb.2021.695420]

52 **Schulz DM**, Böllner C, Thomas G, Atkinson M, Esposito I, Höfler H, Aubele M. Identification of differentially expressed proteins in triple-negative breast carcinomas using DIGE and mass spectrometry. *J Proteome Res* 2009; **8**: 3430-3438 [PMID: 19485423 DOI: 10.1021/pr900071h]

53 **Kabbage M**, Chahed K, Hamrita B, Guillier CL, Trimeche M, Remadi S, Hoebeke J, Chouchane L. Protein alterations in infiltrating ductal carcinomas of the breast as detected by nonequilibrium pH gradient electrophoresis and mass spectrometry. *J Biomed Biotechnol* 2008; **2008**: 564127 [PMID: 18401453 DOI: 10.1155/2008/564127]

54 **Mei Y**, Zhao L, Jiang M, Yang F, Zhang X, Jia Y, Zhou N. Characterization of glucose metabolism in breast cancer to guide clinical therapy. *Front Surg* 2022; **9**: 973410 [PMID: 36277284 DOI: 10.3389/fsurg.2022.973410]

55 **Tran Q**, Lee H, Park J, Kim SH, Park J. Targeting Cancer Metabolism - Revisiting the Warburg Effects. *Toxicol Res* 2016; **32**: 177-193 [PMID: 27437085 DOI: 10.5487/TR.2016.32.3.177]

56 **Fukushi A**, Kim HD, Chang YC, Kim CH. Revisited Metabolic Control and Reprogramming Cancers by Means of the Warburg Effect in Tumor Cells. *Int J Mol Sci* 2022; **23** [PMID: 36077431 DOI: 10.3390/ijms231710037]

57 **Liu S**, Li Y, Yuan M, Song Q, Liu M. Correlation between the Warburg effect and progression of triple-negative breast cancer. *Front Oncol* 2022; **12**: 1060495 [PMID: 36776368 DOI: 10.3389/fonc.2022.1060495]

58 **Mittal L**, Aryal UK, Camarillo IG, Ferreira RM, Sundararajan R. Author Correction: Quantitative proteomic analysis of enhanced cellular effects of electrochemotherapy with Cisplatin in triple-negative breast cancer cells. *Sci Rep* 2019; **9**: 19124 [PMID: 31819154 DOI: 10.1038/s41598-019-55880-7]

59 **Wang Z**, Jiang Q, Dong C. Metabolic reprogramming in triple-negative breast cancer. *Cancer Biol Med* 2020; **17**: 44-59 [PMID: 32296576 DOI: 10.20892/j.issn.2095-3941.2019.0210]

60 **Chen Y**, Cen L, Guo R, Huang S, Chen D. Roles and mechanisms of phosphoglycerate kinase 1 in cancer. *Bull Cancer* 2022; **109**: 1298-1307 [PMID: 36096942 DOI: 10.1016/j.bulcan.2022.07.004]

61 **He Y**, Wang X, Lu W, Zhang D, Huang L, Luo Y, Xiong L, Li H, Zhang P, Li Q, Liang S. PGK1 contributes to tumorigenesis and sorafenib resistance of renal clear cell carcinoma *via* activating CXCR4/ERK signaling pathway and accelerating glycolysis. *Cell Death Dis* 2022; **13**: 118 [PMID: 35121728 DOI: 10.1038/s41419-022-04576-4]

62 **Yuan Y**, Li H, Pu W, Chen L, Guo D, Jiang H, He B, Qin S, Wang K, Li N, Feng J, Wen J, Cheng S, Zhang Y, Yang W, Ye D, Lu Z, Huang C, Mei J, Zhang HF, Gao P, Jiang P, Su S, Sun B, Zhao SM. Cancer metabolism and tumor microenvironment: fostering each other? *Sci China Life Sci* 2022; **65**: 236-279 [PMID: 34846643 DOI: 10.1007/s11427-021-1999-2]

63 **Duncan L**, Shay C, Teng Y. PGK1 : An Essential Player in Modulating Tumor Metabolism. *Methods Mol Biol* 2022; **2343**: 57-70 [PMID: 34473315 DOI: 10.1007/978-1-0716-1558-4_4]

64 **Li X**, Jiang Y, Meisenhelder J, Yang W, Hawke DH, Zheng Y, Xia Y, Aldape K, He J, Hunter T, Wang L, Lu Z. Mitochondria-Translocated PGK1 Functions as a Protein Kinase to Coordinate Glycolysis and the TCA Cycle in Tumorigenesis. *Mol Cell* 2016; **61**: 705-719 [PMID: 26942675 DOI: 10.1016/j.molcel.2016.02.009]

65 **Xu M**, Liu X, Zhou X, Qin Y, Yang L, Wen S, Qiu Y, Chen S, Tang R, Guo Y, Liu M, Sun Y. Hypoxia-induced circSTT3A enhances serine synthesis and promotes H3K4me3 modification to facilitate breast cancer stem cell formation. *Pharmacol Res* 2023; **197**: 106964 [PMID: 37865128 DOI: 10.1016/j.phrs.2023.106964]

66 **Williams SD**, Smith TM, Stewart LV, Sakwe AM. Hypoxia-Inducible Expression of Annexin A6 Enhances the Resistance of Triple-Negative Breast Cancer Cells to EGFR and AR Antagonists. *Cells* 2022; **11** [PMID: 36230969 DOI: 10.3390/cells11193007]

67 **Jin MS**, Lee H, Park IA, Chung YR, Im SA, Lee KH, Moon HG, Han W, Kim K, Kim TY, Noh DY, Ryu HS. Overexpression of HIF1α and CAXI predicts poor outcome in early-stage triple negative breast cancer. *Virchows Arch* 2016; **469**: 183-190 [PMID: 27184798 DOI: 10.1007/s00428-016-1953-6]

68 **Li X**, Zheng Y, Lu Z. PGK1 is a new member of the protein kinome. *Cell Cycle* 2016; **15**: 1803-1804 [PMID: 27105392 DOI:

10.1080/15384101.2016.1179037]

69 **Yan M**, Rayoo M, Takano EA; KConFab Investigators, Fox SB. BRCA1 tumours correlate with a HIF-1alpha phenotype and have a poor prognosis through modulation of hydroxylase enzyme profile expression. *Br J Cancer* 2009; **101**: 1168-1174 [PMID: 19724277 DOI: 10.1038/sj.bjc.6605287]

70 **Sun S**, Wu H, Wu X, You Z, Jiang Y, Liang X, Chen Z, Zhang Y, Wei W, Jiang Y, Chen Y, Song Y, Pang D. Silencing of PGK1 Promotes Sensitivity to Paclitaxel Treatment by Upregulating XAF1-Mediated Apoptosis in Triple-Negative Breast Cancer. *Front Oncol* 2021; **11**: 535230 [PMID: 33747900 DOI: 10.3389/fonc.2021.535230]

71 **Uhlen M**, Zhang C, Lee S, Sjöstedt E, Fagerberg L, Bidkhori G, Benfeitas R, Arif M, Liu Z, Edfors F, Sanli K, von Feilitzen K, Oksvold P, Lundberg E, Hober S, Nilsson P, Mattsson J, Schwenk JM, Brunnström H, Glimelius B, Sjöblom T, Edqvist PH, Djureinovic D, Micke P, Lindskog C, Mardinoglu A, Ponten F. A pathology atlas of the human cancer transcriptome. *Science* 2017; **357** [PMID: 28818916 DOI: 10.1126/science.aan2507]

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