

Description of Additional Supplementary Files

Supplementary Data 1

Description:

- Gene lists used for GSEA
- MSigDB Gene lists used for GSEA
- FACs strategy. First, cells were selected from cellular debris based on the FSC area/SSC area; then singlets were selected based on the FSC area/ FSCHeight and FSC area / FSC weight. Finally, live cells were selected as negative for the Fixable Viability Dye Fluor. This last gating was determined with cells non-incubated with Fixable Viability Dye. (Related to Fig. 3b)

Supplementary Data 2

Description:

- Selected differentially expressed genes in CD45+ cells from p16-3MR-GBMs (pct.1) compared to WT+GCV GBMs (pct.2) (Early time point /10X scRNAseq/related to Fig. 4f) Statistical significance of the expression of genes in p16-3MR+GCV compared with WT+GCV clusters was determined by Wilcoxon-Mann-Whitney test (ns, not significant, *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$).
- *p16^{Ink4a}* fold change per CD45+ cluster in p16-3MR+GCV GBMs (pct.1) compared with WT+GCV GBMs (pct.2) (related to Fig.3h)

Supplementary Data 3

Description:

- Differentially downregulated genes in the p16-3MR+GCV vs the WT+GCV astrocyte cluster (Early time point/10X scRNAseq) avg-logFC ≤ -0.25 ; FDR ≤ 0.05 (related to Fig.5)
- Differentially upregulated genes in p16^{Ink4a} positive vs p16^{Ink4a} negative malignant cells (Late timepoint/ddSeq scRNAseq) avg-logFC ≥ 0.25 ; FDR ≤ 0.05 (related to Fig.5)
- Differentially down-regulated genes in the p16-3MR+GCV vs the WT+GCV GBMs (Late time point/Bulk RNAseq) avg-logFC ≤ -0.5 ; FDR ≤ 0.05 (related to Fig.5)
- NRF2 putative targets (related to Fig. 5)

Supplementary Data 4

Description:

- Univariate Cox analysis (related to Fig.7)
- Cox proportional hazards assumption (related to Fig.7)

Supplementary Data 5

Description:

- Antibodies for IHC/IF analysis
- Antibodies for WB analysis
- RT-qPCR primers
- miR oligonucleotides
- Suppliers for compounds