Co-expression and prognosis analyses of GLUT1–4 and RB1 in breast cancer

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Abstract

Background: Current treatment methods for patients with triple-negative breast cancer (TNBC) are very limited, and the prognosis of TNBC is relatively poor. It has been reported that glucose transporter 1 (GLUT1) is overexpressed in breast cancer cells, however, its association with the prognosis is mostly unclear. Moreover, retinoblastoma gene 1 (RB1) might be used as a biomarker for the sensitivity of breast cancer cells to GLUT1 inhibitors, which brought us to the hypothesis that there might be a close correlation between the expression of GLUT1–4 and the expression of RB1.

Methods: In this study, we systematically analyzed the co-expression of GLUT1–4 and the influence of GLUT1–4 gene expression on the prognosis of breast cancer using data mining methods. We also explored possible relationships between GLUT1–4 and RB1 expression in breast cancer tissues. We used public databases such as ONCOMINE, GEPIA, LinkedOmics, and COEXPEDIA.

Results: According to the results, the mRNA expression of SLC2A1 was significantly higher in breast cancer, while the expression levels of SLC2A2–4 were downregulated. The results also indicate that GLUT1 expression does not have significant influence on the overall survival of patients with breast cancer. The mRNA expression of SLC2A1 and RB1 is significantly correlated, which means that tissues with high RB1 mRNA expression might have relatively higher mRNA expression of SLC2A1; however, further study analyzing their roles in the expression regulation pathways with human samples is needed to verify the hypothesis.

Conclusions: The mRNA expression of SLC2A1 was significantly higher in breast cancer. The overall survival of breast cancer patients wasn’t significantly correlated with GLUT1–4 expression. The mRNA expression of SLC2A1 and RB1 is significantly correlated according to the analysis conducted in LinkedOmics. It provides reference for future possible individualized treatment of TNBC using GLUT1 inhibitors, especially in patients with higher mRNA expression of RB1. Further study analyzing the roles of these two genes in the regulation pathways is needed.

Keywords: Triple-negative breast cancer, Glucose transporters, Metabolic inhibitory therapy, Individualized treatment, Metabolic plasticity

Background

Glucose Transporters (GLUTs) proteins are encoded by the SLC2 genes and are members of the major facilitator superfamily of membrane transporters [1]. GLUTs are the main facilitators of glucose transport in mammalian cells [2]. Fourteen GLUT proteins are expressed in humans and they can be categorized into three classes based on sequence similarity: Class 1 (GLUTs 1–4, 14), Class 2 (GLUTs 5, 7, 9, and 11), and Class 3 (GLUTs 6, 8, 10, 12, and HMIT) [3]. Several studies have shown that GLUT1 expression is increased in a variety of malignant tumors [4–6]. This is probably because tumor cells show an enhanced level of glucose metabolism compared to normal tissues, and tumor cells have
greater need for glucose, which results in a corresponding increase in the transport of glucose into the cells. In addition, it has been reported that GLUT1 overexpression is closely related to tumor progression and is related to the poor prognosis of a variety of malignant tumors [7–9].

Current treatment methods for triple-negative breast cancer (TNBC) patients are very limited [10], and the prognosis of TNBC is relatively poor [11]. Human glucose transporter 1 (hGLUT1) is overexpressed in breast cancer tissues. A series of GLUT1 inhibitors have been discovered [12–16], and these molecules have the potential to block glucose transport in breast cancer tissue and treat TNBC. However, recent research has found that not all types of TNBC cells are sensitive to GLUT1 inhibitor [17]. Different breast cancer cells showed diverse sensitivities to GLUT1 inhibitors, and the protein level of RB1 strongly correlated with the degree of sensitivity to GLUT1 inhibition in TNBC. It was established in a recently published TNBC related research that RB1-negative cells were insensitive to GLUT1 inhibition [17]. According to the research, the effect of GLUT1 inhibitors on the inhibition of TNBC cells depended largely on the RB1 expression level of the cancer tissue and cells. Based on existing research conclusions, we put forward a hypothesis that there may be a close correlation between the expression of GLUT family, especially the expression of GLUT1–4, and the expression of RB1.

To the best of our knowledge, there has been no study reporting the expression and prognosis analyses of GLUT1–4 (encoded by genes SLC2A1-SLC2A4) in breast cancer using data mining. In this study, we used public databases such as ONCOMINE, GEPIA, LinkedOmics, and COEXPEDIA. We systematically studied the effect of GLUT1–4 gene expression level on the prognosis of breast cancer, and explored the possible relationship between the expression of GLUT1–4 and RB1 in breast cancer tissues. The study provides a reference for future possible treatment of TNBC using GLUT1 inhibitors.

**Methods**

In this study, public databases such as ONCOMINE, GEPIA, LinkedOmics, and COEXPEDIA were used to systematically study the co-expression of GLUT1–4, the influence of GLUT1–4 gene expression on the prognosis of breast cancer, and to explore the possible relationship between the expression of GLUT1–4 and RB1 in breast cancer tissues.

**ONCOMINE analysis**

ONCOMINE gene expression array database (https://www.oncomine.org/) is an online cancer microarray database. In this study, it was used to analyze the transcription levels of SLC2A1–4 genes in different cancers. The mRNA expression levels of SLC2A1–4 were especially compared between clinical breast cancer samples and normal controls, using a Student’s t test to generate the p-value. The cutoff values of p and fold change were respectively defined as $1 \times 10^{-4}$ and 2. ONCOMINE was also used for gene co-expression analyses of the four GLUT family genes.

**GEPIA dataset**

GEPIA (Gene Expression Profiling Interactive Analysis) is a newly developed interactive web server for analyzing the RNA sequencing expression data of 9736 tumors and 8587 normal samples from the TCGA and the GTEx projects, using a standard processing pipeline. GEPIA provides customizable functions such as tumor/normal differential expression analysis, profiling according to cancer types or pathological stages, patient survival analysis, similar gene detection, correlation analysis, and dimensionality reduction analysis [18]. In our study, GEPIA was used to analyze the mRNA levels of SLC2A1–4 in breast cancer vs. normal tissues. Scatter diagrams, bar charts, and box plots were automatically generated according to the combined conditions put into the website. GEPIA was also used to conduct survival analyses and to correlation analyses between two genes.

**LinkedOmics dataset**

LinkedOmics (http://www.linkedomics.org/login.php) is a publicly available portal that includes multi-omics data from all 32 TCGA cancer types. It also includes mass spectrometry-based proteomics data generated by the Clinical Proteomics Tumor Analysis Consortium for TCGA breast, colorectal, and ovarian tumors [19]. In this study, LinkedOmics was used to conduct OS analyses in relation to GLUT1–4 expression. It was also used in the correlation analyses among genes SLC2A1–4 and RB1.

**COEXPEDIA**

Massive amounts of array-based transcriptomics data have been deposited in several public depositories such as Gene Expression Omnibus (GEO) and ArrayExpress. COEXPEDIA is a database of context-associated co-expression networks inferred from an individual series of microarray samples for humans and mice of GEO. COEXPEDIA is a distinctive co-expression database by the following three aspects: 1) All co-expression links were evaluated for functional association by statistical assessment. 2) All co-expression links are associated with particular biomedical contexts. 3) All co-expression links have associated medical subject heading terms, which provide anatomical or disease context information.
In our study, COEXPEDIA was used to conduct correlation analyses among genes.

**Results**

**Transcriptional levels of SLC2A1-SLC2A4 (GLUT1–4) in patients with breast cancer**

The mostly studied GLUTs in humans are GLUT1–4. The transcriptional levels of the corresponding genes SLC2A1 through four in cancers are compared with those in normal samples by using ONCOMINE database. The disease summary of the transcriptional levels of SLC2A1–4 is shown in Fig. 1. As is shown in the figure, 10 out of 53 analyses (4 out of 14 datasets) revealed SLC2A1 upregulation in breast cancer, while 1 out of 53 analyses (1 out of 14 datasets) displayed SLC2A1 downregulation. As is shown in Table 1, the expression levels of GLUT1 were significantly upregulated in patients with different subtypes of invasive and non-invasive breast cancer in four datasets. In the Zhao Breast dataset [21], SLC2A1 was overexpressed in invasive ductal breast carcinoma and lobular breast carcinoma compared with that in the normal samples, with a fold change of 2.800 and 2.075 separately. In the TCGA Breast dataset [22], SLC2A1 was overexpressed compared with that in the normal samples in intraductal cribriform breast adenocarcinoma (fold change = 2.172), in male breast carcinoma (fold change = 3.575), in invasive ductal breast carcinoma (fold change = 2.557) and in invasive breast carcinoma (fold change = 2.251). In the Richardson Breast 2 [23] dataset, SLC2A1 was also overexpressed in ductal breast carcinoma with a fold change of 2.340. The Curtis Breast dataset [24] indicated that compared to normal samples, SLC2A1 overexpression is also found in medullary breast carcinoma (fold change = 2.728), in mucinous breast carcinoma (fold change = 2.100) and in invasive breast carcinoma (fold change = 2.317). (Table 1) Conversely, the transcriptional levels of SLC2A2–4 were not significantly upregulated, but showed downregulation in breast cancer (Fig. 1).

**Relationship between the mRNA levels of SLC2A1–4 and the clinicopathological parameters of patients with breast cancer**

The GEPIA (Gene Expression Profiling Interactive Analysis) dataset was used to compare the mRNA expression levels of GLUT1–4 in different types of cancers (ONCOMINE).

![Table and Figure](image-url)
of $SLC2A1$ between breast cancer and normal tissue samples. Each of Fig. 2A-D consisted of 2 diagrams: the corresponding gene expression profile across all tumor samples and paired normal tissues (dot plot: with each dot representing expression of samples; and bar plot: with the height of bar representing the median expression of certain tumor type or pairing normal tissue). Figure 2E is the dot plot revealing the expression profile of $SLC2A1$ in breast invasive carcinoma, with each dot representing expression of samples; Fig. 2F is the bar plot displaying the expression profile of $SLC2A1$ in breast cancer, with the height of bar representing the median expression of certain tumor type or pairing normal tissue. The results showed that the expression level of $SLC2A1$ were higher in breast invasive carcinoma than in pairing normal tissues, and the expression levels

\[
\begin{array}{|c|c|c|c|c|}
\hline
\text{Gene ID} & \text{Types of Breast cancer versus Normal} & \text{Fold Change} & \text{P Value} & \text{t Test} & \text{References} \\
\hline
SLC2A1 & Invasive Ductal Breast Carcinoma versus Normal & 2.800 & 1.03E-11 & 9.276 & Zhao Breast \\
 & Lobular Breast Carcinoma versus Normal & 2.075 & 6.62E-6 & 5.631 & Zhao Breast \\
 & Intraductal Cribriform Breast Adenocarcinoma versus Normal & 2.172 & 2.50E-09 & 11.263 & TCGA Breast \\
 & Male Breast Carcinoma vs. Normal & 3.575 & 2.84E-5 & 11.010 & TCGA Breast \\
 & Invasive Ductal Breast Carcinoma vs. Normal & 2.557 & 4.19E-27 & 13.974 & TCGA Breast \\
 & Invasive Breast Carcinoma vs. Normal & 2.251 & 8.98E-15 & 8.629 & TCGA Breast \\
 & Ductal Breast Carcinoma vs. Normal & 2.340 & 1.07E-6 & 6.053 & Richardson Breast 2 \\
 & Medullary Breast Carcinoma vs. Normal & 2.728 & 4.82E-10 & 8.059 & Curtis Breast \\
 & Mucinous Breast Carcinoma vs. Normal & 2.100 & 6.44E-13 & 8.635 & Curtis Breast \\
 & Invasive Breast Carcinoma vs. Normal & 2.317 & 1.49E-5 & 5.207 & Curtis Breast \\
\hline
\end{array}
\]

Fig. 2 The expression of SLC2A1–4 in pan-cancer and breast cancer (GEPIA). (A)-(D): The expression of SLC2A1–4 (GLUT1–4) in pan-cancer (BRCA: Breast invasive carcinoma); (E)-(F): The expression of SLC2A1–4 in breast cancer (BRCA: Breast invasive carcinoma). Please see supplementary Table S1 for all the cancer type abbreviations in PEGIA.
of SLC2A3 and SLC2A4 were significantly lower in breast invasive carcinoma than in pairing normal tissues (Fig. 2A-F).

The prognostic values of SLC2A1–4 and RB1 in breast cancer
As mentioned in the Introduction, it has been suggested that RB1 expression in TNBC might be used as a biomarker for the inhibitory effect of GLUT1 inhibitors on breast cancer. Here, we used GEPIA and LinkedOmics databases to investigate the prognostic value of SLC2A1–4 and RB1 gene expression in breast cancer. We generated survival curves reflecting the relationship between the overall survival (OS) rate of the patients and the corresponding gene expression levels.

Survival curves generated in GEPIA for SLC2A1,3,4 and RB1 are shown in Fig. 3A-D. The sample size was insufficient to generate a survival curve for SLC2A2. According to shape of the curves shown in the figure, decreased RB1 might be associated with poor OS in breast cancer, but its p value showed no significance (p > 0.05).

Survival curves generated in LinkOmics [19] for
SLC2A1–4, RB1 are shown in Fig. 3E-I. As we can see from the shape of the curves, decreased RB1 might be associated with poor OS in breast cancer, but the p value showed no significance (p > 0.05). SLC2A1–4 expression level does not have a significant influence on the OS in breast cancer.

Co-expression gene analyses for SLC2A1–4
Genes co-expressed with SLC2A1–4 were analyzed using the COEXPEDIA website. The co-expressed network of SLC2A1 is shown in Fig. 4, and the co-expressed network figures of SLC2A2–4 are in the Supplementary materials (Fig. S1, S2 and S3). The sum of log likelihood scores from all co-expression links (LLS score) are listed in supplementary Table S2. The smaller distance between the linked genes in the figures, the higher LLS score they had in the table, the more probable that the corresponding gene pairs were co-expressed. According to the results, the top six genes found to be co-expressed with SLC2A1 were MYL4, SLC6A8, ANK1, TRIM10, FECH, and GYPB, with the sum of log likelihood scores from all co-expression links (LLS score) of 29.435, 28.116, 25.847, 25.183, 24.849, and 23.899. The top six genes shown to be co-expressed with SLC2A2 were KNG1, HRG, SERPINC1, MAT1A, ALDOB, and CFHR2, with the sum of edges’ LLS score of 16.558, 15.079, 14.500, 14.474, 13.897, and 13.729. The top six genes analyzed to be co-expressed with SLC2A3 were...
MAFF, MCL1, FOSL2, PLAUR, NR4A2, and BHLHE40, with scores of 36.855, 33.949, 30.075, 29.411, 27.156, and 27.073. Only five genes were shown to be co-expressed with SLC2A4, including PFKB1, ADAM23, AQP5, SH2D3C, and TTYH2, with scores of 1.862, 1.803, 1.303, 1.261, and 1.137 respectively.

Subsequently, we also conducted co-expression gene analyses on ONCOMINE; the co-expression color maps are shown in Fig. 5(A-D). Genes co-expressed with SLC2A1 were analyzed in Haverty Breast [25], and the results showed that SLC2A1 is co-expressed with FAML183A, ZNF691, ERMAP, CCDC23, C1orf50, LEPRE1, CLDN19, YBX1, PPIH, CCDC30, RIMKLA, etc. (Fig. 5A). Genes co-expressed with SLC2A2 were analyzed in Landemaine Breast [26]; the result of which showed that SLC2A2 is co-expressed with F9, AFM, ITIH2, IGFBP1, AKR1D1, ANGPTL3, ACSM2A, LOC100131613, MTPP, KNG1, C9, ALDOB, etc. (Fig. 5B). Gene co-expression analyses for SLC2A3 were conducted with Gruvberger Breast [27], and the results showed that SLC2A3 is co-expressed with EMP3, EPHB3, GPSM3, IL2RB, LCK, ENPP2, C2, FCER1G, IL10RA, CCL18, CIITA, etc. (Fig. 5C). Gene co-expression analyses for SLC2A4 were conducted with West Breast [28], and the results showed that SLC2A4 is co-expressed with FADD, BLOC151, RHOB, DCTN6, CELF2, SNTB2, NPPB, TIE1, FGFR1, IDH1, ECH1, etc. (Fig. 5D).

Correlation analyses among SLC2A1–4 and RB1

Finally, we analyzed the possible association among SLC2A1–4 and RB1, using LinkedOmics database and PEGIA. All the P values are shown in Table 2, P values < 0.05 were seen as results indicating significant correlation between genes. The positive results analyzed in PEGIA and LinkedOmics are shown in Fig. 6. The negative results are shown in Supplementary materials (Fig. S4 and S5). As is shown in Fig. 6, the positively associated gene pairs included: SLC2A1-SLC2A3, SLC2A1-SLC2A4, SLC2A3-SLC2A4, and SLC2A4-RB1 in PEGIA analyses (Fig. 6 a-d); and SLC2A1-SLC2A3, SLC2A1-SLC2A4, SLC2A1-RB1, SLC2A2-SLC2A4, SLC2A3-SLC2A4, and SLC2A3-RB1 in LinkedOmics analyses (Fig. 6e-j). As is shown in Table 2, the RNA expression of some gene pairs was significantly correlated in both

![Fig. 5 Co-expressed genes of SLC2A1–4, analyzed by ONCOMINE. The correlation scores on the left side of the figures represent the level of co-expression between SLC2A1 or SLC2A2–4 with other genes.](image-url)
PEGIA and LinkedOmics analyses. These gene pairs are: SLC2A1-SLC2A3, SLC2A1-SLC2A4, and SLC2A3-SLC2A4. This indicates that GLUT1 is significantly correlated with GLUT3 and GLUT4, and GLUT3 is also significantly correlated with GLUT4. Four other gene pairs had positive results, which only showed significant positive results in one of the database analyses (either in PEGIA or in LinkedOmics). The correlation between these gene pairs might need further investigation and confirmation. These gene pairs included: SLC2A1-RB1, SLC2A3-RB1, SLC2A4-RB1, and SLC2A2-SLC2A4.

**Discussion**

The expression of GLUT1–4 has been reported in many cancers [29]. The present study is the first to explore the relationship of mRNA expression between SLC2A1–4 and RB1, and to study the prognostic values of GLUT1–4 in breast cancer using data mining methods. We hope that our findings can contribute to available knowledge, report the expression of GLUT1–4 in breast cancer, and more importantly, provide a reference for the potential individualized metabolic inhibition therapy of TNBC using hGLUT1 inhibitors.
In our study, the mRNA expression of SLC2A1 was significantly higher in breast cancer, while the expression levels of SLC2A2–4 were downregulated. The result is in accordance with previously published literature, which state that GLUT1 is crucial for uptake of glucose by breast cancer cells, and is also the main glucose transporter in breast cancer cell lines [30]. Although it has also been reported that a strong correlation between GLUT1 gene expression and breast cancers of higher grade and proliferative index and lower degree of differentiation [31] and higher malignant potential, invasiveness, and consequently poorer prognosis [32] exists, the p-values in our prognosis analyses were all larger than 0.05. The OS of patients with breast cancer was not significantly correlated with GLUT1–4 expression. With 20 years’ survival data of more than 1000 subjects included in the analyses, we think of the results to be quite convincing. It is considered that the relationship between the expression of GLUT1 and the OS of patients with breast cancer is not clear. Further evidence is required to determine whether GLUT1 can be used as a prognostic biomarker for breast cancer.

Moreover, in terms of the correlation between GLUT1 and RB1 expression, the analysis conducted in LinkedO-mics had a positive result for this gene pair, with a sample size of 1093 and p-value of $2.429 \times 10^{-13}$. The result indicates that the mRNA expression of SLC2A1 and RB1 is significantly correlated. Further study analyzing their roles in the expression regulation pathways is required.

**Conclusions**

The mRNA expression of SLC2A1 was significantly higher in breast cancer. The overall survival of breast cancer patients wasn’t significantly correlated with GLUT1–4 expression. The mRNA expression of SLC2A1 and RB1 is significantly correlated according to the analysis conducted in LinkedO-mics. It provides reference for future possible individualized treatment of TNBC using GLUT1 inhibitors, especially in patients with higher mRNA expression of RB1. Further study analyzing the roles of these two genes in the regulation pathways is needed.

**Abbreviations**

TNBC: Triple negative breast cancer; GLUTs: Glucose transporters; GLUT1: Glucose transporter 1; RB1: Retinoblastoma gene 1; GEPIA: Gene Expression Profiling Interactive Analysis; TCGA: The Cancer Genome Atlas

**Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s12885-021-08763-y.

**Additional file 1: Figure S1.** Co-expression network of SLC2A2 (Coexpedia)

**Additional file 2: Figure S2.** Co-expression network of SLC2A3 (Coexpedia)

**Additional file 3: Figure S3.** Co-expression network of SLC2A4 (Coexpedia)

**Additional file 4: Figure S4.** Negative results of the correlation analyses in GEPIA

**Additional file 5: Figure S5.** Negative results of the correlation analyses in LinkedO-mics

**Additional file 6: Table S1.** List of Abbreviations for all cancer types in PEGIA database

**Additional file 7: Table S2.** LLS scores of gene co-expression analyses for SLC2A1–4 in COEXPEDIA

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Not applicable.

**Authors’ contributions**

X.Z. and Q.X. were in charge of the conceptualization of the study. X.Z. wrote the main manuscript text and X.P. and Z.Z. prepared the Figs. Q.L. and H.Z. prepared the Tables. Y.C. and Q.X. participated in the revision and further editing of the manuscript. X.Z., Q.X., Y.C., and X.P. contributed to funding acquisition. All the authors reviewed the manuscript.

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**Availability of data and materials**

The datasets analysed during the current study are available in ONCOMINE, GEPIA, LinkedO-mics, and COEXPEDIA. [https://www.oncomine.org/; http://gepia.cancer-pku.cn/index.html; http://www.linkedomics.org/login.php; https://www.coexpedia.org/].

All data and outcomes generated during this study are included in this published article and its supplementary information files.

**Ethics approval and consent to participate**

This is a bioinformatics study based on online databases. Since all of the datasets were retrieved from published literature, it was confirmed that all written informed consent were obtained.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

**Declarations**

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**References**

1. Mueckler M, Thorens B. The SLC2 (GLUT) family of membrane transporter. Mol Asp Med. 2013;34(2-3):121–38. https://doi.org/10.1016/j.mam.201207.001.
2. Wilson-O’Brien AL, Patron N, Rogers S. Evolutionary ancestry and novel functions of the mammalian glucose transporter (GLUT) family. BMC Evol Biol. 2010;10(1). https://doi.org/10.1186/1471-2148-10-152.

3. Chai YJ, Yi JW, Oh SW, Kim YA, Yi KH, Kim JH, et al. Upregulation of SLC2 (GLUT) family genes is related to poor survival outcomes in papillary thyroid carcinoma: analysis of data from the Cancer genome atlas. Surgery. 2016; 161(1):188–94. https://doi.org/10.1016/j.surg.2016.04.050.

4. Jiwa LS, van Dext PJ, Hoeflagd LD, Wesseling J, Wesseling P. Dutch Distant Breast Metastases Consortium, et al. Upregulation of Claudin-4, CAIX and GLUT-1 in distant breast cancer metastases. BMC Canc. 2014;14:8464.

5. Tang Z, Li C, Kang B, Gao G, Li C, Zhang Z. GEPIA: a web server for cancer and normal gene expression profiling and interactive analyses. Nucleic Acids Res. 2017;45(7):D871–8.

6. Haber RS, Rathan A, Weiser KR, Pritsker A, Itzkowitz SH, Bodian C, et al. Predicting the clinical status of human breast cancer by using gene expression profiles. Proc Natl Acad Sci U S A. 2001;98(20):11462–7. https://doi.org/10.1073/pnas.111098.

7. Ancey PB, Contat C, Mieylan E. Glucose transporters in cancer: from tumor cells to the tumor microenvironment. FEBs J. 2018;285(16):2926–43. https://doi.org/10.1111/febs.14577.

8. Barbosa AM, Martel F. Targeting glucose transporters for breast cancer therapy: the effect of natural and synthetic compounds. Cancers (Basel). 2020;12:1.

9. Pinheiro C, Sousa B, Albergaria A, Paredes J, Dufloth R, Vieira D, et al. GLUT1 and CAIX expression profiles in breast cancer correlate with adverse prognostic factors and MCT1 overexpression. Histol Histopathol. 2011;26(5):721–32. https://doi.org/10.1111/1365-2559.12058.

10. Estrogen receptor status in breast cancer is associated with remarkably distinct gene expression patterns. Cancer Res. 2001;61(16):5979–84.

11. West M, Blanchette C, Dressman H, Huang E, Ishida S, Spang R, et al. Interactions of androgens, green tea catechins and the antiandrogen flutamide with the external glucose-binding site of the human erythrocyte glucose transporter Glut1. FEBS J. 2018;285(16):2926–43. https://doi.org/10.1111/febs.14577.