Figure S1. GLO 1 and PKC $\lambda$ gene expression is enhanced at all breast cancer tumor stages compared with that of normal tissue samples. P-values were generated using the Kruskal-Wallis test with a Steel-Dwass test. The $\alpha$-level was fixed at 0.05 , and $\mathrm{P}<0.05$ was considered to indicate a statistically significant difference. ${ }^{*} \mathrm{P}<0.05,{ }^{* *} \mathrm{P}<0.01$. GLO 1 , glyoxalase $1 ; \mathrm{PKC} \lambda$, protein kinase $\mathrm{C} \lambda$.


Figure S2. Kaplan-Meier analysis of GLO 1 and $P K C \lambda$ gene based on breast cancer subtype. P-values were calculated using a Gehan-Breslow generalized Wilcoxon test. Adjusted P-values were calculated using Holm's method for post-hoc analysis. The $\alpha$-level was fixed at 0.05 , and $\mathrm{P}<0.05$ was considered to indicate a statistically significant difference. GLO 1 , glyoxalase $1 ; \mathrm{PKC} \lambda$, protein kinase $\mathrm{C} \lambda$; ER, estrogen receptor; PgR, progesterone receptor; TNBC, triple-negative breast cancer.





















ER and/or PgR






— GLO $\prod_{\text {high }} P K C \lambda_{\lambda}^{\text {high }}(\mathrm{n}=29)$


- GLO flow PKCX ${ }^{\text {nigh }}$ ( $n=90$ )



|  | Adjusted P-value (Holm method) |
| :---: | :---: |
|  | 0.95 |
| GLO $1^{\text {tigh }}$ PKC $\chi^{\text {nigh }}$ vs GLO $1^{\text {tow }}$ PKC $\chi^{\text {nigh }}$ | h 1.00 |
| GLO $1^{\text {tigh }}$ PKC $\lambda^{\text {nigh }}$ vs GLO $1^{\text {nigh }}$ PKC $\lambda^{\text {low }}$ | 1.00 |

Figure S3. Basal-like type breast cancer accounts for a larger fraction of cancer classed as GLO $1^{\text {high }} P K C \lambda^{\text {high }}$ among the subtypes in stage III-IV breast cancer. GLO 1 , glyoxalase $1 ; \mathrm{PKC} \lambda$, protein kinase $\mathrm{C} \lambda$.


Figure S4. Correlation between $G L O 1$ and $P K C \lambda$ expression in breast cancer subtypes. r and P-values are indicated. P-values were generated using a non-correlation test. The $\alpha$-level was fixed at 0.05 , and $\mathrm{P}<0.05$ was considered to indicate a statistically significant difference. GLO 1, glyoxalase 1; PKC $\lambda$, protein kinase $\mathrm{C} \lambda$; r, Pearson's correlation coefficient; ER, estrogen receptor; PgR , progesterone receptor; TNBC, triple-negative breast cancer.


Claudin-low
PKC入


Table SI. Clinicopathological data of the 99 patients with breast cancer.

| Variable | Value |
| :--- | :---: |
| Median age, years (range) | $59(34-82)$ |
| Tumor size, n (\%) |  |
| Tis | $6(6)$ |
| T1 | $34(34)$ |
| T2 | $46(46)$ |
| T3 | $3(3)$ |
| T4 | $2(2)$ |
| Unknown | $8(8)$ |
| Nodal metastasis, n (\%) |  |
| N0 | $59(60)$ |
| N1-3 | $38(38)$ |
| Unknown | $2(2)$ |
| TNM stage, $\mathrm{n}(\%)$ |  |
| 0 | $6(6)$ |
| 1 | $24(24)$ |
| 2 | $37(37)$ |
| 3 | $3(3)$ |
| 4 | $2(2)$ |
| Unknown | $27(27)$ |
| ER, $\mathrm{n}(\%)$ |  |
| Positive | $74(75)$ |
| Negative | $24(24)$ |
| Unknown | $1(1)$ |
| PgR, n (\%) |  |
| Positive | $54(55)$ |
| Negative | $44(44)$ |
| Unknown | $1(1)$ |
| HER2, $\mathrm{n}(\%)$ |  |
| Positive | $63(64)$ |
| Negative | $35(35)$ |
| Unknown | $1(1)$ |
| TNBC, n (\%) | $6(6)$ |

ER, estrogen receptor; PgR , progesterone receptor; TNBC, triple-negative breast cancer.

Table SII. Clinicopathological data of the 1,904 patients with breast cancer.

| Variable | Value |
| :--- | :---: |
| Median age, years (range) | $61.8(21.9-96.3)$ |
| Tumor stage, n (\%) |  |
| 0 | $4(0.2)$ |
| I | $475(24.9)$ |
| II | $800(42.0)$ |
| III | $115(6.0)$ |
| IV | $5(0.3)$ |
| Unknown | $501(26.3)$ |
| Tumor size, n (\%) |  |
| 0-20 mm | $594(31.2)$ |
| $\geq 20$ mm | $1,292(67.9)$ |
| Unknown | $18(0.9)$ |
| Pam50 + Claudin-low subtype, $\mathrm{n}(\%)$ |  |
| Normal-like | $140(7.4)$ |
| Luminal A | $679(35.7)$ |
| Luminal B | $461(24.2)$ |
| HER2-enriched | $220(11.6)$ |
| Claudin-low | $199(10.5)$ |
| Basal-like | $199(10.5)$ |
| ER, n (\%) |  |
| Positive | $1,459(76.6)$ |
| Negative | $445(23.4)$ |
| PgR, n (\%) |  |
| Positive | $1,009(53.0)$ |
| Negative | $895(47.0)$ |
| HER2, n (\%) | $236(12.4)$ |
| Positive | $1,668(87.6)$ |
| Negative | $1,478(77.6)$ |
| ER and/or PgR, $\mathrm{n}(\%)$ | $299(15.7)$ |
| Triple negative, $\mathrm{n}(\%)$ |  |

ER, estrogen receptor; PgR, progesterone receptor; Pam50, a minimal gene set for classifying 'intrinsic' subtypes of breast cancer.

Table SIII. Association between the clinicopathological parameters and GLO 1 and $P K C \lambda$ gene expression in 1,904 patients.

| Characteristics | GLO $1^{\text {low }}$ | $G L O 1^{\text {high }}$ | P -value | $P K C \lambda^{\text {low }}$ | $P K C \lambda^{\text {high }}$ | P -value | GLO $1^{\text {low }} P K C \lambda^{\text {low }}$ | $G L O 1{ }^{\text {high }} P K C \lambda^{\text {high }}$ | P -value |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Age, years |  |  |  |  |  |  |  |  |  |
| <61.77 | 720 | 232 | 0.53 | 700 | 252 | 0.14 | 537 | 69 | 0.82 |
| $\geq 61.77$ | 708 | 244 |  | 728 | 224 |  | 552 | 68 |  |
| Tumor stage |  |  |  |  |  |  |  |  |  |
| $0-\mathrm{II}$ | 972 | 307 | 0.07 | 952 | 327 | 0.89 | 740 | 95 | 0.77 |
| III-IV | 85 | 39 |  | 93 | 31 |  | 63 | 9 |  |
| Tumor size, mm |  |  |  |  |  |  |  |  |  |
| 0-20 | 456 | 136 | 0.15 | 456 | 136 | 0.16 | 360 | 40 | 0.34 |
| $\geq 20$ | 955 | 337 |  | 956 | 336 |  | 715 | 96 |  |

P-values were calculated using the $\chi^{2}$ test. GLO 1 , glyoxalase $1 ; \mathrm{PKC} \lambda$, protein kinase $\mathrm{C} \lambda$.

Table SIV. Multivariable Cox regression analysis of the association between GLO 1 and $P K C \lambda$ expression based on breast cancer subtype.
Comparison
Normal-like
$G L O I^{\text {high }}$ vs. $G L O I^{\text {low }}$
$P K C \lambda^{\text {high }}$ vs. $P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. $G L O I^{\text {low }} P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. $G L O I^{\text {low }} P K C \lambda^{\text {high }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $I^{\text {high }} P K C \lambda^{\text {low }}$
Luminal A
$G L O I^{\text {high }}$ vs. GLO $1^{\text {low }}$
$P K C \lambda^{\text {high }}$ vs. $P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $1^{\text {low }} P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $1^{\text {low }} P K C \lambda^{\text {high }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $l^{\text {high }} P K C \lambda^{\text {low }}$
Luminal B
$G L O 1^{\text {high }}$ vs. GLO $1^{\text {low }}$
$P K C \lambda^{\text {high }}$ vs. $P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. $G L O I^{\text {low }} P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $1^{\text {low }} P K C \lambda^{\text {high }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $l^{\text {high }} P K C \lambda^{\text {low }}$
HER2-enriched
$G L O I^{\text {high }}$ vs. GLO $1^{\text {low }}$
$P K C \lambda^{\text {high }}$ vs. $P K C \lambda^{\text {low }}$
GLO $1^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $1^{\text {low }} P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $1^{\text {low }} P K C \lambda^{\text {high }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $l^{\text {high }} P K C \lambda^{\text {low }}$
Claudin-low
$G L O 1^{\text {high }}$ vs. GLO $1^{\text {low }}$
$P K C \lambda^{\text {high }}$ vs. $P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $1^{\text {low }} P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $1^{\text {low }} P K C \lambda^{\text {high }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $l^{\text {high }} P K C \lambda^{\text {low }}$
Basal-like
$G L O I^{\text {high }}$ vs. GLO $I^{\text {low }}$
$P K C \lambda^{\text {high }}$ vs. $P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $1^{\text {low }} P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $I^{\text {low }} P K C \lambda^{\text {high }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $1^{\text {high }} P K C \lambda^{\text {low }}$
ER and/or PgR
$G L O l^{\text {high }}$ vs. GLO $1^{\text {low }}$
$P K C \lambda^{\text {high }}$ vs. $P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. $G L O 1^{\text {low }} P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $1^{\text {low }} P K C \lambda^{\text {high }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $l^{\text {high }} P K C \lambda^{\text {low }}$
HER2
$G L O I^{\text {high }}$ vs. GLO $1^{\text {low }} \quad 1.03(0.71-1.49) \quad 0.86$
$P K C \lambda^{\text {high }}$ vs. $P K C \lambda^{\text {low }}$
GLO $1^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $1^{\text {low }} P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $1^{\text {low }} P K C \lambda^{\text {high }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $l^{\text {high }} P K C \lambda^{\text {low }}$
TNBC
GLO $1^{\text {high }}$ vs. GLO $1^{\text {low }}$
$P K C \lambda^{\text {high }}$ vs. $P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $1^{\text {low }} P K C \lambda^{\text {low }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $1^{\text {low }} P K C \lambda^{\text {high }}$
$G L O I^{\text {high }} P K C \lambda^{\text {high }}$ vs. GLO $I^{\text {high }} P K C \lambda^{\text {low }}$

P -value

| $1.64(0.87-3.06)$ | 0.12 |
| :--- | ---: |
| $1.72(0.86-3.45)$ | 0.13 |
| $9.11(2.07-40.15)$ | $<0.01$ |
| $2.83(0.49-16.37)$ | 0.25 |
| $3.21(0.63-16.48)$ | 0.16 |
|  |  |
| $1.20(0.92-1.55)$ | 0.17 |
| $1.26(0.96-1.64)$ | 0.09 |
| $1.81(1.10-2.97)$ | 0.02 |
| $1.35(0.76-2.39)$ | 0.30 |
| $1.54(0.89-2.65)$ | 0.12 |
|  |  |
| $0.85(0.67-1.07)$ | 0.17 |
| $1.04(0.81-1.33)$ | 0.77 |
| $0.78(0.54-1.14)$ | 0.21 |
| $0.61(0.40-0.93)$ | 0.02 |
| $0.84(0.55-1.26)$ | 0.40 |

$1.32(0.93-1.89) \quad 0.12$
$0.94(0.67-1.33) \quad 0.73$
$1.22(0.64-2.30) \quad 0.54$
$1.30(0.66-2.58) \quad 0.45$
$0.96(0.48-1.92) \quad 0.91$
$0.87(0.45-1.69) \quad 0.68$
$1.06(0.66-1.71) \quad 0.80$
$1.47(0.59-3.69) \quad 0.41$
$1.42(0.53-3.83) \quad 0.48$
2.16 (0.62-7.52) 0.23
$0.86(0.57-1.30) \quad 0.48$
$1.08(0.74-1.58) \quad 0.68$
0.96 (0.53-1.77) 0.91
$1.01(0.54-1.90) \quad 0.96$
$1.27(0.63-2.55) \quad 0.50$
1.09 (0.94-1.28) 0.26
$1.26(1.08-1.47)<0.01$
$1.21(0.93-1.57) \quad 0.16$
$0.89(0.66-1.19) \quad 0.43$
$1.06(0.79-1.42) \quad 0.69$
1.03 (0.71-1.49) 0.86
$0.90(0.63-1.27) \quad 0.54$
$0.83(0.43-1.62) \quad 0.59$
$0.90(0.44-1.84) \quad 0.77$
$0.81(0.39-1.70) \quad 0.58$
$0.89(0.61-1.30) \quad 0.55$
$1.03(0.75-1.42) \quad 0.84$
0.98 (0.56-1.72) 0.95
$1.06(0.59-1.90) \quad 0.86$
$1.26(0.64-2.47) \quad 0.50$

[^0]
[^0]:    ${ }^{\text {a }}$ Hazard ratio adjusted by age estimated using Cox proportional hazard model. GLO 1, glyoxalase $1 ; \mathrm{PKC} \lambda$, protein kinase $\mathrm{C} \lambda$; ER, estrogen receptor; PgR , progesterone receptor; TNBC , triple-negative breast cancer.

