

Extended Data Figure 6 | Pan-glioma and multi-cancer analysis of F3–T3 fusion-positive samples. **a, b**, Hierarchical (a) and consensus clustering (b) of 11 F3–T3-positive samples (red) out of 627 pan-glioma samples. The 11 F3–T3-positive samples (red) in **b** fall in one cluster (blue). **c**, Enrichment map network of statistically significant GO categories ($Q < 0.001$, NES > 0.6 ; upper-tailed MWW-GST) in the 11 F3–T3 fusion-positive pan-glioma samples. Nodes represent GO terms and lines demonstrate their connectivity. Size of nodes is proportional to number of genes in the GO category and thickness of lines indicates the fraction of genes shared between the groups. **d**, MWW enrichment plot of the 'hallmark oxidative phosphorylation' GO category in F3–T3-positive samples in the pan-glioma cohort. **e**, Hierarchical clustering of four F3–T3-positive (red) samples out of 86 lung squamous cell carcinoma (LUSC) samples. **f**, Enrichment map network of statistically significant GO categories ($Q < 0.001$, NES > 0.6 ; upper-tailed MWW-GST) in four F3–T3-positive LUSC. Nodes represent GO terms and lines demonstrate their connectivity. Size of nodes is proportional to number of genes in the GO category and thickness of lines indicates the fraction of genes shared between the groups. **g**, Hierarchical clustering of two F3–T3-positive, human papilloma virus (HPV)-positive head and neck squamous cell carcinoma (HNSC) samples (in red) out of 36 samples. **h**, Enrichment map network of statistically significant GO categories ($Q < 0.001$, NES > 0.6 ; upper-tailed MWW-GST) in two F3–T3-positive HNSC samples. Nodes represent GO terms and lines demonstrate their connectivity. Size of nodes is proportional to number of genes in the GO category and thickness of lines indicates the fraction of genes shared between the groups. **i**, Hierarchical clustering of two F3–T3-positive samples (red) out of 184 oesophageal carcinoma (ESCA) samples. Heat maps of the two

F3–T3-positive samples are enlarged to the left. **j**, Hierarchical clustering of four F3–T3-positive samples (red) out of 305 cervical squamous cell carcinoma and endocervical adenocarcinoma (CESC) samples. **k**, Hierarchical clustering of five F3–T3-positive samples (red) out of 408 urothelial bladder carcinoma (BLCA) samples. **l**, TDA network of pan-glioma samples ($n = 627$) reconstructed using variance normalized Euclidean distance and locally linear embedding as filter function. The nodes containing F3–T3-positive samples are highlighted in red. **m**, Correlation between the expression of F3–T3 (\log_2 of total fragment, x axis) and NES (y axis) of three top ranking mitochondrial functional categories in a multi-cancer cohort including F3–T3-positive samples ($n = 19$) from eight tumour types (r and P values are indicated, upper-tailed Spearman's rank correlation test). **n**, Analysis of the activity of master regulators in the pan-glioma cohort ($n = 627$ glioma). Grey curves represent the activity of each master regulator with tumour samples ranked according to master regulator activity. Red and blue lines indicate individual F3–T3-positive GBM samples displaying high and low master regulator activity, respectively. P values, two-sided MWW test, for differential activity (left) and mean of the activity (right) of the master regulator in F3–T3-positive versus F3–T3-negative samples are indicated. **o**, Gene expression analysis of *PPARGC1A* and *ESRRG* genes in F3–T3-positive and F3–T3-negative GBM; $n = 9$ F3–T3-positive tumours; $n = 525$ F3–T3-negative tumours. Box plot spans the first to third quartiles and whiskers show the $1.5 \times$ interquartile range. P value, two-sided MWW test. Data in **a**, **e**, **g**, **i–k**, were obtained using the Euclidean distance and Ward linkage method and are based on the top and bottom 50 genes having the highest and lowest probability to be upregulated, respectively.