## Supplementary Figures



Supplementary Figure 1. Number of unique p52 and ETS1 ChIP peaks in both untreated and TWEAK treated U-87 MG cells.



Supplementary Figure 2. p52 and ETS1 expression in U-87 MG and U-251 MG cells following *NFKB2* knockdown and TWEAK treatment analysed through western blotting.



Supplementary Figure 3. Gene expression of ETS transcription factors in glioma patients (n = 702) from TCGA RNA-seq dataset. The box plots define the median, upper and lower quartiles.



Supplementary Figure 4. p52 and ETS1 expression in U-87 MG and U-251 MG cells following *ETS1* knockdown and TWEAK treatment analysed through western blotting.



Supplementary Figure 5. Images of primary tumours extracted 35 days after mice were injected with U-87 MG cells that express either CRISPR control, *NFKB2* KD or *ETS1* KD and overexpression control or TWEAK.



Supplementary Figure 6. Uncropped western blot images for Figure 1b. Proteins were probed on two western blots that were loaded with the same amount of protein and performed at the same time.



Supplementary Figure 7. Uncropped western blot images for Figure 4e U-87 MG. Proteins were probed on two western blots that were loaded with the same amount of protein and performed at the same time.



Supplementary Figure 8. Uncropped western blot images for Figure 4e and Supplementary Figure 2 U-251 MG. Proteins were probed on two western blots that were loaded with the same amount of protein and performed at the same time.



Supplementary Figure 9. Uncropped western blot images for Figure 5a. All bands were probed on the same blot.



## <u>U-87 MG</u>



Supplementary Figure 10. Uncropped western blot images for Supplementary Figure 2 U-87 MG. Proteins were probed on two western blots that were loaded with the same amount of protein and performed at the same time.



Supplementary Figure 11. Uncropped western blot images for Supplementary Figure 4 U-87 MG. Proteins were probed on two western blots that were loaded with the same amount of protein and performed at the same time.



Supplementary Figure 12. Uncropped western blot images for Supplementary Figure 4 U-251 MG. Proteins were probed on two western blots that were loaded with the same amount of protein and performed at the same time.

## CRISPR sgRNA sequences

| Primer name      | Sequence                  |
|------------------|---------------------------|
| ETS1 guide #1 F  | CACCGGGTTTCTGTCCACTGCCGG  |
| ETS1 guide #1 R  | CCGGCAGTGGACAGAAACCCGGTG  |
| ETS1 guide #2 F  | CACCGCTGGGCTCTGAGAACTCCGA |
| ETS1 guide #2 R  | AAACTCGGAGTTCTCAGAGCCCAGC |
| NFKB2 guide #1 F | CACCGTGGCCCCTACCTGGTGATCG |
| NFKB2 guide #1 R | AAACCGATCACCAGGTAGGGGCCAC |
| NFKB2 guide #2 F | CACCGCTTTCGGCCCTTCTCACTGG |
| NFKB2 guide #2 R | AAACCCAGTGAGAAGGGCCGAAAGC |

shIRE1α sequences

| Primer name | Sequence              |
|-------------|-----------------------|
| shIRE1α #1  | GCGTAAATTCAGGACCTATAA |
| shIRE1α #2  | TCAACGCTGGATGGAAGTTTG |

TWEAK overexpression primer sequences

| Primer name | Sequence                                 |
|-------------|--|
| sTWEAK F    | ATACCGGTCGCCACCATGAAAACACGGGCTCGAAG      |
| sTWEAK R    | CGTATTCGAATCAGTGAACCTGGAAGAGTCCGAAGTAGGT |

Supplementary Table 1. Primer sequences for CRISPR sgRNA, shIRE1 $\alpha$  and TWEAK overexpression construct.

| Genotype                                | Plasmid combination              |
|---|----------------------------------|
| CRISPR control + Overexpression control | lentiCRISPR v2 + pLJM-EGFP-hygro |
| CRISPR control + sTWEAK overexpression  | lentiCRISPR v2 + pLJM-sTWEAK     |
| ETS1 KD + sTWEAK overexpression         | lentiCRISPR ETS1 guide #1 +      |
|   | pLJM-sTWEAK                      |
| NFKB2 KD + sTWEAK overexpression        | lentiCRISPR NFKB2 guide #1 +     |
|   | pLJM-sTWEAK                      |

Supplementary Table 2. Combinations of plasmids transduced into U-87 MG cells that were injected into immunocompromised mice and the presented genotype of the cells.