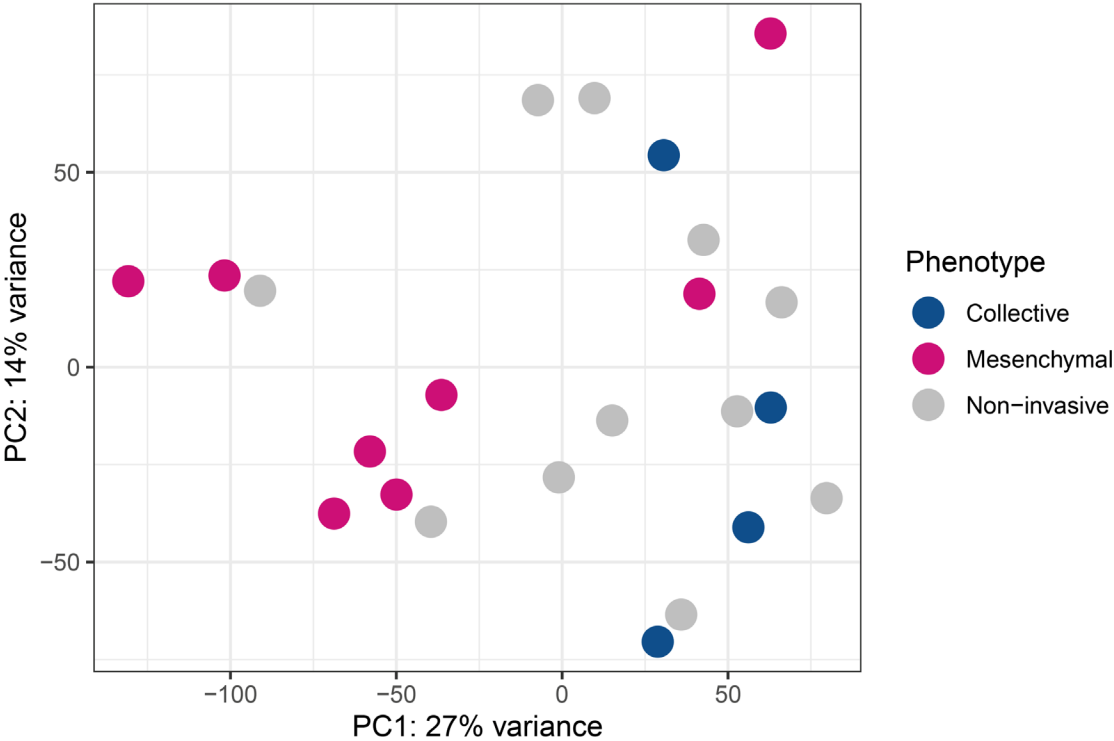
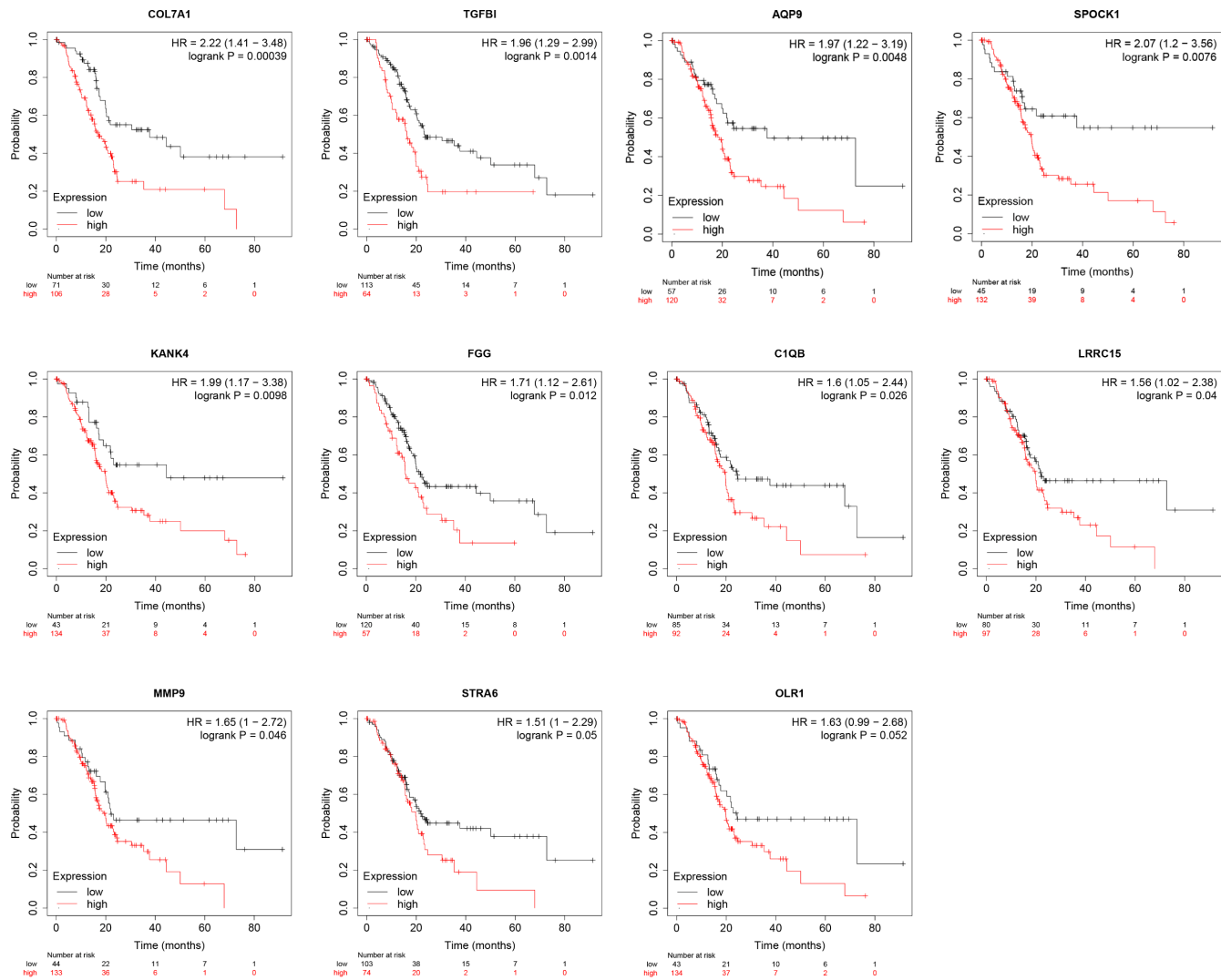


Supplemental figure 1



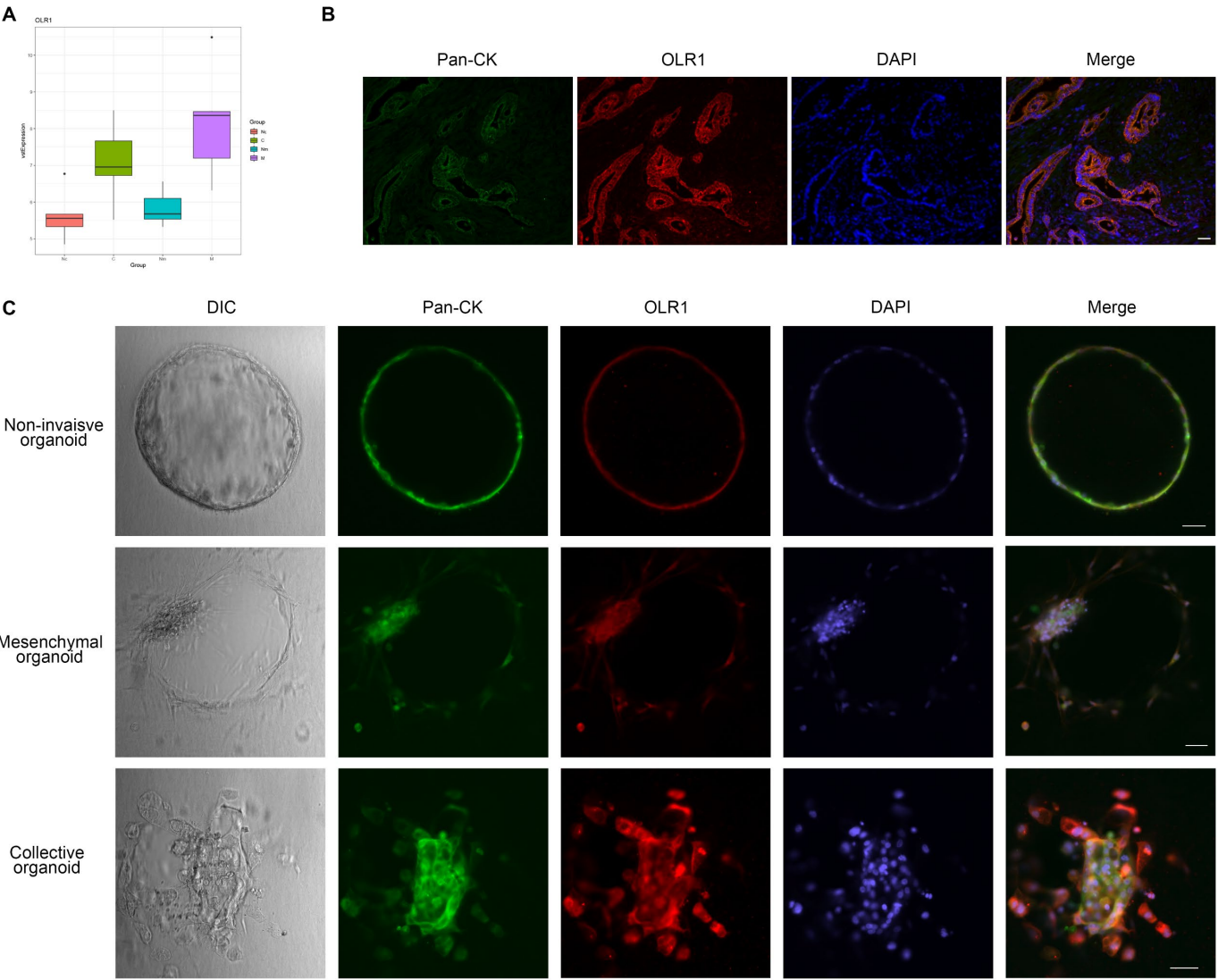
**Supplemental figure 1. Principal component analysis of all invasive PDAC organoids and matched non-invasive organoids** Principal component analysis shows clustering of the matched invasive and non-invasive organoids from the same primary tumors and also segregates by the invasive morphology as indicated.

Supplemental figure 2



**Supplemental figure 2. Kaplan Meier curves of TCGA PDAC cohort based on expression levels of 11 shared DE genes** Kaplan Meier curves show statistically significant differences in survival time between tumors showing low and high quartile expression of indicated DE genes upregulated in invasive organoids ( $p < 0.05$ ).

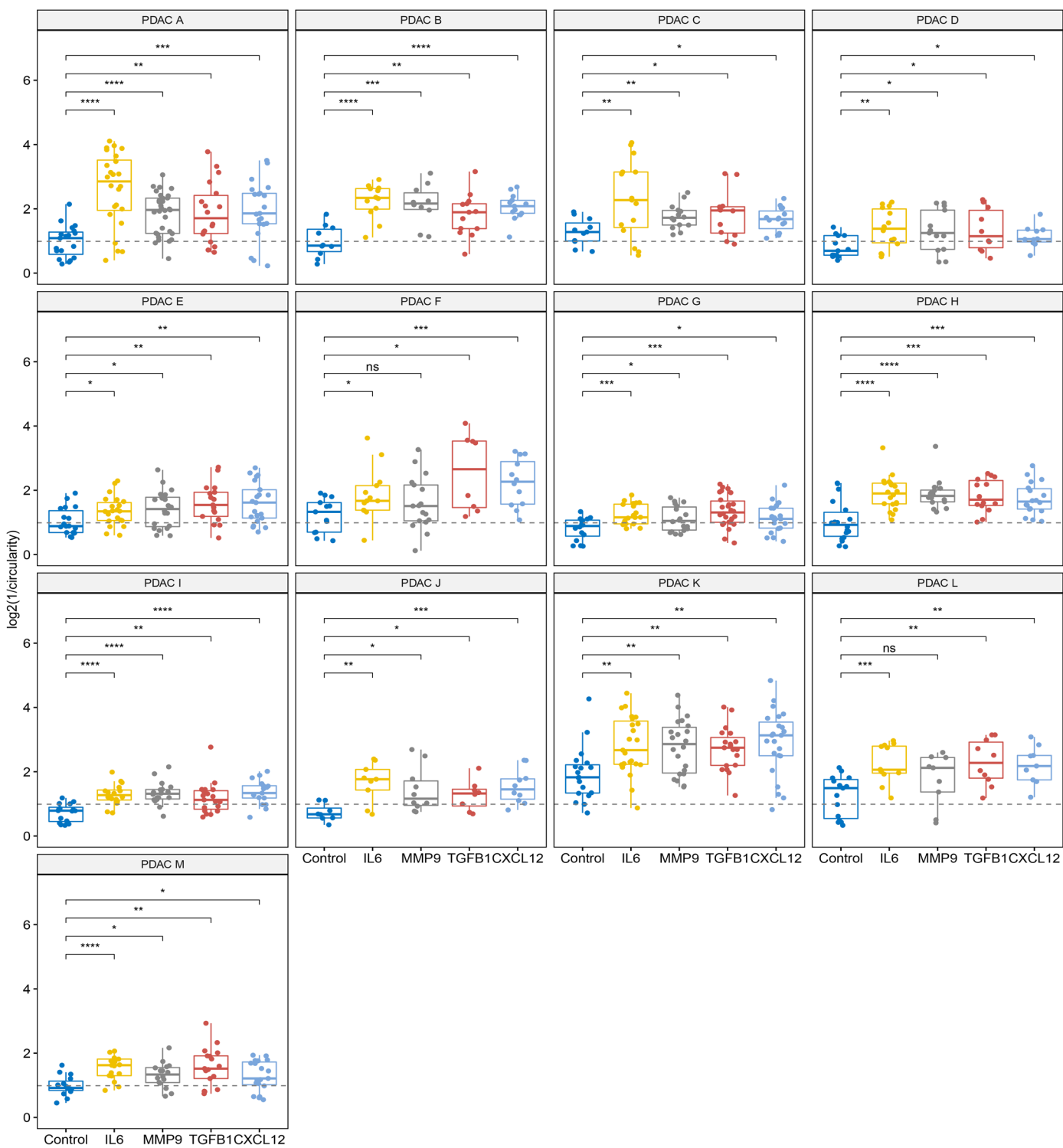
Supplemental figure 3



### **Supplemental figure 3 - OLR1 Immunofluorescence assay on PDAC**

**organoids and tissue section** (A) A bar plot of OLR1 mRNA expression in indicated organoid groups. (B) Immunofluorescence images of Pan-CK, OLR1 and DAPI staining in primary PDAC tissue sections. Scale bar: 50µm (C) Phase and immunofluorescence images of Pan-CK, OLR1 and DAPI staining in invasive and non-invasive organoids. Scale bars: 50µm

Supplemental figure 4



**Supplemental figure 4 – Inverse circularity of PDAC organoid cultures after ligand treatment.** Organoid invasion ( $\log_2(1/\text{circularity})$ ) analysis for control and ligand-treated cultures from twelve PDACs. Organoids derived from each PDAC are shown separately, with cultures labeled as A to M. One PDAC produced organoids with both invasive phenotypes; each phenotype from this culture was analyzed separately in graph K (collective) and graph L (mesenchymal) (ns>0.05, \*≤0.05, \*\*≤0.01, \*\*\*≤0.001, \*\*\*\*≤0.0001, Mann-Whitney U test).