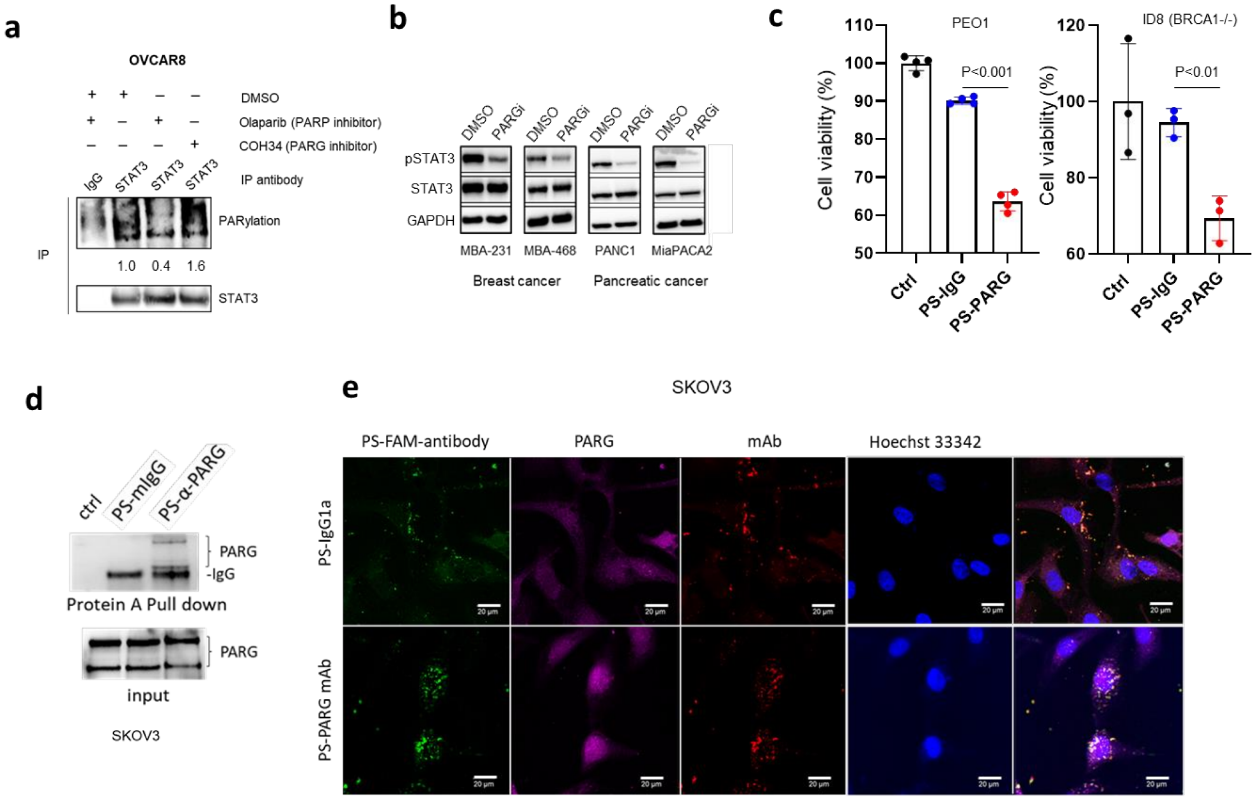
SUPPLEMENTARY FIGURES

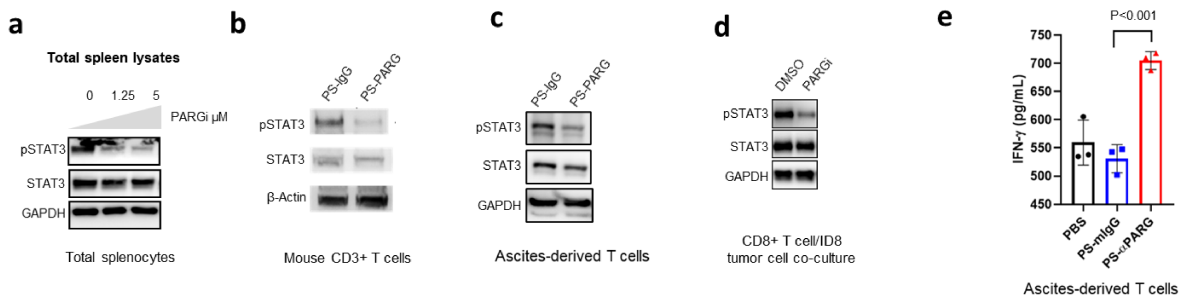
Supplementary Figure 1



Supplementary Figure 1: PARG inhibition reduces STAT3 activity in tumor cells. a. OVCAR8 ovarian cancer cells whole cell lysates were immunoprecipitated with anti-STAT3 antibody and endogenous PARG along with poly(ADP-ribosyl)ated STAT3 proteins were detected by immunoblotting with indicated antibodies. The protein levels of PAR shown under immunoblotting images were quantified by band intensity using ImageJ software and normalized with the levels of total STAT3. **b**. Immunoblotting analysis of pSTAT3 in indicated TNBC breast and pancreatic cancer cells following 24h PARGi treatment. **c**. Cell viability analysis of indicated ovarian cancer cells cultured with 1.56 µM of PS-IgG or PARG antibody with for 5 d. **d.** SKOV3 ovarian cancer cells were treated with either control or PARG cell-penetrating

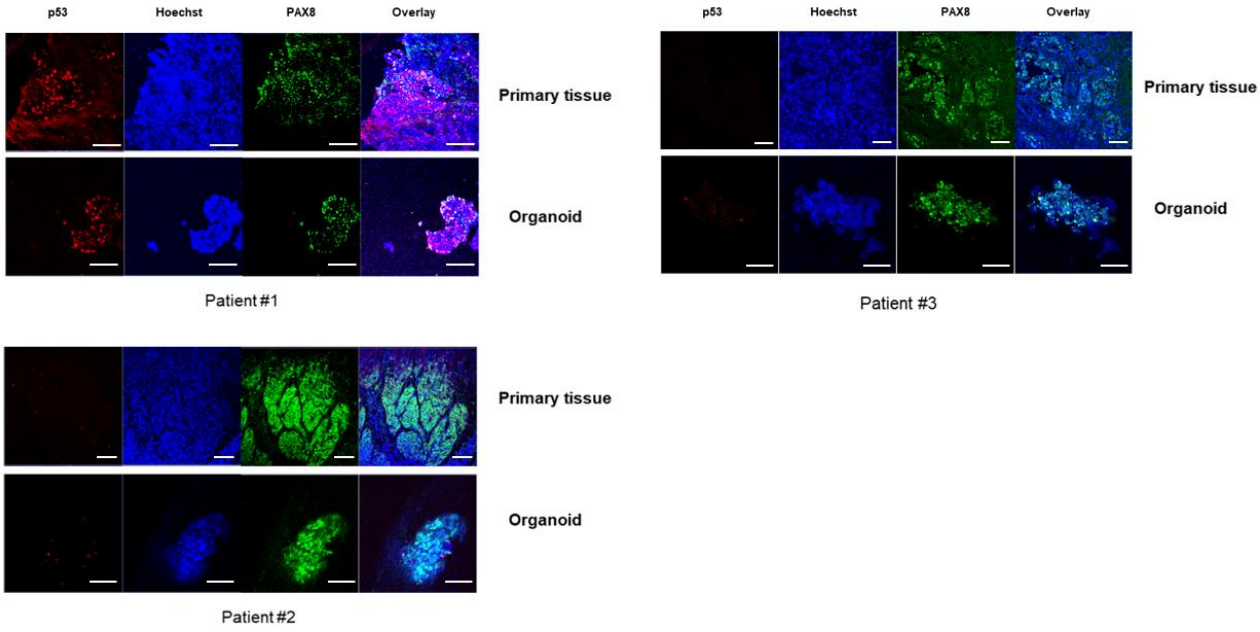
antibodies and protein A pull-down assay was performed to detect bound endogenous PARG proteins. **e.** The subcellular localization of PS-PARG antibody and PS-control antibody, relative to PARG (detected by an anti-PARG antibody), nucleus (Hoechst 33342 staining) was visualized by immunofluorescence and confocal microscopy. 0.14 µM of PS-conjugated antibodies were incubated with SKOV3 cells for 1 h. The scale bars represent 20 µm.

Supplementary Figure 2



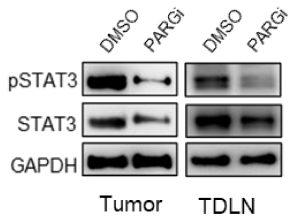
Supplementary Figure 2: PARG inhibition decreases basal pSTAT3 in immune cells and stimulates immune activation in vitro. a. Mouse splenic cells were incubated with 1-5μM PARGi overnight and changes in pSTAT3 after were assessed by immunoblotting**. b.** Mouse splenic CD3+ T cells were incubated with either control PS-IgG or PS-PARG antibody for 24h and changes in pSTAT3 were analyzed by immunoblotting. **c**. Ovarian cancer patient ascites-derived T cells were treated either with PS-IgG or PS-PARG cell-penetrating antibodies and pSTAT3 was measured by immunoblotting. **d**. Immunoblotting analysis of CD8+ T cell/ID8 co-culture after 24h treatment with either DMSO or PARGi **e.** The supernatant from the treated ascites-derived T cells were subject to ELISA for IFNγ expression.

Supplementary Figure 3



Supplementary Figure 3: Ovarian ALI-PDTO organoids retained PAX8 and p53 expression status as observed for their corresponding tumor tissue. Histological comparison of ovarian cancer patient-derived organoids from three different HGSOC patients and their corresponding primary tumor tissue. Top and bottom panels show p53 and PAX8 staining of primary tumor tissue and ALI-cultured organoids prior to drug and antibody treatment. The scale bars represent 100 µm.

Supplementary Figure 4



Supplementary Figure 4: In vivo PARG inhibition reduces pSTAT3 levels in tumors and tumor-draining lymph nodes. Whole cell lysates were prepared from mice tumors and tumor-draining lymph nodes (TDLN), as described in figure 5A. Total STAT3 and pSTAT3 levels were analyzed by immunoblotting.