Figure S1. M2-like TAMs infiltrate in CGGA cohort.

(A) ssGSEA of M2-like TAMs signature genes in CGGA-glioma dataset showed M2-like TAMs signature score increased with higher grade gliomas. ****P < 0.0001, ANOVA, analysis of variance. (B) Violin plot of M2-like TAMs signature score in IDH-WT and IDH-mutant gliomas from the CGGA database. ****P < 0.0001, Student’s t-test. (D) Kaplan–Meier survival plots of M2-like TAMs signature score showed a higher score indicated a poorer prognosis. P < 0.001, log-rank test.
Figure S2. TGFBI is preferentially secreted by M2-like TAMs and indicates a poor prognosis in GBM patients.

(A) The volcano plot shows the differentially expressed genes in GSE37475 (fold change ≥ 2) [1]. (B) Kaplan-Meier survival plots of TGFBI, TIMP1, AOAH of TCGA-GBM patients. Statistical test: Log-rank test. (C) t-SNE analysis of 3533 cells of 4 glioma patients (GSE84465) [2]. Differential coloring in cell clusters is annotated according to the dominant cell type (left). Expression of cell-type-specific TGFBI, TIMP1, CD163 and CD206 overlaid on the t-SNE space (right). (D) Correlation analyses of TGFBI and CD163 in TCGA-GBM, CGGA-GBM, Rembrandt-GBM, Gravendeel-GBM databases. Pearson’s r test. (E) qRT-PCR analyses of the expressions of M2 markers (CD163 and CD206), M1 markers (iNOS and CD86) and TGFBI between primed-U937 and the U937-derived M2-like TAMs. *p < 0.05, ****p <
0.0001, Student’s t-test. (F) Immunofluorescent staining of TGFBI and IBA1, CD86, CD163 in M0, M1 and M2 macrophages. Scale bar represents 50 μm. (G) The quantification of the TGFBI signal is shown. ****p < 0.01, ANOVA, analysis of variance. (H) Immunoblot analysis of TGFBI in GSCs (456 and 3691) and TAMs. (I) Representative immunofluorescent (IF) staining of TGFBI and the M2-like TAM marker (CD163) in human GBM tissues. Areas indicated with solid and dashed square lines respectively represent the CD163 high and low expression groups. Scale bar represents 20 μm.
Figure S3 TGFBI is distributed around GSCs and mediates the pro-tumorigenic effect of M2-like TAMs.

(A) Representative IF images of Ki67, TGFBI, and SOX2 in mouse models. Scale bar represents 10 μm. (B) The ratio of Ki67+ cells in SOX2+ cells. n = 3, **p < 0.01, Student’s t-test. (C) Representative IF images of total TAMs (labeled with CD163 antibody recognizes human and murine-derived antigen) and injected TAMs (labeled with CD163 antibody recognizes human-derived antigen) in mouse models. Scale bar represents 20 μm. (D) The statistical result indicated the injected TAMs (human-derived TAMs) account for about 90% of the total TAMs (human and murine-derived TAMs), n = 3.
Figure S4 Integrin αvβ5 is a receptor for TGFBI on GSCs.

(A, B) The correlation analyses of ITGAV, ITGB5, and TGFBI expression in TCGA-GBM (A) and CGGA-GBM (B) databases. ***p < 0.001, Pearson’s r test. (C) The mRNA levels of ITGAV and ITGB5 between matched TCGA GBM and normal brain from the genotype-tissue expression (GTEx) dataset. *p < 0.05, Student’s t-test. (D) Kaplan-Meier survival plots of ITGAV and ITGB5 of TCGA-GBM patients. P=0.04, log-rank test.
Figure S5. TGFBI mediates the pro-tumorigenic effect via the integrin αvβ5-Src-Stat3 axis.

(A) KEGG pathways were enriched with TGFBI$^{\text{high}}$-ITGAV$^{\text{high}}$-ITGB5$^{\text{high}}$ in TCGA-GBM. (B) The protein-protein interaction (PPI) network of TGFBI-ITGAV-ITGB5-Src-Stat3 was built using STRING (http://string-db.org/). (C) Immunoblot analyses of ITGA5, ITGB5, phospho-Src (P-Src-Y527), total Src, phospho-Stat3 (P-Stat3-Y705), total Stat3, P53 and CCND1 in 456GSCs and 3691GSCs, indicated that rhTGFBI stimulation significantly increased Src and Stat3-activating phosphorylation, while the inhibitor of ITGAV and ITGB5 (SB273005) compromised rhTGFBI-stimulated P-Src and P-Stat3 activation in GSCs.
# Table S1 The list of chemicals.

| Chemicals                        | Source         | Identifier   |
|----------------------------------|----------------|--------------|
| PMA                              | Sigma-Aldrich  | P1585        |
| LPS                              | Sigma-Aldrich  | L4516        |
| IFN-γ                            | Peprotech      | AF300-02     |
| IL4                              | Peprotech      | AF200-04     |
| IL10                             | Peprotech      | AF200-10     |
| TGF-β                            | Peprotech      | AF100-21C    |
| EGF                              | R&D            | Cat#236-EG   |
| bFGF                             | R&D            | Cat#4114-TC  |
| Fetal bovine serum               | Gbico          | 10099141C    |
| protease and phosphatase inhibitors | Thermo Scientific | Cat# 78442 |
| ChamQ SYBR Master Mix            | Vazyme         | Cat# Q311-02/03 |
| HiScript II Q RT SuperMix for qPCR (+gDNA wiper) | Vazyme | Cat# R223-01 |
| B27                              | BasalMedia     | S441J7       |
| Neurobasal media                 | BasalMedia     | X087G1       |
| Sodium pyruvate                  | BasalMedia     | Cat# 11360070 |
| Glutamax                         | BasalMedia     | Cat# 35050061 |
| penicillin/streptomycin          | BasalMedia     | S110JV       |
| RPMI Medium 1640 basic           | Gbico          | Cat# 11875093 |
| Triton X-100                     | Solarbio       | Cat# T8200   |
| SB273005                         | Selleck        | S7540        |
Table S2 The clinical information of the six human GBM specimens.

| Specimen  | Histopathology | WHO Grade | Gender | Age (years) | Predominant side of tumor location | Predominant lobe of tumor location | Extent of surgical resection |
|-----------|----------------|-----------|--------|-------------|----------------------------------|----------------------------------|-----------------------------|
| GBM5336   | GBM            | 4         | Male   | 64          | Left                             | Temporal                        | TR                          |
| GBM3871   | GBM            | 4         | Female | 49          | Right                            | Temporal                        | TR                          |
| GBM4698   | GBM            | 4         | Female | 46          | Left                             | Temporal                        | TR                          |
| GBM7611   | GBM recurrent  | 4         | Female | 56          | Right                            | Parietal                        | GTR                         |
| GBM8733   | GBM            | 4         | Male   | 54          | Left                             | Temporal                        | TR                          |
| GBM7715   | GBM recurrent  | 4         | Female | 45          | Right                            | Frontal                         | TR                          |

Abbreviations: GBM, Glioblastoma; TR, Total resection; GTR, Gross total resection.
Table S3 The clinical information of the 78 gliomas.

| TMA number | Gender | Age (year) | WHO grade | Survival time (month) | Survival state |
|------------|--------|------------|-----------|-----------------------|----------------|
| 1          | Male   | 63         | 2         | 13.32                 | Dead           |
| 2          | Male   | 47         | 4         | 4.80                  | Dead           |
| 3          | Male   | 33         | 3         | 21.37                 | Dead           |
| 4          | Male   | 44         | 4         | NA                    | NA             |
| 5          | Female | 73         | 4         | 42.08                 | Alive          |
| 6          | Male   | 55         | 4         | 9.24                  | Dead           |
| 7          | Male   | 63         | 4         | 5.92                  | Dead           |
| 8          | Male   | 58         | 4         | 8.52                  | Dead           |
| 9          | Female | 47         | 2         | 36.36                 | Alive          |
| 10         | Female | 44         | 2         | 36.07                 | Alive          |
| 11         | Male   | 65         | 4         | 15.78                 | Dead           |
| 12         | Male   | 68         | 4         | 18.12                 | Dead           |
| 13         | Male   | 35         | 4         | NA                    | NA             |
| 14         | Female | 42         | 2         | 35.38                 | Alive          |
| 15         | Male   | 30         | 4         | 35.34                 | Alive          |
| 16         | Female | 35         | 2         | 34.49                 | Alive          |
| 17         | Female | 53         | 2         | 34.49                 | Alive          |
| 18         | Male   | 48         | 4         | 1.35                  | Dead           |
| 19         | Male   | 47         | 2         | 34.19                 | Alive          |
| 20         | Female | 44         | 2         | 34.16                 | Alive          |
| 21         | Male   | 46         | 2         | 29.36                 | Dead           |
| 22         | Female | 43         | 3         | NA                    | NA             |
| 23         | Male   | 60         | 4         | 13.87                 | Dead           |
| 24         | Male   | 65         | 4         | 11.51                 | Dead           |
| 25         | Female | 56         | 3         | 13.48                 | Dead           |
| 26         | Female | 50         | 2.3       | NA                    | NA             |
| 27         | Female | 50         | 4         | NA                    | NA             |
| 28         | Male   | 50         | 4         | NA                    | NA             |
| 29         | Female | 42         | 4         | 6.64                  | Dead           |
| 30         | Male   | 45         | 3         | 28.77                 | Alive          |
| 31         | Male   | 44         | 4         | 13.18                 | Dead           |
| 32         | Male   | 46         | 4         | 28.47                 | Alive          |
| 33         | Female | 51         | 4         | 9.40                  | Dead           |
| 34         | Male   | 65         | 4         | 16.34                 | Dead           |
| 35         | Male   | 62         | 4         | 14.50                 | Dead           |
| 36         | Female | 36         | 2         | 27.48                 | Alive          |
| 37         | Female | 35         | 4         | 18.67                 | Dead           |
| 38         | Male   | 30         | 4         | NA                    | NA             |
| 39         | Male   | 65         | 4         | 6.90                  | Dead           |
| 40         | Male   | 11y5m      | 4         | 10.75                 | Dead           |
|   | Gender | Age   | Sex | Temperature | Status |
|---|--------|-------|-----|-------------|--------|
| 42 | Female | 26    | 4   | 24.36       | Dead   |
| 43 | Male   | 43    | 4   | 2.89        | Dead   |
| 44 | Male   | 61    | 4   | 9.53        | Dead   |
| 45 | Female | 38    | 2   | 24.72       | Alive  |
| 46 | Female | 38    | 4   | 21.80       | Alive  |
| 47 | Female | 54    | 4   | 16.93       | Dead   |
| 48 | Male   | 46    | 4   | 23.61       | Alive  |
| 49 | Female | 48    | 3   | 2.73        | Dead   |
| 50 | Male   | 31    | 2   | 18.87       | Alive  |
| 51 | Female | 47    | 3   | NA          | NA     |
| 52 | Male   | 55    | 4   | 18.31       | Alive  |
| 53 | Female | 37    | 2.3 | 17.62       | Alive  |
| 54 | Male   | 53    | 4   | 30.31       | Alive  |
| 55 | Male   | 47    | 2   | 35.34       | Alive  |
| 56 | Male   | 31    | 2   | 34.26       | Alive  |
| 57 | Male   | 49    | 4   | 13.78       | Alive  |
| 58 | Female | 50    | 4   | 18.77       | Alive  |
| 59 | Female | 9     | 3   | 15.81       | Alive  |
| 60 | Male   | 46    | 4   | 10.45       | Dead   |
| 61 | Female | 62    | 4   | 10.78       | Dead   |
| 62 | Male   | 1y6m  | 3.4 | 21.14       | Alive  |
| 63 | Female | 32    | 2.3 | 0.33        | Alive  |
| 64 | Female | 55    | 4   | 6.87        | Dead   |
| 66 | Male   | 34    | 2   | 23.21       | Alive  |
| 67 | Female | 34    | 2   | 2.86        | Dead   |
| 68 | Male   | 69    | 4   | 11.64       | Dead   |
| 69 | Female | 57    | 4   | NA          | NA     |
| 70 | Male   | 17    | 3   | NA          | NA     |
| 71 | Male   | 45    | 2   | NA          | NA     |
| 73 | Female | 55    | 3.4 | 3.68        | Dead   |
| 74 | Female | 59    | 2.3 | 13.94       | Dead   |
| 75 | Male   | 48    | 2   | NA          | NA     |
| 76 | Male   | 52    | 2   | 16.14       | Dead   |
| 77 | Male   | 40    | 2   | 31.96       | Alive  |
| 78 | Male   | 56    | 4   | 4.83        | Dead   |
| 79 | Female | 61    | 2   | NA          | NA     |
| 80 | Male   | 1y8m  | 2   | 26.89       | Alive  |
| 81 | Male   | 16    | 3   | NA          | NA     |

Abbreviations: NA, Not available
Table S4 The list of antibodies.

| Antibodies | Source       | Identifier            |
|------------|--------------|-----------------------|
| P-stat3 Y705 | Cell Signaling | 9145S                |
| Stat3      | Cell Signaling | 9139S                |
| P-src Y527  | Cell Signaling | 2105S                |
| Src        | Cell Signaling | 2109S                |
| CCND1      | Cell Signaling | 2978T                |
| Ki67       | Proteintech   | 27309-1-AP            |
| P53        | Santa cruz    | SC126(D0-1)           |
| TGFBI      | Proteintech   | 60007-1-Ig            |
| TGFBI      | Proteintech   | 10188-1-AP            |
| TGFBI      | Abclone       | A11222                |
| TGFBI      | Abcam         | ab170874              |
| CD206      | Proteintech   | 60143-1-Ig            |
| CD163      | Santa cruz    | SC-33715              |
| CD163      | Proteintech   | 16646-1-AP            |
| IBA1       | Cell Signaling | 17198S               |
| ITGAV      | Abclone       | A2091                 |
| ITGB5      | Cell Signaling | 3629S                |
| SOX2       | Proteintech   | 66411-1-Ig            |
| Olig2      | Proteintech   | 66513-1-Ig            |
| CD133      | Affinity      | BF0403                |
| GFAP       | Cell Signaling | 80788                |
| CD86       | Proteintech   | 13395-1-AP            |
| iNOS       | Proteintech   | 18985-1-AP            |
| SOX2       | Abcam         | ab196637              |
Table S5 Short hairpin RNA sequences used for lentiviral vector construction

| Source | Identifier | Sequence (5' to 3')          |
|--------|------------|------------------------------|
| shTGF  | Sigma-TRCN000 | CCGGGCGCTTGAGATCTCTTTCAAAACAAACTCG |
| BI-417 | Aldrich-0291417 | AGTTGTCTTGAAGATCTCAAGCGCTTTTTTG |
| shTGF  | Sigma-TRCN000 | CCGGAAGGTATTGCACTAATACTCG |
| BI-419 | Aldrich-0291419 | AGTATTAGTGCCAAATAACCTTCTTTTTTG |
| shITG  | Sigma-TRCN000 | CCGGGTGAGGCTCAGGATAACTC |
| AV-1   | Aldrich-0010768 | GAGTTTTATCCTTGTTCGACCTCACTTTTT |
| shITG  | Sigma-TRCN000 | CCGCGACAGGCTCACATTCTACTTCTCG |
| AV-3   | Aldrich-0010769 | AGAAGTAGAATGTGAGCCTGCGTTTTT |


Table S6 The list of primer sequences used for the qRT-PCR.

| Gene   | Forward primer (5' to 3') | Reverse primer (5' to 3') |
|--------|---------------------------|---------------------------|
| TGFBI  | ATGACCCTCACCTCTATGTACC    | CACAGTTCAAGTTACAATCCCA    |
| CD163  | CATGTCTCTGAGGCTGACCA      | TGACACAGATCTACCCACAT      |
| CD206  | TACCTGACCCCCACACCTGCT     | GCGGTTGTCATGGTTTCCC      |
| CD86   | CCGCAGAGGATGTTGGGCAATA    | TCACAAGGGAGGAGGACCACA     |
| iNOS   | TTCAGTATACAAACCTAGCAAGA   | TGGACCTGCAAAGTTAAATCCCC  |
| SOX2   | TACAGCATGTCTCTACTCGCAG    | GAGGAAGAGGTAACACAGGG     |
| GFAP   | CTGGGCTGATCAACTCA         | TCCAGCGACTCAATTTTCTC     |
| ITGAV  | GCTGTCGGAGATTTCAATGGT     | TCTGTCGGCCAGTAAATGGT     |
| ITGA3  | GTCACACGATGTTGGAAAGA      | CCGAAGTACACAGTGTTTCTG    |
| ITGA5  | GGCTTCATAATGAGCCGGAG      | TGGCGTATTAGCCTTGGG       |
| ITGA6  | GGGCAGTGTTGTCATCTGAGTC    | AATCGCCCATCAACAGGCTC     |
| ITGB1  | GGTGGAAGTGGTCTACCTGGG     | CAGCAGCGAGTTCTGAATGTC    |
| ITGB3  | AATCTCCCTGTACCATACATTCT   | TCTAGATGCTGCAAGTACGGT    |
| ITGB5  | TCTCAGTGTGATCTCGAGGG      | TGCGCAAAGTCTGAGCTGA      |
| ACTB   | CTCCCTGGAGTCAAGAGATCCA    | CAACAGCTTCTGAGGAGGGA     |
| GAPDH  | AAGGTTAAGGTCAGCGATCAC     | GGGGTATTGATGGCAACAATA    |

References

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[2]. Darmanis S, Sloan SA, Croote D, et al. Single-Cell RNA-Seq Analysis of Infiltrating Neoplastic Cells at the Migrating Front of Human Glioblastoma. *Cell reports*. 2017 **21**: 1399-1410.