

Supplementary Figure S2. A. Autocorrelation scores (see methods) of hallmark pathways with FDR <0.01. **B.** UMAPs with pathway scores for each persister nucleus of TNF α via NF- κ B signaling (autocorrelation score 0.54, FDR <0.01), IFN α response (autocorrelation score 0.45, FDR <0.01) and Myogenesis (autocorrelation 0.41, FDR <0.01). **C.** Module to module similarity heatmap. Rows and columns correspond to modules from different Hotspot runs using different number of topmost informative pathways (see methods). The Jaccard similarity (percent of overlapping genes between modules) between modules is calculated and modules are clustered according to their Jaccard similarity resulting in five clusters, i.e. meta-modules. Only genes recurrent in all modules within a meta-module were subsequently retained. Meta-Module #3 was composed of housekeeping genes and was excluded. Purple – high similarity, yellow – low similarity. MX_Y; – M- module, X- number of module, Y- the autocorrelation cutoff used to select the top most informative pathways. **D.** Pearson correlation heatmap between cell cycle phase (S and G2M) scores and module scores assigned to persister cells. Yellow – high, Blue - low. **E.** Pathway enrichment analysis of genes comprising the four persister meta-modules. Yellow – high enrichment score, Blue – low enrichment score. **F.** Percent of persister subtypes by regions in 16 tumors for which samples from two regions were available at time of definitive surgery. ns, not significant