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*Original Research*

# Molecular Subtypes of Ovarian Cancer Based on Lipid Metabolism and Glycolysis Reveals Potential Therapeutic Targets

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**Abstract**

**Background**: Ovarian cancer (OC) is one of the most lethal gynecological malignant neoplasms. The aim of this study was to use high-throughput sequencing data to investigate the molecular and clinical characteristics of OC subtypes related to lipid metabolism and glycolysis, thus providing a theoretical basis for clinical decision-making. **Methods**: Molecular data and clinicopathological characteristics of OC patients were extracted from the Cancer Genome Atlas (TCGA), Genotype-Tissue Expression Project (GTEx), and the Gene Expression Omnibus (GEO). Following analysis of genes involved in lipid metabolism and glycolysis, OC was classified into subtypes by unsupervised clustering. The molecular features and clinical outcomes of these subtypes were then evaluated. **Results**: OC patients were divided into five subtypes based on the analysis of nine genes of interest. Amongst these, patients in subtype D had longer overall survival and more benign clinical features. Subtypes B and E had shorter overall- and progression-free survival, respectively. Both the B and E subtypes were closely related to lipid metabolism and to the glycolytic process. Subtype D was positively correlated with the infiltration of $CD8^+$ T cells, $CD4^+$ T cells, and macrophages, all of which play essential anti-tumor roles. Several risk models for selected subtypes were also constructed based on the expression of select genes. **Conclusions**: The present work revealed that irregular metabolism in OC tissues was an indicator of poor clinical outcome and altered homeostasis in cancer-related pathways. Moreover, aberrant gene expression signatures associated with lipid metabolism and glycolysis were also correlated with an immunosuppressive tumor microenvironment. Based on lipid metabolism and glycolysis, we have therefore identified several OC molecular subtypes that may prove useful for the development of potential therapeutic targets.

**Keywords:** ovarian cancer; lipid metabolism; glycolysis; molecular subtypes; bioinformatics

## 1. Introduction

Ovarian cancer (OC) is one of the most common malignant neoplasms in women globally. Because of the insidious onset of OC and its rapid progress, most patients are diagnosed at an advanced stage [1]. The altered metabolism of OC and other cells within the tumor microenvironment is a critical factor that drives OC progression [2]. Recent genomic analysis has revealed that remodeling of metabolic pathways may play an important role in several tumor types [3,4]. The classification of OC into different subtypes with distinct metabolic characteristics may therefore help with tumor diagnosis and with the prediction of patient outcomes.

Other recent work has revealed that cancer cells have unusual lipid metabolism and activation of related pathways [5]. Lipids generally regarded as being associated with cancer development and resistance to chemotherapy include fatty acids, glycerolipids, glycerophospholipids, sphingolipids, and sterol lipids [6]. Differences in lipid metabolism between benign and cancer tissues have long been considered to represent possible targets for cancer therapy [7,8]. An association has also been reported between a high-fat diet, which can alter lipid metabolism, and the development of prostate cancer [9]. Moreover, exosomes originating from colorectal cancer cells can promote pre-metastatic niche formation and liver metastasis via aberrant lipid metabolism in cancer-associated fibroblasts [10].

Molecular subtypes that are based on lipid-metabolism-related signatures and have significant clinical value have been reported in several cancer types, including bladder, gastric, lung, and colon [11–14]. Although associations between lipid metabolism and many different tumor types have been reported, the overall influence of lipid metabolism on OC development remains poorly understood.

Similar to lipogenesis, glycolysis is often aberrantly activated in cancer [15]. This supplies cancer cells with abundant energy while also suppressing oxidative stress by avoiding the electron transport chain responsible for the

generation of reactive oxygen species [16,17]. Moreover, it has been shown that lactate, which is the final product of glycolysis, mediates the reprogramming of immune cells. This helps to establish disease-specific conditions via post-translational histone lactylation [18]. Elevated glycolysis is a prominent feature of OC, and the modulation of glucose metabolism has been reported to increase drug resistance [19].

Glucose is the direct source of lipid synthesis in most tumor cells. Glucose-derived acetyl-CoA is converted to citrate via the tricarboxylic acid cycle, which is then exported by mitochondria to the cytoplasm, where it is involved in lipid synthesis [20]. In prostate cancer, androgen can promote the utilization of glucose for *de novo* lipid synthesis by upregulating hexokinase 2 (*HK2*) and 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 2 (*PFKFB2*), thus demonstrating the relationship between glycolysis and lipid synthesis [21]. However, little is known about the crosstalk between lipid metabolism and glycolysis that can drive the aggressive features of OC, such as motility, invasiveness, and tumor-initiating capacity. It seems important, therefore, to identify potential biomarkers and OC subtypes related to lipid metabolism and glycolysis.

The aim of the present study was to comprehensively investigate the metabolic signatures in OC that are associated with altered metabolic transcriptional profiles. To achieve this, we analyzed genomic data from The University Of Cingifornia Santa Cruz (UCSC) Xena and Gene Expression Omnibus (GEO). Three metabolic subtypes of OC were identified based on nine signatures associated with lipid metabolism or glycolysis. In addition, we found some unique clinicopathological features associated with two other subtypes, although patient survival was not significantly different. The clinical features of patients with distinct metabolic features revealed the occurrence of tumor-specific molecular events within these subtypes. Our results led to the construction of a clinically useful OC classification scheme that could help to further clarify the relationship between lipid metabolism and glycolysis, as well as guide the design of targeted therapy for OC.

## 2. Materials and Methods

### *2.1 Data Extraction and Processing*

RNA-Seq data and clinical information from OC patients were derived from the Cancer Genome Atlas (TCGA)-TARGET- Genotype-Tissue Expression Project (GTEx) cohort in the UCSC Xena database. GEO data was downloaded from GEO Series (GSE)18520, GSE18521, GSE27651, GSE26193, GSE14764, GSE26712, GSE32062, GSE63885, and GSE26942. Lipid metabolism and glycolysis-related gene sets were obtained from the Molecular Signatures Database (MSigDB v7.0) and the Kyoto Encyclopedia of Genes and Genomes (KEGG).

RNA-Seq data from the UCSC Xena and GEO cohorts were processed as follows: (1) samples without full clinical information were excluded; (2) the Ensemble or probe IDs were converted to Gene Symbol; (3) the mean value was recorded if there were multiple Gene Symbol expressions; and (4) Open source softwares including Linear Models for Microarray Data (limma v3.56.2, Victoria, Australia in Bioconductor v3.17, Heidelberg, Germany) and Surrogate Variable Analysis (sva v3.48.0, Baltimore, MD, USA in Bioconductor v3.17) operating in R 4.3.0 (Vienna, Austria) were used to remove batch effects and to normalize the data.

### *2.2 Identification of Metabolism Subtypes in OC*

The R package "ConsensusClusterPlus" v1.64.0 (Chapel Hill, NC, USA) was used to identify different subtypes based on lipid metabolism and glycolysis-related genes. Metabolism subtypes were obtained using the following parameters: reps = 50, pItem = 0.8, pFeature = 1, and distance = pearson. After performing unsupervised hierarchical clustering with the same parameters according to the expression of critical genes obtained from lipid metabolism and glycolysis pathways, 5 molecular-based subtypes were obtained.

### *2.3 Functional Enrichment Analyses and Gene Set Variation Analysis*

The functions of critical genes associated with lipid metabolism and glycolysis were investigated using the online tool DAVID (Database for Annotation, Visualization and Integrated Discovery). This was used to annotate signatures with a potential role in the development of OC based on Gene Ontology (GO) terms. Terms with $p$ values $< 0.05$ were deemed to be statistically significant.

In addition, gene sets associated with lipid metabolism were downloaded from the MSigDB v7.0, while genes involved in glycolysis were downloaded from KEGG. Each gene set was comprehensively analyzed using the gene set variation analysis (GSVA v1.48.1, Catalonia, Spain) algorithm, with an evaluation of the specific variation in biological processes between subtypes. In order to visualize the differences in pathways between different subtypes, heat maps were constructed using the "pheatmap" R package.

### *2.4 Immune Analyses*

The ESTIMATE (Estimation of Stromal and Immune cells in Malignant Tumor tissues using Expression data) method was used to calculate the stromal score, immune score, and tumor purity. The CIBERSORT (Cell-type Identification By Estimating Relative Subsets Of RNA Transcripts) algorithm was then used to analyze the RNA-Seq data of OC patients in order to determine the relative proportions of 22 types of infiltrating immune cells.

*2.5 Construction of Risk Models for Different OC Subtypes*

The critical genes identified from both the TCGA and GEO databases were selected for least absolute shrinkage and selection operator (LASSO) regression analysis via the "glmnet" package. The selected genes were used to calculate the risk score by adding the gene expression multiplied by the corresponding coefficient.

## 3. Results

*3.1 Identification of Critical Metabolic Genes in OC*

Following the analysis of data from TCGA-TARGET-GTEx and GEO, 71 lipid metabolism-related genes were found to be significantly upregulated in OC (Fig. 1A, **Supplementary Tables 1–5**). GO results revealed that in addition to lipid metabolism, these genes were also involved in ion transport, cell response to peroxides, and adenosine triphosphate (ATP) binding. This piqued our interest since they are also involved in glycolysis (Fig. 1B, **Supplementary Table 6**). Therefore, we obtained 25 key components of the glycolysis pathway derived from KEGG and performed subsequent analysis (**Supplementary Table 7**). After building a protein-protein interaction (PPI) network via the STRING database, we found interactions between four lipid metabolism-related genes (Mini-chromosome Maintenance Complex Component 2 (*MCM2*), nucleolar and spindle associated protein (*NUSAP1*), Isocitrate Dehydrogenase ($NADP^+$) 2 (*IDH2*), and (*BUB1*) and five critical genes for glycolysis (Glucose-6-Phosphate Isomerase (*GPI*), glyceraldehyde-3-phosphate dehydrogenase (*GAPDH*), *BPGM*, Lactate dehydrogenase B (*LDHB*), and *PFKP*) (Fig. 1C and **Supplementary Table 8**). To further explore the relationships among these, we performed a correlation analysis of the transcriptomic profiles from OC samples in the TCGA. As shown in Fig. 1D, strong correlations were found between these genes. *GPI*, *GAPDH*, *BPGM*, and *PFKP* were also found to be upregulated in OC, whereas *LDHB* was downregulated (Fig. 1E). Genomic mutation analysis revealed these genes had significant copy number variation in OC, which could affect their messenger RNA (mRNA) expression (Fig. 1F). The chromosomal location of the nine genes is shown in Fig. 1G. By analyzing the survival of OC patients using KMplotter (https://kmplot.com), high expression levels for *MCM2*, *NUSAP1*, *IDH2*, *BUB1*, *GPI*, and *LDHB* were found to associate with poor outcomes, whereas upregulation of *GAPDH* expression was associated with better survival (Fig. 1H). The expression of *BPGM* and *PFKP* was not significantly correlated with prognosis; however, patients with high expression of these genes showed trends for poor outcomes (**Supplementary Fig. 1**).

*3.2 Patient Outcomes and Clinical Features of the Five Metabolic OC Subtypes*

We next investigated the clinical features of patients with OC subtypes classified by expression signatures for lipid metabolism and glycolysis genes, as well as the enrichment scores for metabolism-related pathways. The RNA sequencing data of 1164 OC patients was extracted from TCGA (n = 378) and GEO datasets, including GSE14764 (n = 80), GSE18521 (n = 53), GSE26193 (n = 107), GSE26712 (n = 185), GSE32062 (n = 260) and GSE63885 (n = 101). Unsupervised cluster analysis classified the OC patients into five subtypes (maxK = 5) (Fig. 2A). After deleting samples missing patient survival data, 1138 OC samples were available for analysis. Subtype D patients had longer overall survival time compared to the other four subtypes (66.56 months, Mantel-Cox $p$ value $< 0.0001$), whereas subtype B patients had the shortest overall survival (40 months, Mantel-Cox $p$ value $< 0.05$) (Fig. 2B). Subtype E patients had the shortest progression-free survival (17.08 months, Mantel-Cox $p$ value = 0.042) (Fig. 2B).

We next analyzed the clinicopathological features of the five OC subtypes; the clinical information of patients was shown in **Supplementary Table 9**. Subtype D patients showed significant differences in age, The International Federation of Gynecology and Obstetrics (FIGO) stage, The World Health Organization (WHO) classification, Breast Cancer Susceptibility Protein 1 (*BRCA1*) mutation, platinum-based chemotherapy sensitivity, and clinical response compared to the other subtypes (Fig. 2C–E,G,I,J). The histological composition and Tumor Protein P53 (*TP53)* mutation status of subtype B patients were also significantly different (Fig. 2F,H). Overall, these results suggest that lipid metabolism and glycolysis processes may differ between OC patients and are significantly correlated with clinical features and outcomes. It is, therefore, important to be able to distinguish between the five subtypes.

*3.3 GSVA Reveals that OC Subtypes have Distinct Metabolic Characteristics*

The five subtypes described above showed different expression levels for lipid metabolism and glycolysis-related genes. The expression levels for the nine aforementioned genes were also significantly different between the five subgroups. We further analyzed the possible molecular mechanisms relating to these subtypes based on their different clinical features. The GSVA score of the metabolism-related gene set in subtype B was significantly higher than that of subtype D. Interestingly, in addition to a high metabolism-related gene set score, subtype E was significantly enriched for gene sets or pathways related to DNA replication and the cell cycle (Fig. 3). This suggests that subtype B and E patients may have a poor prognosis due to disruptions in their metabolic processes and that lipid metabolism and glycolytic metabolism may be necessary for OC cell division.

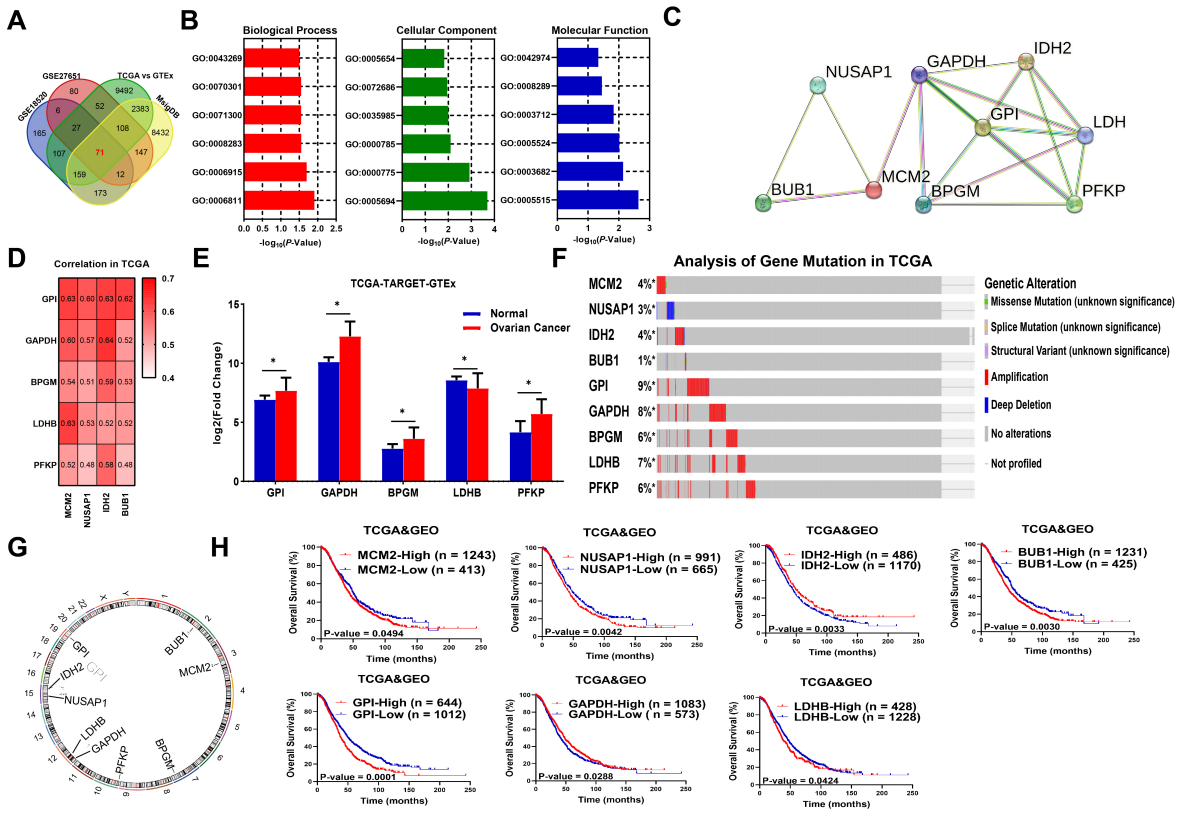


**Fig. 1. Distinct gene expression signatures associated with lipid metabolism and glycolysis in ovarian cancer (OC).** (A) The expression of 11,436 genes involved in lipid metabolism and obtained with Molecular Signatures Database (MSigDB v7.0) using three datasets (the Cancer Genome Atlas (TCGA)-TARGET- Genotype-Tissue Expression Project (GTEx), GSE18520, and GSE27651) are displayed as a Venn diagram. Each dataset is represented by distinct colors. A total of 71 genes were upregulated in all three datasets (|log2 Fold Change| >2, adjust *p*-value < 0.05). (B) GO analysis of these 71 lipid metabolic genes in OC. (C) Correlation analyses for expression of the critical signature genes associated with lipid metabolism and glycolysis in TCGA. (D) Protein-protein interaction (PPI) network of 9 genes involved in the regulation of lipid metabolism and glycolysis. (E) Expression of 5 glycolysis-related genes in TCGA-TARGET-GTEx. (F) Mutation analysis of 9 genes in TCGA OC samples analyzed via cBioportal. (G) Chromosome locations of the 9 genes. (H) KMplotter analysis of the relationship between overall survival of OC patients and the expression of 5 genes (*$p <$ 0.05). Abbreviation: GTEx, Genotype-Tissue Expression Project; GEO, Gene Expression Omnibus.

### *3.4 The Tumor Immune Microenvironment and Aberrant Metabolism in OC*

Immunotherapy is safe and effective, especially for OC patients who do not respond well to chemotherapy and poly ADP-ribose polymerase inhibitor (PARPi) therapy. We, therefore, compared the immune microenvironment between different OC metabolic subtypes in order to evaluate the correlation between lipid metabolism and glycolysis processes. Not surprisingly, subtype D showed a higher infiltration with $CD8^+$ T cells, $CD4^+$ T cells, and macrophages compared to the other subtypes. Subtype E showed lower infiltration of most immune cell types compared to the other subtypes. These differences in immune cell signatures between OC metabolic subtypes indicate potential variation in therapeutic sensitivity to immunotherapy and could therefore help to guide the choice of individual therapies for OC patients (Fig. 4).

### *3.5 Construction of a Prognostic Model with the 9 Genes Associated with Lipid Metabolism and Glycolysis*

We next constructed risk models for three OC subtypes (B, D, and E) based on the expression of nine critical genes and the survival outcome of patients. OC samples were divided in a ratio of 7:3 into training and test sets, respectively. The prognostic value of the nine genes in the different subtypes was analyzed in the training set using LASSO-Cox analysis. Variables with Cox $p < 0.05$ were incorporated into the LASSO procedure, and corresponding variables were retrieved subject to a minimum Lambda ($\lambda$) value (Fig. 5). The formulae for the final 9-gene signatures in the three subtypes were:

Subtype B: Risk score = MCM2 × 0.390754 + NUSAP1 × 0.074372 + IDH2 × –0.222335 + BUB1 × 0.379793 + GPI × –0.216464 + GAPDH × 0.22577 + BPGM × –0.091337 + LDHB × 0.001043 + PFKP × 0.046298

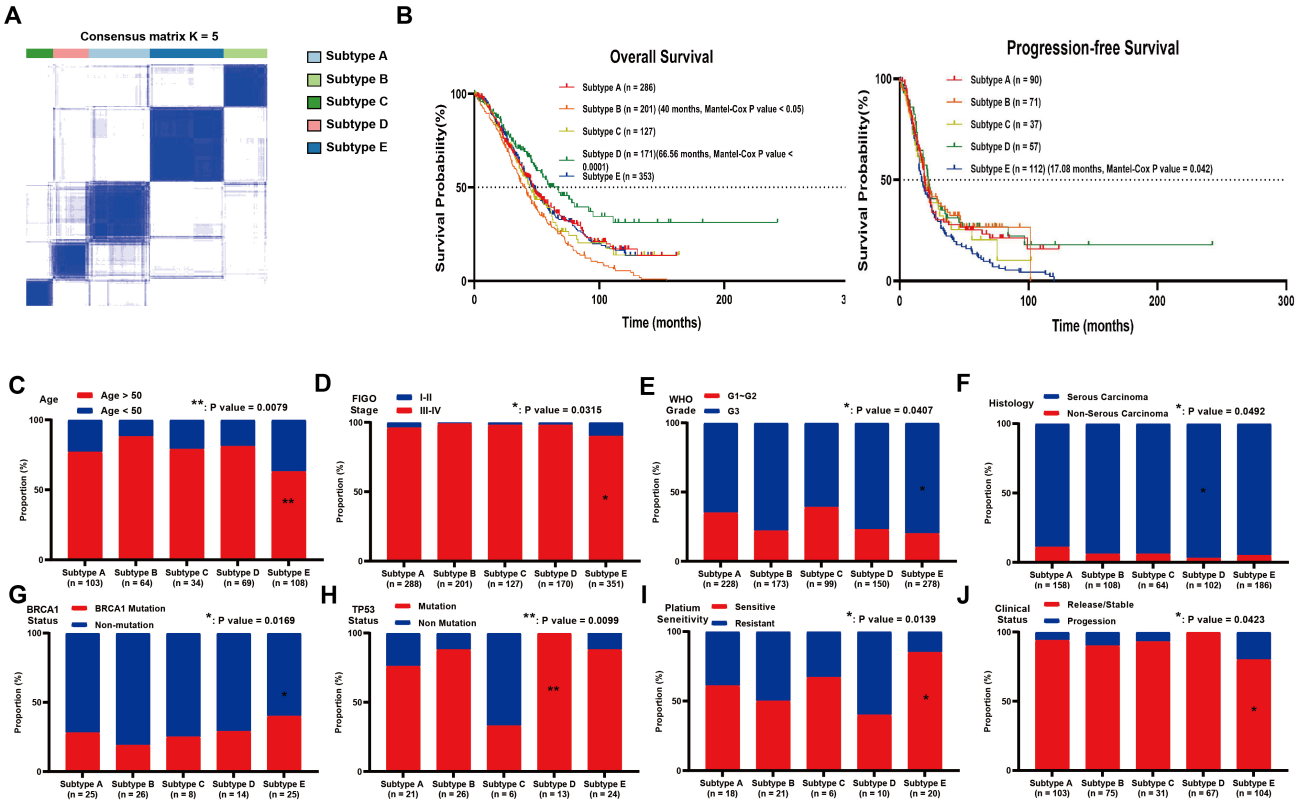


**Fig. 2. Clinical features of different OC subtypes identified by lipid metabolism and glycolysis.** (A) The ConsensusClusterPlus package was used to perform unsupervised hierarchical clustering for 1164 OC samples. Five OC subtypes were identified using this method. (B) Results from Kaplan–Meier analysis revealed marked differences in overall- and progression-free patient survival for the 5 metabolic subtypes of OC. The log-rank test was used to statistically evaluate the survival differences. (C–J) Fisher's exact test was performed to evaluate differences in the following clinical features between patients from subtypes B, D, and E: (C) age, (D) Gynecology and Obstetrics (FIGO) Stage, (E) grade, (F) histology, (G) Breast Cancer Susceptibility Protein (BRCA) status, (H) Tumor Protein P53 (TP53) status, (I) platinum sensitivity, (J) clinical status. The proportions of each clinical feature in the different OC subtypes are shown (*$p < 0.05$, **$p < 0.01$).

Subtype D: Risk score = MCM2 × –0.1327 + NUSAP1 × 0.3433 + IDH2 × –0.39141 + BUB1 × 0.17157 + GPI × 0.08761 + GAPDH × 0.53605 + BPGM × 0.08978 + LDHB × 0.16939 + PFKP × 0.09034

Subtype E: Risk score = MCM2 × –0.275412 + NUSAP1 × –0.048727 + IDH2 × –0.028002 + BUB1 × 0.316162 + GPI × 0.407496 + GAPDH × –0.106956 + BPGM × 0.007721 + LDHB × 0.144628 + PFKP × –0.011904

## 4. Discussion

The TCGA and GEO databases were used in the present study to identify five metabolic subtypes of OC according to lipid metabolism and glycolysis. These were then linked to underlying gene expression patterns that play critical roles in tumor biology, clinical outcome, and the tumor immune microenvironment.

Although the specific mechanisms remain unclear, the abnormal energy metabolism of tumor cells is related to their aberrant proliferation, invasion, and metastasis [22]. Furthermore, the reprogramming of lipid metabolism and glycolysis affects the normal response to tumors, as well as the body's sensitivity to chemotherapeutic drugs [23–25]. A pan-cancer study found that gene expression profiles associated with metabolic pathways can indicate whether important metabolites in the body are altered [26]. The study of closely related molecular subtypes and associated clinical characteristics of OC patients can shed light on the metabolic differences in OC and lead to a better understanding of patient outcomes. Moreover, the development of a risk prediction model based on metabolic features should provide a novel approach to clinical diagnosis and treatment.

We used bioinformatic methods in the current study to identify five OC subtypes with distinct metabolic features. Subtype D had an inactive profile for lipid metabolism and glycolysis-relevant pathways and better patient prognosis than subtypes B and E. Other analyses revealed that subtype D also displayed a high level of immune cell infiltration, which is known to be associated with immune activation

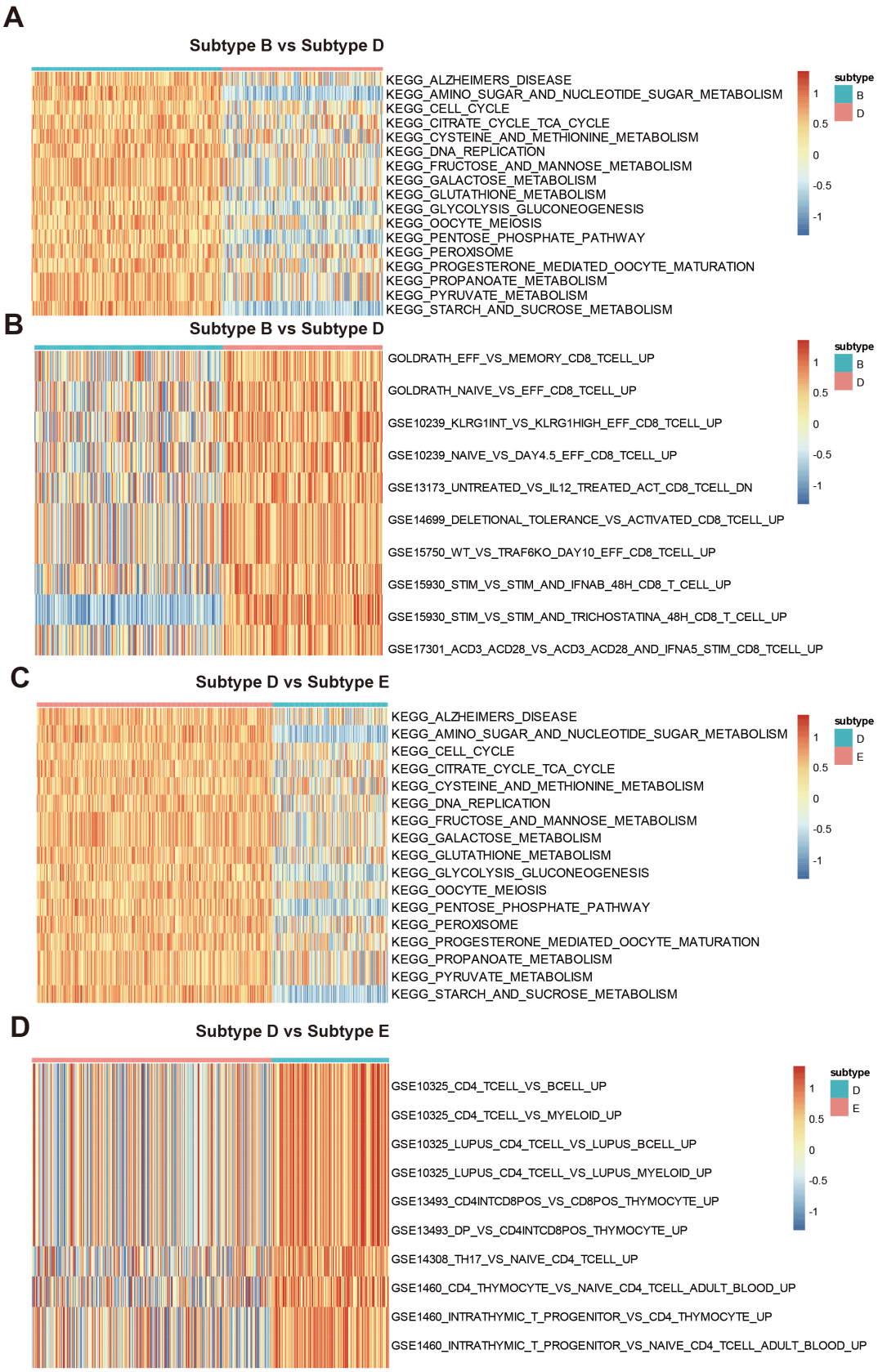


**Fig. 3. Significantly enriched gene sets in OC subtypes classified according to critical metabolic signatures.** (A) and (B) Gene Set Variation Analysis (GSVA) results for OC samples in the TCGA and GEO cohorts. The heat map shows the normalized enrichment scores for subtypes B and D. (C,D) GSVA results for OC samples in the TCGA and GEO cohorts. The heat map shows the normalized enrichment scores for subtypes E and D.

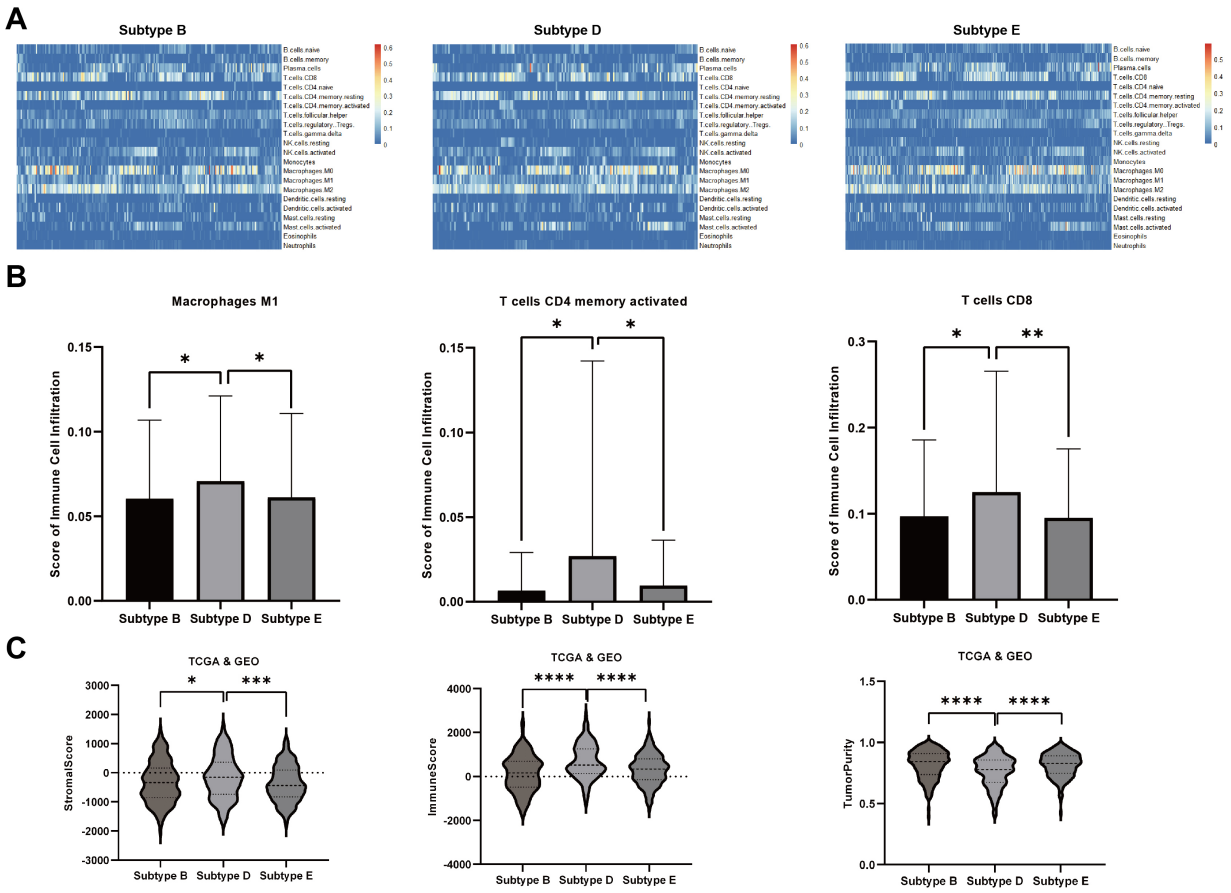


**Fig. 4. The immune microenvironment in different OC subtypes.** (A) Cell-type Identification By Estimating Relative Subsets Of RNA Transcripts (CIBERSORT) scores for immune cell infiltration in OC subtypes are displayed as heat maps. (B) Infiltration scores for three immune cell types in three OC metabolic subtypes. $^{**}p < 0.01$, $^{*}p < 0.05$. (C) Integrated Estimation of Stromal and Immune cells in Malignant Tumor tissues using Expression data (ESTIMATE) scores for different OC subtypes are presented as violin plots. ($^{*}p < 0.05$, $^{***}p < 0.001$, $^{****}p < 0.0001$).

[27–29]. Subtype D is also correlated with TP53 mutation, which is indicative of stromal invasion and mesenchymal activation [30]. Overall, subtype D OC, therefore, exhibits an ideal metabolic phenotype, and targeting metabolic pathways might potentially reverse the poor clinical status of patients in subgroups B and E.

Although we focused on three subtypes in the present study, further investigation of the remaining two subtypes could prove worthwhile. Examination of the clinical characteristics for the five OC subtypes revealed a higher proportion of non-serous carcinoma in subtype A patients. The evaluation of treatment response in this study was based on platinum-based therapy. Therefore, our results suggest that subtype A could be more sensitive to treatment with other drugs, although more in-depth research is required. Subtype C showed a lower percentage of *TP53* mutations, which could result in fewer mutations and, therefore, fewer changes in cancer-associated antigens, thereby explaining the small number of immune cell infiltrates. Subtypes A and C can be further classified in more detail in future studies.

The present study also developed a risk model for predicting patient outcomes. The nine metabolism-related genes used to identify the B, D, and E subtypes showed good predictive value. Thus, lipid metabolism and glycolysis are key factors in the body's resistance to cancer.

Previous studies have also implicated the nine metabolic genes in tumorigenesis. Mini-chromosome Maintenance Complex Component 2 (MCM2) was first implicated in chromosome initiation in eukaryotic cells, and the inhibition of *MCM2* promotes the sensitivity of OC to carboplatin [31]. Hiramatsu K *et al.* [32] reported that knockdown of MCM2 via siRNA interference significantly decreased the proliferation rate of ovarian cancer cell line. Nucleolar and spindle associated protein (NUSAP1) is an important chromosome-chromosome interaction protein that also has an important role in the OC cell cycle [33]. Moreover, the tumor-promoting effects of NUSAP1 in gastric cancer are mediated mainly through Yes-associated protein 1 (YAP1), with the aberrant expression of NUSAP1 and YAP1 being highly correlated in gastric cancer cells and tissues [34]. Isocitrate Dehydrogenase ($NADP^+$) 2

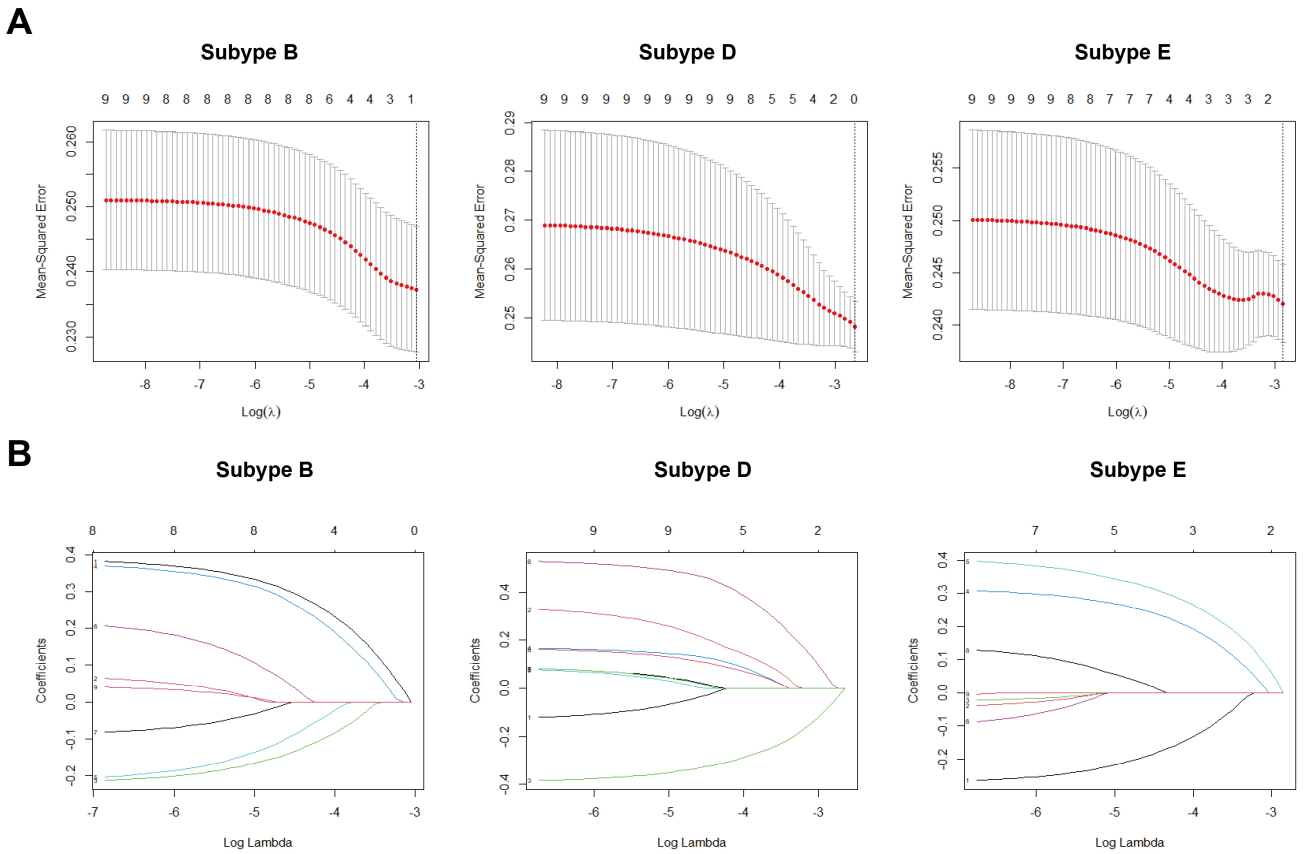


**Fig. 5. Construction of multigene risk models using LASSO-Cox regression analysis.** (A) The trajectory of each independent variable, where the horizontal axis represents the log-value of the independent variable lambda and the vertical axis represents the coefficient of the independent variable. (B) The confidence interval under each lambda.

(IDH2) has an important function in the conversion of 2-hydroxyglutaric acid (2-HA). It is expressed in many tumor types, including acute myeloid leukemia, cholangiocarcinoma, chondrosarcoma, and glioma [35–37]. BUB1 mitotic checkpoint serine/threonine kinase (BUB1) is a serine/threonine kinase that plays a key role in mitosis. It can activate the Signal transducer and activator of transcription 3 (STAT3) pathway, thereby affecting tumor development and progression [38]. Zhu *et al.* [39] found that BUB1 overexpression increased SMAD family member 2 (SMAD2) phosphorylation, which may be linked to the epithelial–mesenchymal transition in liver cancer. Genetic variants of Glucose-6-Phosphate Isomerase (GPI) have prognostic significance in liver cancer and can also be used as molecular markers of overall survival [40]. A previous study reported that activation of Akt2 can reduce tumor cell apoptosis induced by glyceraldehyde-3-phosphate dehydrogenase (GAPDH), thus enhancing their viability [41]. Das *et al.* [42] reported that GAPDH is associated with GPI in Ehrlich ascites carcinoma (EAC) cells and in 3-methylcholanthrene-induced mouse tumor tissue. GPI may also regulate the enzymatic activity of GAPDH. Lactate dehydrogenase B (LDHB) catalyzes the interconversion of pyruvate and lactate with concomitant interconversion of NADH and $NAD^+$ in a post-glycolysis process. Brisson *et al.* [43] reported that LDHB regulates lysosomal acidification, vesicle maturation, and intracellular proteolysis. LDHB activity is essential for basal autophagy and cell proliferation in oxidative cancer cells and in glycolytic cancer cells. However, some of the metabolites identified in our study were not significantly related to the prognosis of OC. It is currently unclear how these metabolites regulate the survival of OC cells.

There are several shortcomings to this study. First, public gene chip and RNA-seq data were used to screen 1164 cases, with the results possibly influenced by the platform used. Moreover, this analysis was carried out on retrospective data, and more prospective trials and tests are therefore needed. In addition, the results of this project are based on publicly available data obtained from OC tissue samples and are discussed in relation to the relevant molecular mechanisms and possible impact on cancer tissues. Furthermore, the roles of several metabolic factors closely related to the molecular mechanisms of OC development were studied.

## 5. Conclusions

Overall, this study describes several different OC subtypes from the perspective of lipid metabolism and glycolysis, thereby providing novel information on the pathogenesis and clinical classification of OC. These results provide a theoretical foundation for the prevention and treatment of OC and for further drug research and development in this area.

## Availability of Data and Materials

The datasets used or analysed during this study are available from the corresponding author on reasonable request.

## Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by XW, WX, ML, WL, LC, RW, HY and DZ. The first draft of the manuscript was written by XW and all authors commented on previous versions of the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Ethics Approval and Consent to Participate

Not applicable.


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## Conflict of Interest

The authors declare no conflict of interest.

## Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/j.fbl2810253.

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