

Supplemental information

Table S1. IHC of EGFR in Human Protein Atlas database.

| No. | Tissue type | ID | Age | Gender | staining |
|-----|----------------|------|-----|--------|--------------|
| 1 | Normal | 2268 | 49 | Female | Low |
| 2 | Normal | 2417 | 59 | Male | Low |
| 3 | Adenocarcinoma | 4923 | 57 | Male | Not detected |
| 4 | Adenocarcinoma | 2003 | 61 | Female | Not detected |

Table S2. Correlation analysis between MCM4 and biomarkers of immune cells using TIMER.

| Description | Gene markers | LUAD | |
|---------------------|------------------------|---------------|--|
| | | Cor | p-value |
| CD8+ T cell | CD8A | 0.125 | 4.54×10^{-03} |
| | CD8B | 0.132 | 2.63×10^{-03} |
| T cell (general) | CD3D | -0.038 | 3.91×10^{-01} |
| | CD3E | -0.049 | 2.71×10^{-01} |
| | CD2 | -0.055 | 2.14×10^{-01} |
| B cell | CD19 | -0.11 | 1.26×10^{-02} |
| | CD79A | -0.106 | 1.60×10^{-02} |
| Monocyte | CD86 | 0.061 | 1.69×10^{-01} |
| | CD115 (CSF1R) | 0.009 | 8.34×10^{-01} |
| TAM | CCL2 | 0.047 | 2.87×10^{-01} |
| | CD68 | 0.058 | 1.89×10^{-01} |
| | IL10 | 0.018 | 6.80×10^{-01} |
| M1 Macrophage | INOS (NOS2) | 0.072 | 1.02×10^{-01} |
| | IRF5 | 0.07 | 1.13×10^{-01} |
| | COX2 (PTGS2) | 0.139 | 1.63×10^{-03} |
| M2 Macrophage | CD163 | 0.155 | 4.37×10^{-04} |
| | VSIG4 | 0.003 | 9.52×10^{-01} |
| | MS4A4A | -0.018 | 6.89×10^{-01} |
| Neutrophils | CD66b (CEACAM8) | -0.259 | 2.62×10^{-09} |
| | CD11b (ITGAM) | -0.03 | 4.97×10^{-01} |
| | CCR7 | -0.174 | 7.34×10^{-05} |
| Natural killer cell | KIR2DL1 | 0.015 | 7.27×10^{-01} |
| | KIR2DL3 | 0.14 | 1.49×10^{-03} |
| | KIR2DL4 | 0.324 | 5.14×10^{-14} |
| | KIR3DL1 | 0.008 | 8.58×10^{-01} |
| | KIR3DL2 | 0.119 | 6.73×10^{-03} |
| | KIR3DL3 | 0.119 | 7.02×10^{-03} |
| | KIR2DS4 | 0.031 | 4.82×10^{-01} |
| Dendritic cell | HLA-DPB1 | -0.31 | 6.02×10^{-13} |
| | HLA-DQB1 | -0.252 | 6.25×10^{-09} |

| | | | |
|-------------------|---------------------------------------|---------------|--|
| | HLA-DRA | -0.252 | 7.25×10^{-09} |
| | HLA-DPA1 | -0.233 | 9.32×10^{-08} |
| | BDCA-1 (CD1C) | -0.42 | 2.03×10^{-23} |
| | BDCA-4 (NRP1) | 0.125 | 4.55×10^{-03} |
| | CD11c (ITGAX) | 0.005 | 9.01×10^{-01} |
| Th1 | T-bet (TBX21) | 0.038 | 3.89×10^{-01} |
| | STAT4 | -0.033 | 4.60×10^{-01} |
| | STAT1 | 0.433 | 0.00 |
| | TNF-γ (IFNG) | 0.218 | 6.08×10^{-07} |
| | TNF- α (TNF) | 0.005 | 9.07×10^{-01} |
| Th2 | GATA3 | 0.075 | 8.80×10^{-02} |
| | STAT6 | -0.129 | 3.50×10^{-03} |
| | STAT5A | 0.008 | 8.61×10^{-01} |
| | IL13 | -0.006 | 8.86×10^{-01} |
| Tfh | BCL6 | -0.005 | 9.15×10^{-01} |
| | IL21 | 0.182 | 3.15×10^{-05} |
| Th17 | STAT3 | 0.106 | 1.61×10^{-02} |
| | IL17A | 0.049 | 2.70×10^{-01} |
| Treg | FOXP3 | 0.082 | 6.34×10^{-02} |
| | CCR8 | 0.124 | 4.99×10^{-03} |
| | STAT5B | 0.088 | 4.49×10^{-02} |
| | TGF β (TGFB1) | -0.044 | 3.21×10^{-01} |
| T cell exhaustion | PD-1 (PDCD1) | 0.171 | 9.89×10^{-05} |
| | CTLA4 | 0.071 | 1.06×10^{-01} |
| | LAG3 | 0.204 | 3.03×10^{-06} |
| | TIM-3 (HAVCR2) | 0.055 | 2.16×10^{-01} |
| | GZMB | 0.331 | 1.35×10^{-14} |

Table S3. Correlation analysis between MCM4 and biomarkers of Neutrophils, Dendritic cell, Natural killer cell, Th1 and T cell exhaustion in LUAD in GEPIA.

| Description | Gene markers | LUAD | |
|---------------------|---------------|-------|-----------------------|
| | | Cor | p-value |
| Neutrophils | CD66b | -0.13 | 0.0059 |
| Dendritic cell | HLA-DPB1 | -0.26 | 5.6×10^{-09} |
| | HLA-DQB1 | -0.19 | 2.5×10^{-05} |
| | HLA-DRA | -0.23 | 1.8×10^{-07} |
| | HLA-DPA1 | -0.18 | 6.8×10^{-05} |
| | BDCA-1 | -0.27 | 2.6×10^{-09} |
| Natural killer cell | KIR2DL4 | 0.12 | 0.0061 |
| Th1 | STAT1 | 0.33 | 7.9×10^{-14} |
| | IFN- γ | 0.18 | 5.8×10^{-05} |
| T cell exhaustion | GZMB | 0.19 | 4.3×10^{-05} |

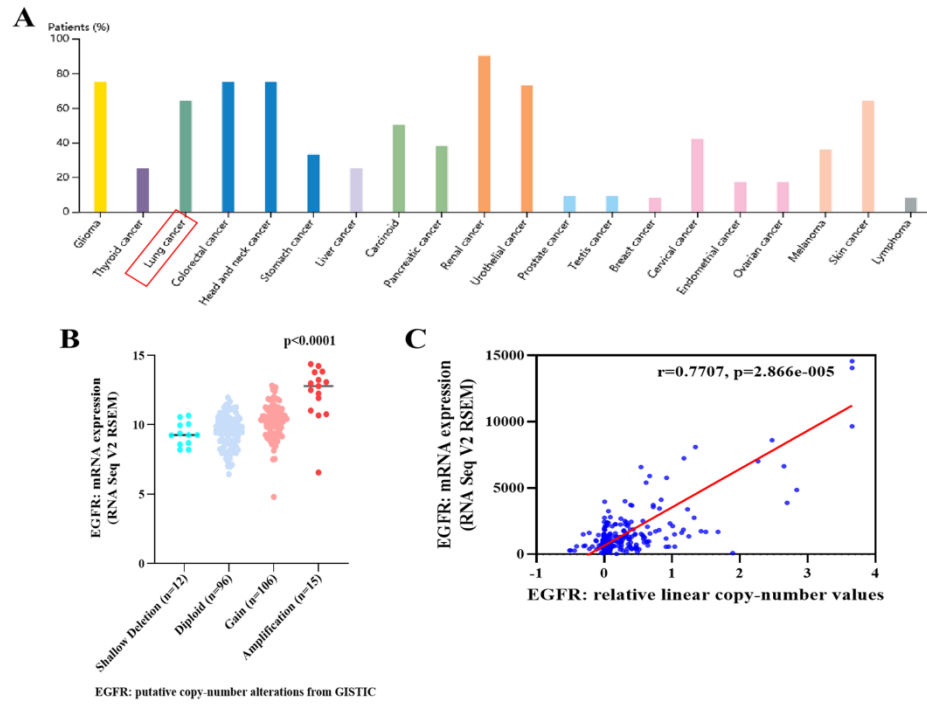


Figure S1. The expression status of EGFR in LUAD. (A) Expression distribution expression of EGFR in various cancer tissues. Dot plot (B) and correlation figure (C) showing the positive correlation between EGFR copy value and mRNA expression values.

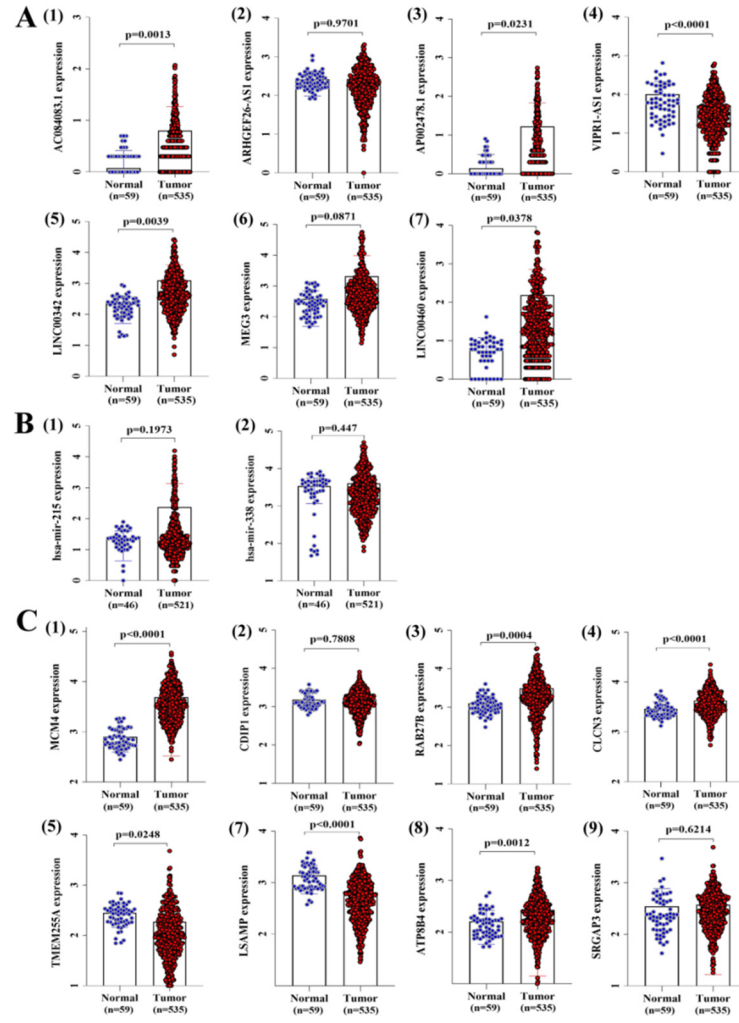


Figure S2. In the TCGA LUAD data set, the distribution of expression values of 17 RNAs from the triple regulatory network in tumor tissues (n=535) and adjacent tissues (n=59). (A) 7 DElncRNAs, (B) 2 DEMiRNAs and (C) 8 DEMRNAs.

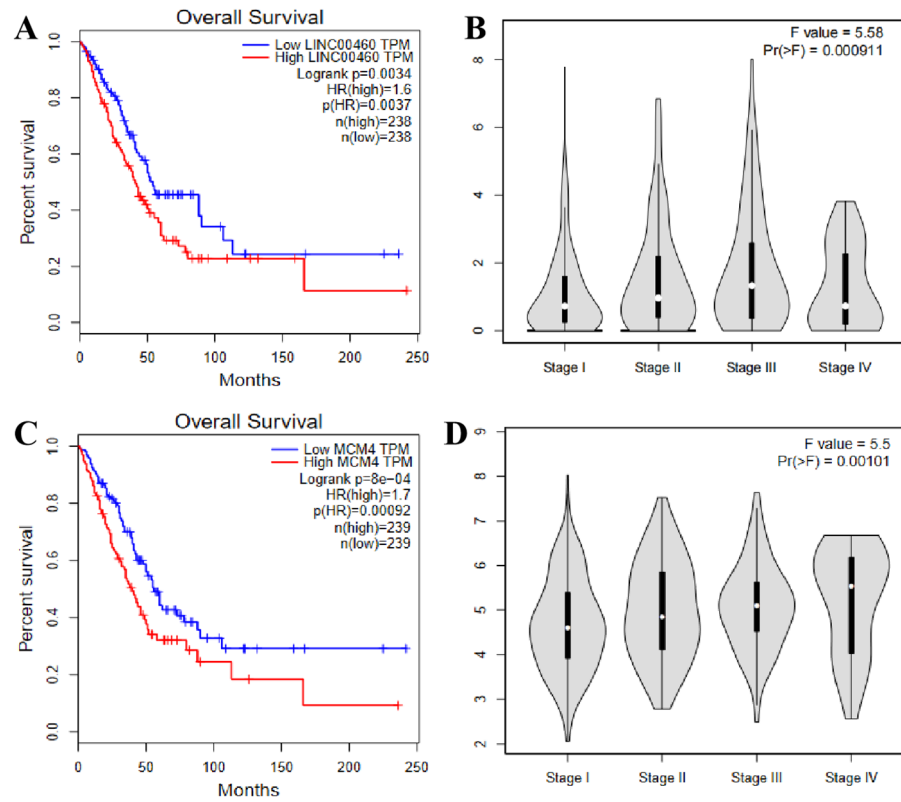


Figure S3. The correlation between LINC00460/MCM4 and overall survival and tumor stage of LUAD patients was detected in the GEPIA database.

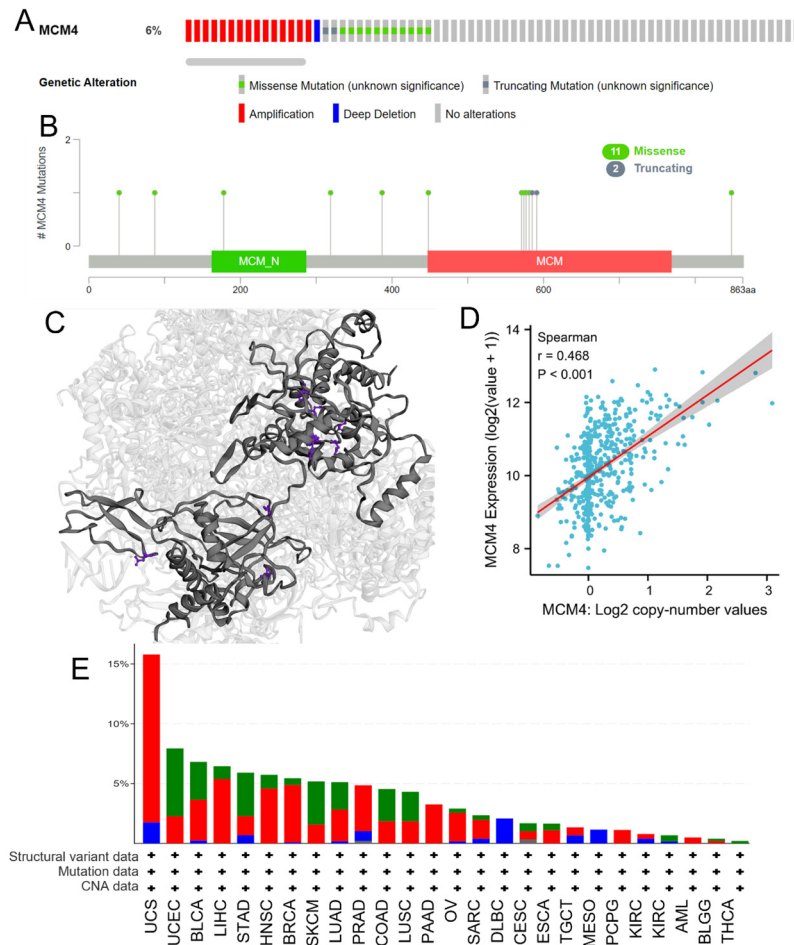


Figure S4. The mutation of MCM4 in LUAD. (A) Mutation site of MCM4. (B) The Mutation site of MCM4. (C) The position of the mutation site in the 3D map of MCM4 gene. (D) The correlation between the expression level of MCM4 and the copy number of the gene. (E) The frequency and type of mutation of MCM4 gene in pan-cancer.

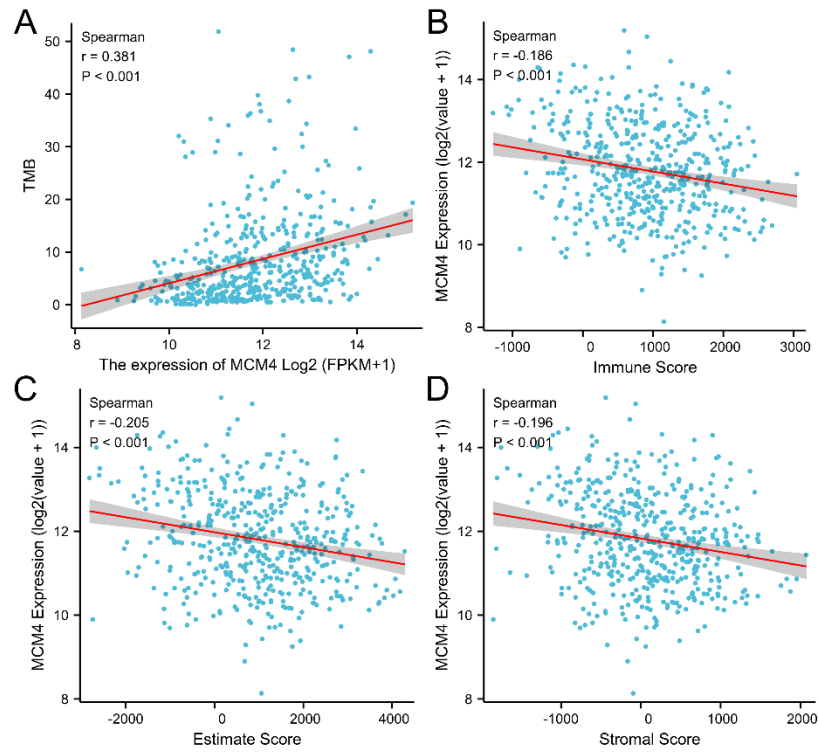


Figure S5. Tumor mutation load and tumor immune microenvironment score. (A) Correlation analysis between TMB and MCM4 expression. (B) The correlation analysis between stromal score and MCM4 expression was evaluated by Estimate. (C) The correlation analysis between immune score and MCM4 expression was evaluated by Estimate. (D) Correlation analysis between the Estimate total score and the expression of MCM4.