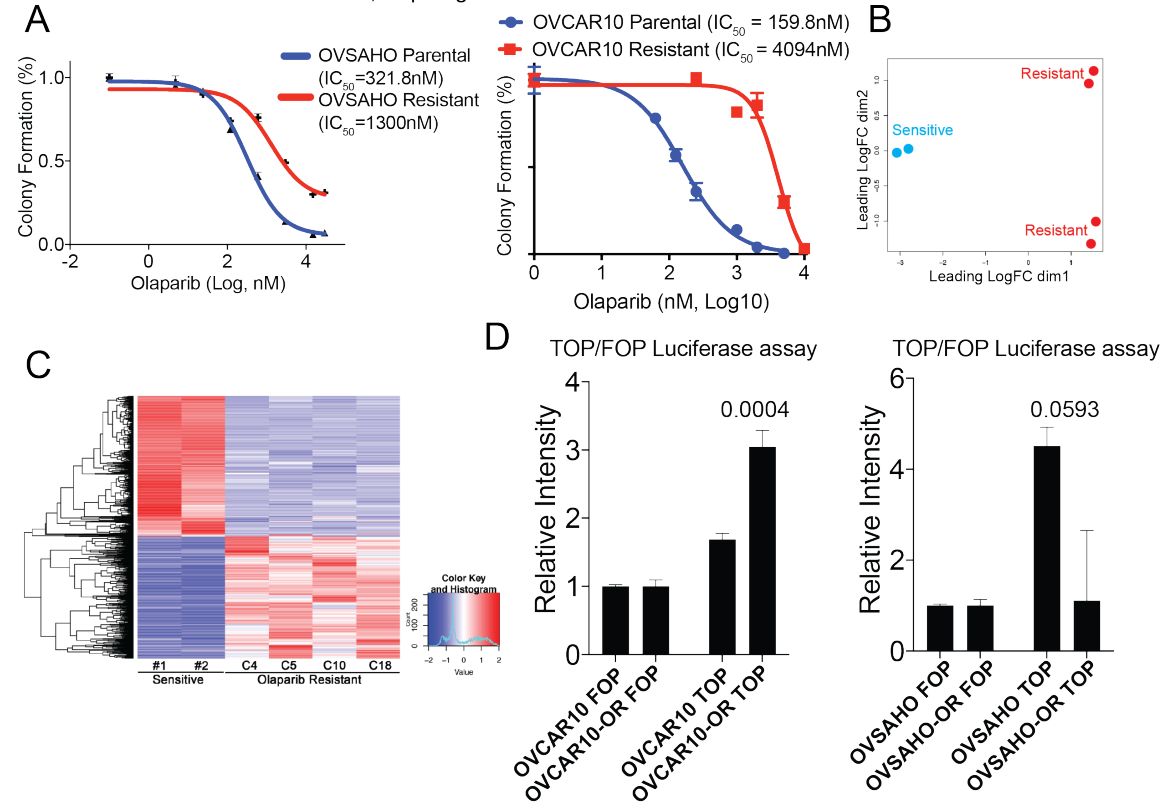


Supplementary Materials and Methods

Immunofluorescence. Immunofluorescence was performed by fixing samples in 4% paraformaldehyde and permeabilizing with 0.5% Triton-X. Samples were incubated with primary antibodies for 2 hours at room temperature, highly cross absorbed secondary antibodies (Invitrogen) for 1 hour at room temperature and mounted with prolong anti-fade reagent (Invitrogen). Immunostained cells were imaged using an Olympus FV1000 confocal microscope.

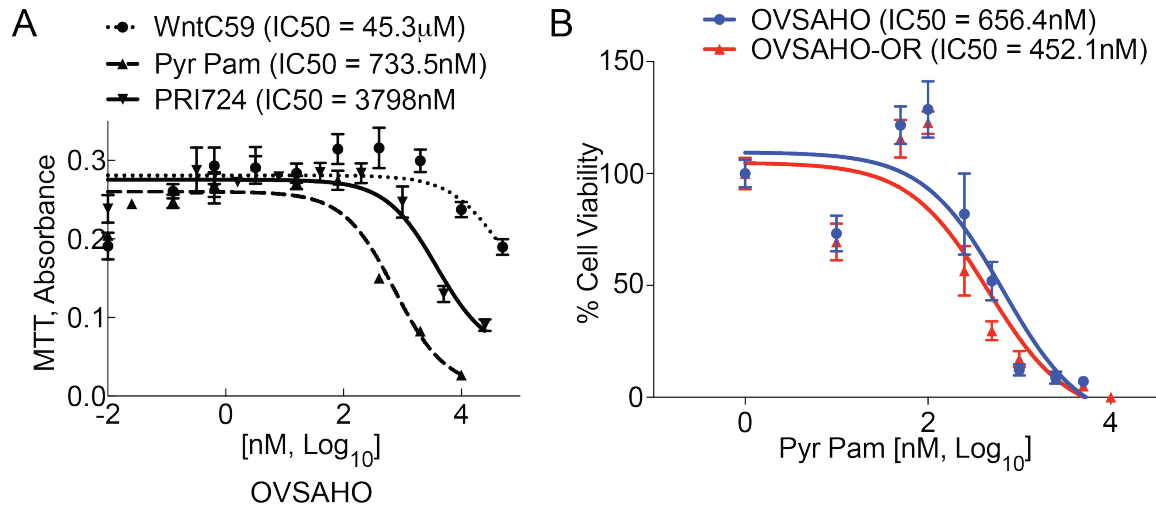
Supplementary Figures

Yamamoto and McMellen et al 2018, Sup. Fig. 1

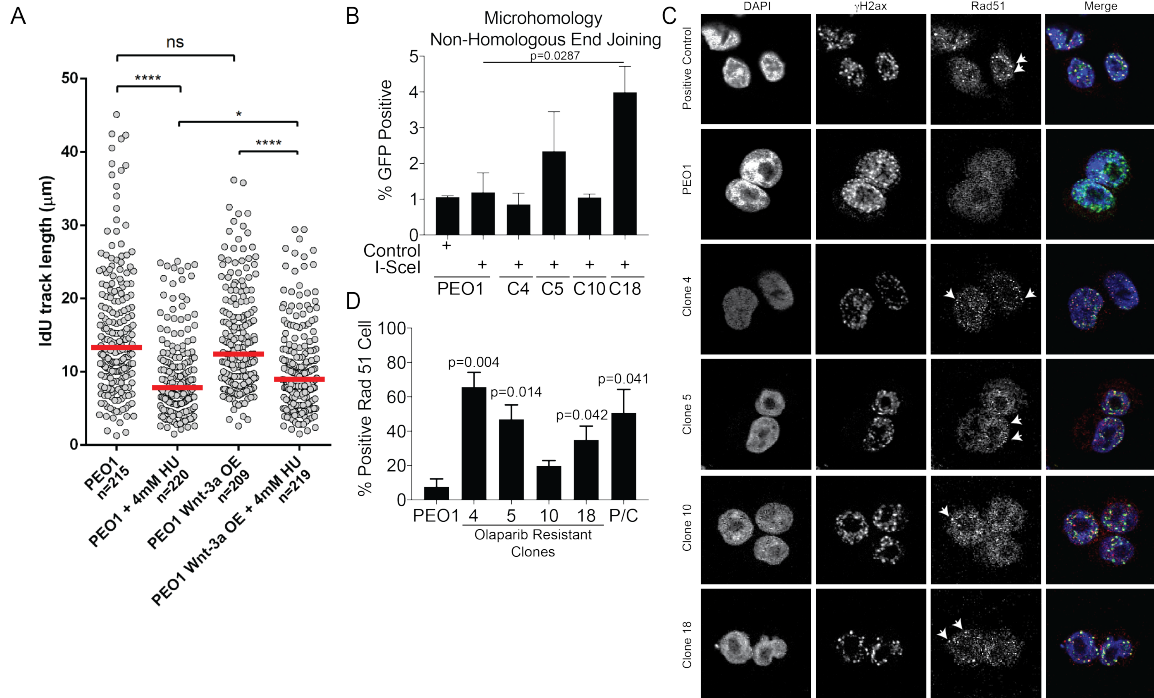


Supplementary Figure 1. Olaparib resistant and RNA-sequencing quality control.

A) HGSOC OVSCHO or OVCAR10 cells were treated in a step-wise fashion with olaparib to establish olaparib resistant cells (OVSCHO-OR and OVCAR10-OR). Confirmation of resistance confirmed via colony formation and crystal violet staining. **B)** Principal component analysis of RNA-sequencing from PEO1 sensitive (n=2) and four independent resistant clonal populations (n=4). **C)** Hierarchical clustering of RNA-sequencing. **D)** OVCAR10, OVCAR10-OR, OVSCHO, and OVSCHO-OR were transfected with TOP/FOP-FLASH and incubated for 72hrs. Luciferase activity was measured. Experiments performed in triplicate. Error bars = SEM.



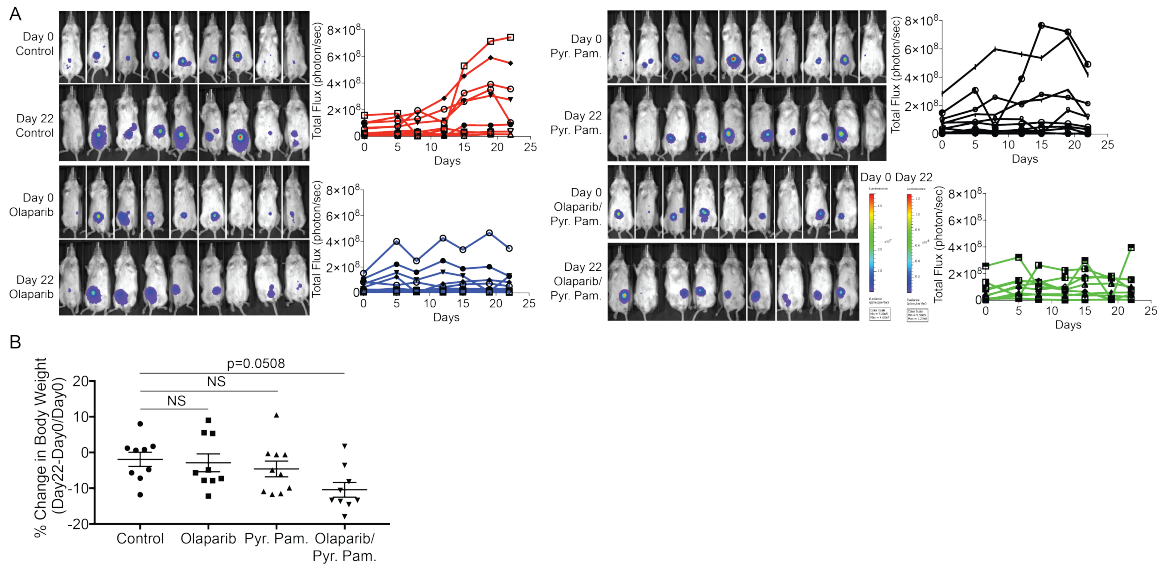
Supplementary Figure 2. Pyr. Pam. inhibits cell viability and TCF transcriptional activity. A) OVSAHO (TP53 and BRCA2-mutated) cells were treated with increasing doses of three different Wnt inhibitors (Wnt-C59, Pyr. Pam., and PRI724). Cells were treated for 48hrs and a MTT assay was used to examine changes in cell viability. IC₅₀ values indicated for each inhibitor. **B)** OVSAHO and OVSAHO-OR were incubated with increasing doses of Pyr. Pam. and a MTT assay was used to examine changes in cell viability. IC₅₀ values indicated. Experiments performed in triplicate. Statistical test used to calculate p-values, unpaired two tailed t-test. Error bars = SEM.



Supplementary Figure 3. WNT3A overexpression partially inhibits replication fork stability and DNA damage repair is rescued in olaparib resistant cells. **A)** PEO1 and PEO1-WNT3A cells were pulsed with 2'-deoxy-5-iodouridine (IdU) for 30 minutes, followed by 4mM hydroxyurea (HU) for 3 hours to promote replication fork stalling, washed, and pulsed with 5-chloro-2'-deoxyuridine (CIdU) for 30 minutes. DNA fibers were obtained using the FiberPrep kit and stretched on glass slides using the FiberComb Molecular Combing instrument (Genomic Vision). The length of IdU tracks occurring adjacent to CIdU tracks were measured to assess replication fork degradation. **B)** Two-plasmid functional assay performed to assess distal non-homologous end joining. PEO1 sensitive and PEO1-OR clones were stably transfected with EJ2GFP and subsequently transfected with I-SceI restriction enzyme. After 72 hours transfected cells were collected and examined via a flow cytometer to quantify GFP positive cells. Statistical test used to calculate p-value, ANOVA. **C)** TOV-21G (Positive control), PEO1, and four PEO1-OR clonal populations were examined for Rad51 via

immunofluorescence following irradiation. Percentage of Rad51 positive cells based on total nuclei (n=200 per cell population). **D)** Same as C, quantification of percent Rad51 positive cells. Statistical test used to calculate p-value, ANOVA.

Sup. Fig. 4, Yamamoto and McMellen et al. 2018



Supplementary Figure 4. Olaparib and Pyr. Pam. inhibits tumor growth. A)

GFP/luciferase PEO1-Wnt3a cells were injected into the intraperitoneal cavity of immunocompromised mice. Tumors were allowed to establish for 4 weeks. Mice were imaged and were randomized based in luminescence intensity on Day 0 and images shown. Mice were treated daily for 21 days with vehicle control (n=9), olaparib (n= 9, 50mg/kg), Pyr. Pam. (n= 10, 0.5mg/kg)and olaparib/Pyr. Pam. (n=9, 0.5mg/kg). Mice were imaged twice a week. Mice were imaged and sacrificed on Day 22 and image shown. All of the luminescence data shown for individual mice from each group. **B)**

Percentage body weight change from Day 0 and 22. Statistical test used to calculate p-value, ANOVA.

Table with multiple columns containing alphanumeric codes and numerical values. The table is organized into sections with headers like 'Z12PHC+4', 'Z12PHC+4', etc., and contains a dense grid of data points.

Sup. Table 2. Wnt inhibitors in PEO1 and OVSAHO cells

<u>Inhibitor Name</u>	<u>Target</u>	<u>PEO1 IC50 [nM]</u>	<u>OVSAHO IC50 [nM]</u>
Pyruvium Pamoate	β -catenin, AKT	370.7	733.5
PRI724	β -catenin/CBP	852	3798
WntC59	Porcupine	>50000	45140

Sup. Table 3. Primers.

PRIMERS	SEQUENCE
FOSL1 forward	CTTGTGAACAGATCAGCCCGGA
FOSL1 reverse	GTCGGTCAGTTCCTTCCTCC
CCND1 forward	GATCAAGTGTGACCCGGACTG
CCND1 reverse	CCTTGGGGTCCATGTTCTGC
WNT3A forward	ATGGTGTCTCGGGAGTT
WNT3A reverse	TGGCACTTGCACTTGAG
WNT5A forward	CATGAACCTGCACAACAACGA
WNT5A reverse	GGCACTTGCAAGCCACAT
WNT7B forward	TCATGCACAGAACTTTCGCA
WNT7B reverse	GATGACAGTGCTCCGAGCTTC
SFRP1 forward	GAGACTTCTGTTCTGGGGGCCGAG
SFRP1 reverse	CCCGATGCCCATGCCGGCTCT
GAPDH forward	GTCTCCTCTGACTTCAACAGCG
GAPDH reverse	ACCACCCTGTTGCTGTAGCCAA
18S forward	AACTTTCGATGGTAGTCGCCG
18S reverse	CCTTGGATGTGGTAGCCGTTT
B2M forward	GGCATTCTGAAGCTGACA
B2M reverse	CTTCAATGTGGATGGATGAAAC