A Prognostic lncRNA Signature Associated with Lipid Metabolism in Glioma

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Primary research

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Abstract

Background: Long noncoding RNAs (lncRNAs) are promising cancer biomarkers and therapeutic targets . And lipid metabolism reprogramming is a trait of cancer metabolism. However, the relationship between lncRNAs and lipid metabolism and their prognostic value are still unclear in glioma. Hence, we screened for prognostic lncRNAs associated with lipid metabolism and explored their potential biological functions and effects on glioma.

Methods: The glioma data were obtained from TCGA and CGGA databases. Correlation analysis was used to identify the lncRNAs associated with lipid metabolism . The Cox and LASSO regression analysis were adopted to find prognostic lncRNAs, and further established ceRNA network, clustering and risk score models. CNV and somatic mutation data were used to explore the correlation between risk score and genomic alterations. GSVA and GSEA was adopted to reveal the potential biological functions of prognostic lncRNAs. The abundance of 22 immune cells was inferred by CIBERSORT algorithm . The TIDE algorithm and GDSC database were used to predict the patient's response to immunotherapy and chemotherapy, respectively. Human glioma cell lines were used for further experimental validation. CCK-8 and colony forming assays were adopted to evaluate the cell viability. The cell proliferation was detected by EdU assay. Transwell assay was used to evaluate the ability of cell invasion and migration.

Results: A total of twenty prognostic lncRNAs associated with lipid metabolism were found, and a prognostic lncRNA signature was established. A high risk-score suggested a poor prognosis , more malignant clinicopathological and genomic aberrations features. The risk score was also an independent prognos tic factor. The high-risk patients were more likely to benefit from anti-PD1 treatment. The biological function of signature lncRNAs was mainly to regulate the biosynthesis and transportation of lipid (especially the fatty acid). Among signature lncRNAs, LINC01614 was associated with prognosis, genomic aberrations characteristics, m6A methylation modification, immune infiltration status, and chemotherapy response of patients with glioma. In vitro experiments, silencing the expression of LINC01614 could inhibit the viability, migration , and proliferation of glioma cells.

Conclusions: A prognostic lncRNA signature containing twenty lncRNAs associated with lipid metabolism was established in glioma. The signature lncRNAs play an important role in the development of glioma by regulating lipid biosynthesis and transportation. Our study also provides a new perspective for understanding the lipid metabolism and the biological role of lncRNAs in glioma.

Full Text

This preprint is available for download as a PDF.

Figures

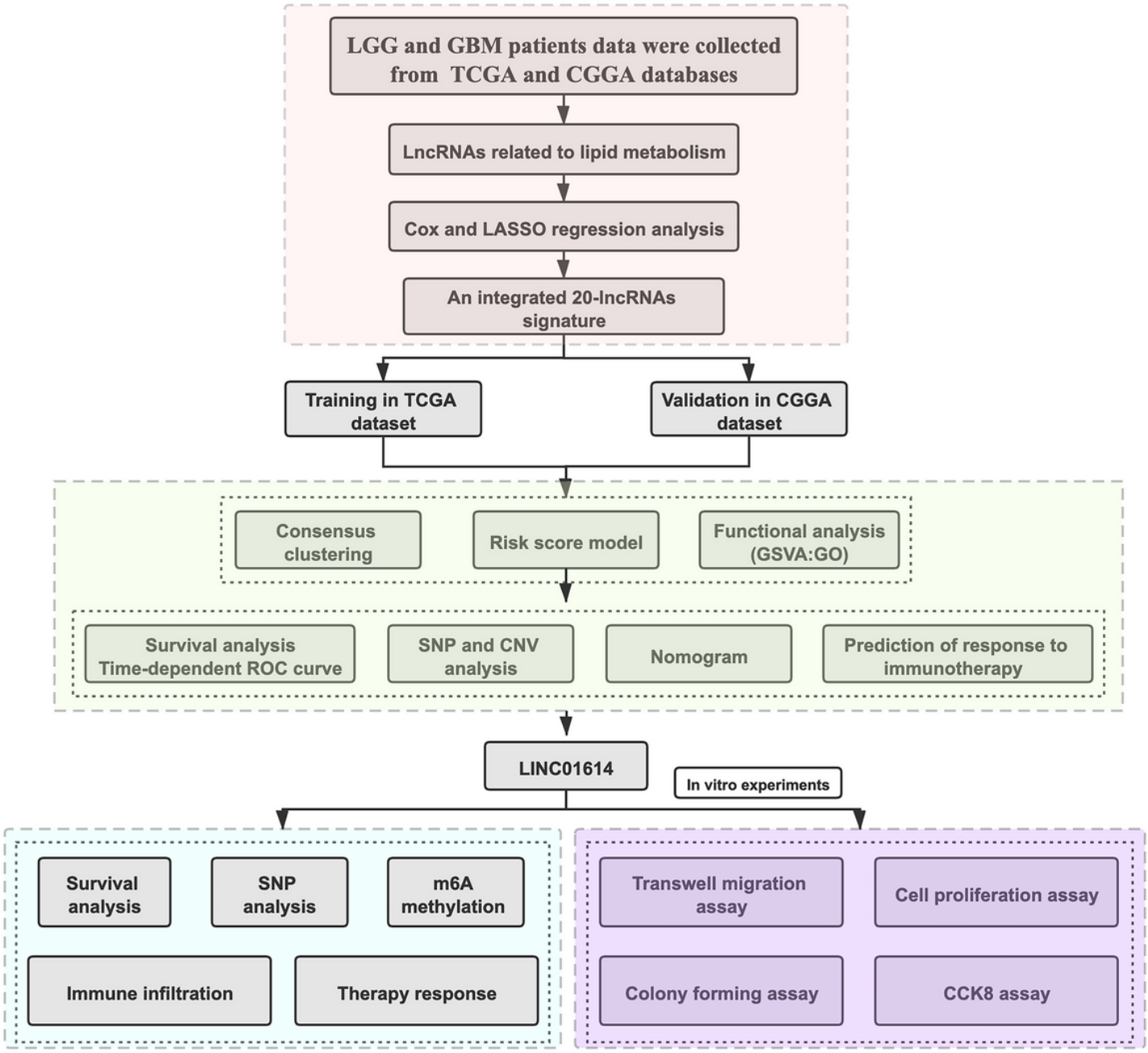

Figure 1

The flowchart designed for the study.

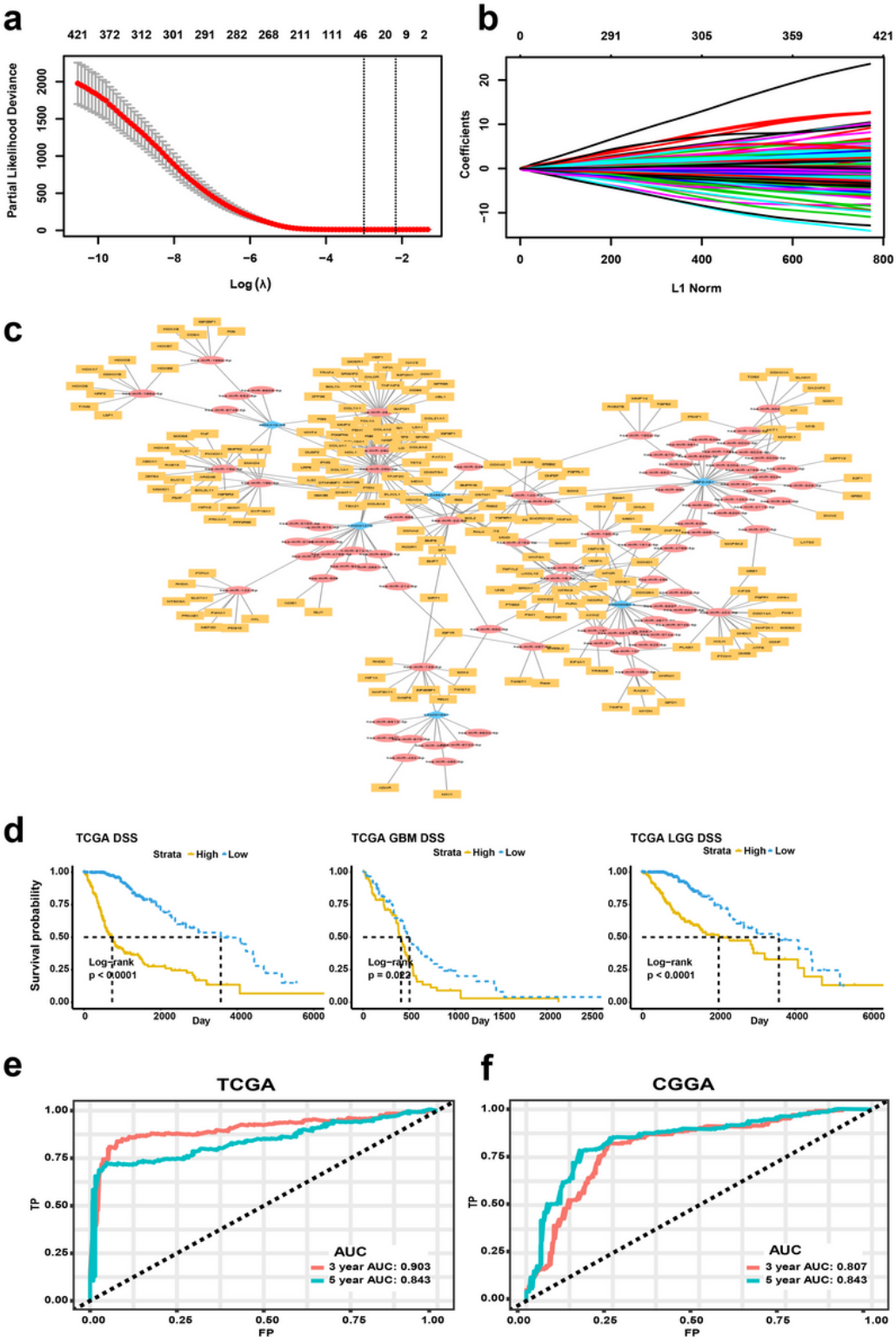

Figure 2

a The cross-validation plot of LASSO regression (the dashed lines signify 735 the optimal log (λ) value). b LASSO coefficients of the lncRNAs with independent prognostic value. c The ceRNA network based on signature lncRNAs. d Comparison of clinical outcomes between high- and low-risk groups using DSS as the endpoint in TCGA dataset. e-f The ROC curves and AUC values of the risk model in TCGA and CGGA datasets.

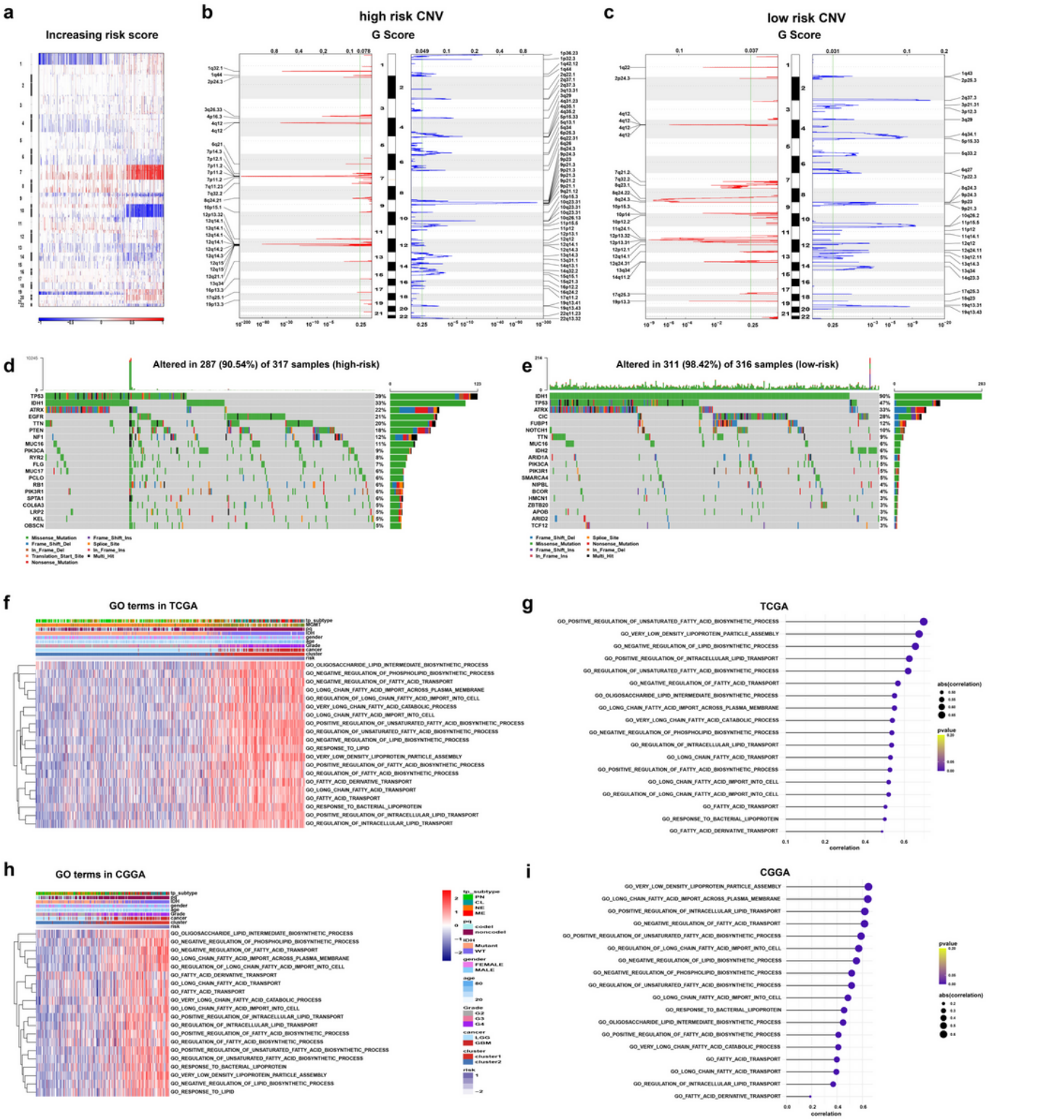

Figure 3

a The overall CNV profile in order of increasing risk score. b-c The deleted (blue) and amplified (red) chromosomal regions in high- and low-risk groups; q value = 0.25 as the threshold (the green line). d-e The somatic mutation profiles in high and low-risk groups. f,h Heatmaps displaying the correlation between the identified lipid metabolism functions, clinicopathological characteristics, and risk score in

TCGA and CGGA datasets. g,i Correlograms showing the 20 biological processes of lipid metabolism most correlated with risk score in TCGA and CGGA datasets

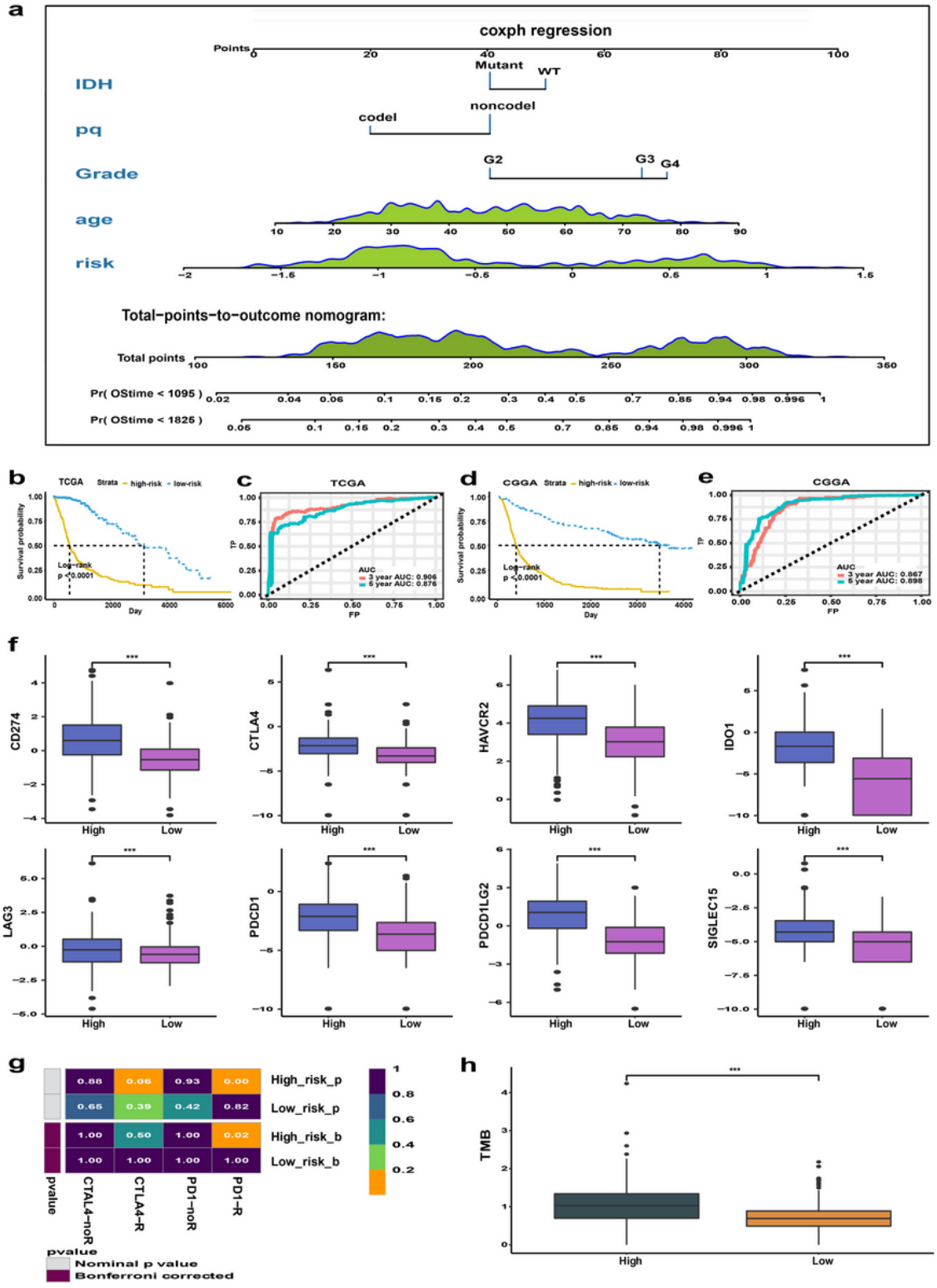

Figure 4

a Nomogram was used by summing the points of each variable. b,d K-M plots showing the difference in OS between high- and low-risk groups in TCGA and CGGA datasets. c,e The ROC curves and AUC values of the nomogram in TCGA and CGGA datasets. f Expression of immune checkpoints in high- and low-risk

groups. g.The analysis of response to immunotherapy. h Comparison of TMB between high- and low-risk groups.

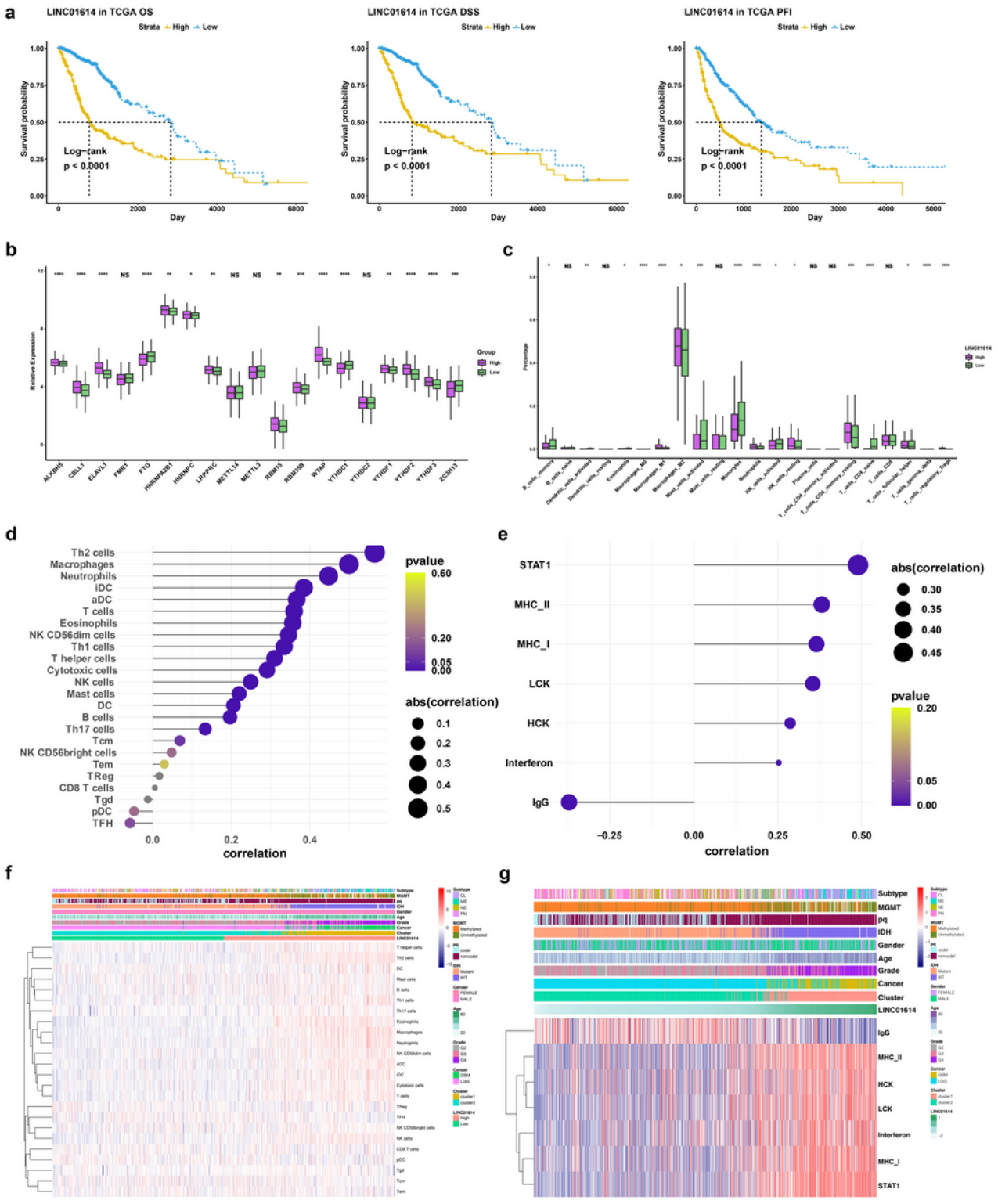

Figure 5

a Comparison of prognosis between LINC01614 high- and low-expression groups. b Difference of m6A-related genes expression between the two groups. c Comparison of 22 immune cell components between high- and low-LINC01614 groups. d-e Correlograms showing the correlation between immune cell

infiltration, inflammation activities, and LINC01614 expression. f-g Heatmaps displaying the activities of immune cells and inflammation.

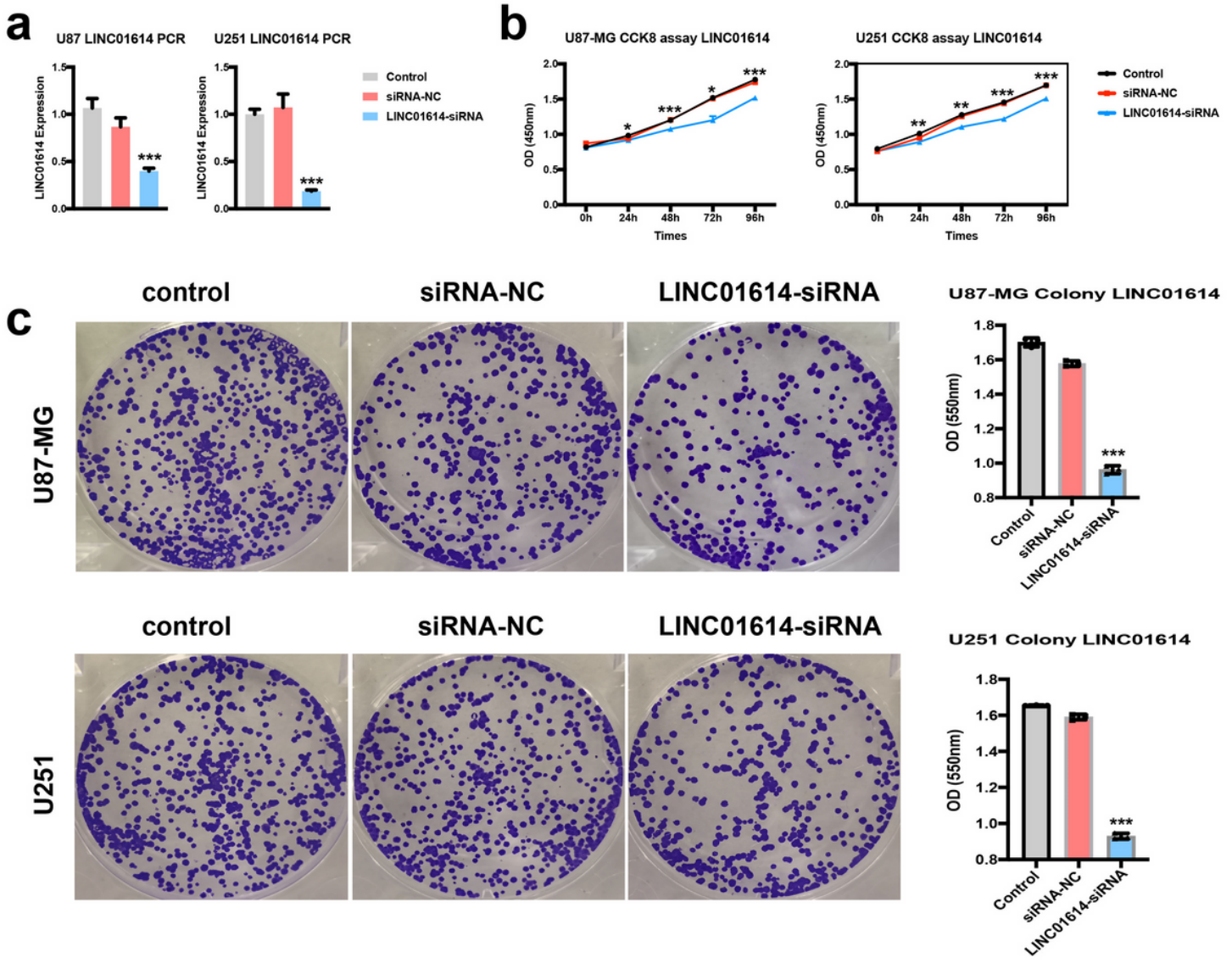

Figure 6

Silencing LINC01614 expression inhibited the viability of U87-MG and U251 cells. a The relative expression levels of LINC01614 in control, siRNA-NC, and LINC01614-siRNA groups were measured by RT-PCR. b Cell viability was measured by CCK-8 assay at 24 h, 48 h, 72 h, and 96h after silencing the expression of LINC01614. c Cell cloning was reduced by interfering with LINC01614 expression in colony-forming assay. *p < 0.05, **p < 0.01, ***p < 0.001

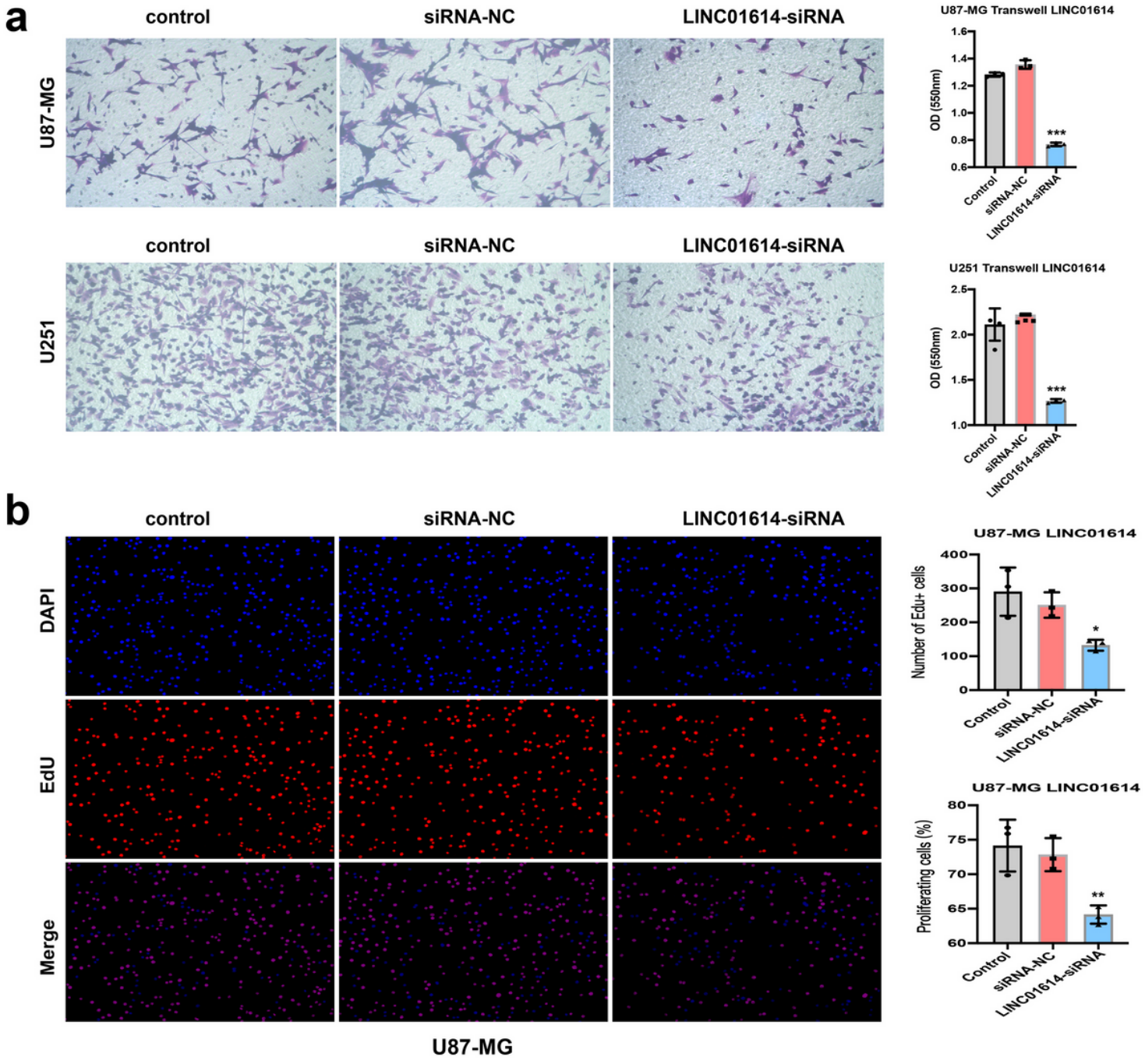

Figure 7

Silencing LINC01614 expression inhibited the proliferation and migration of U87-MG and U251 cells. a Transwell assay was performed to assess the migration ability of glioma cells in control, siRNA-NC, and LINC01614-siRNA groups. b EdU assay was used to evaluate the proliferation of U87-MG cells; Cells were stained with EdU (red) and DAPI (blue).

Supplementary Files

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