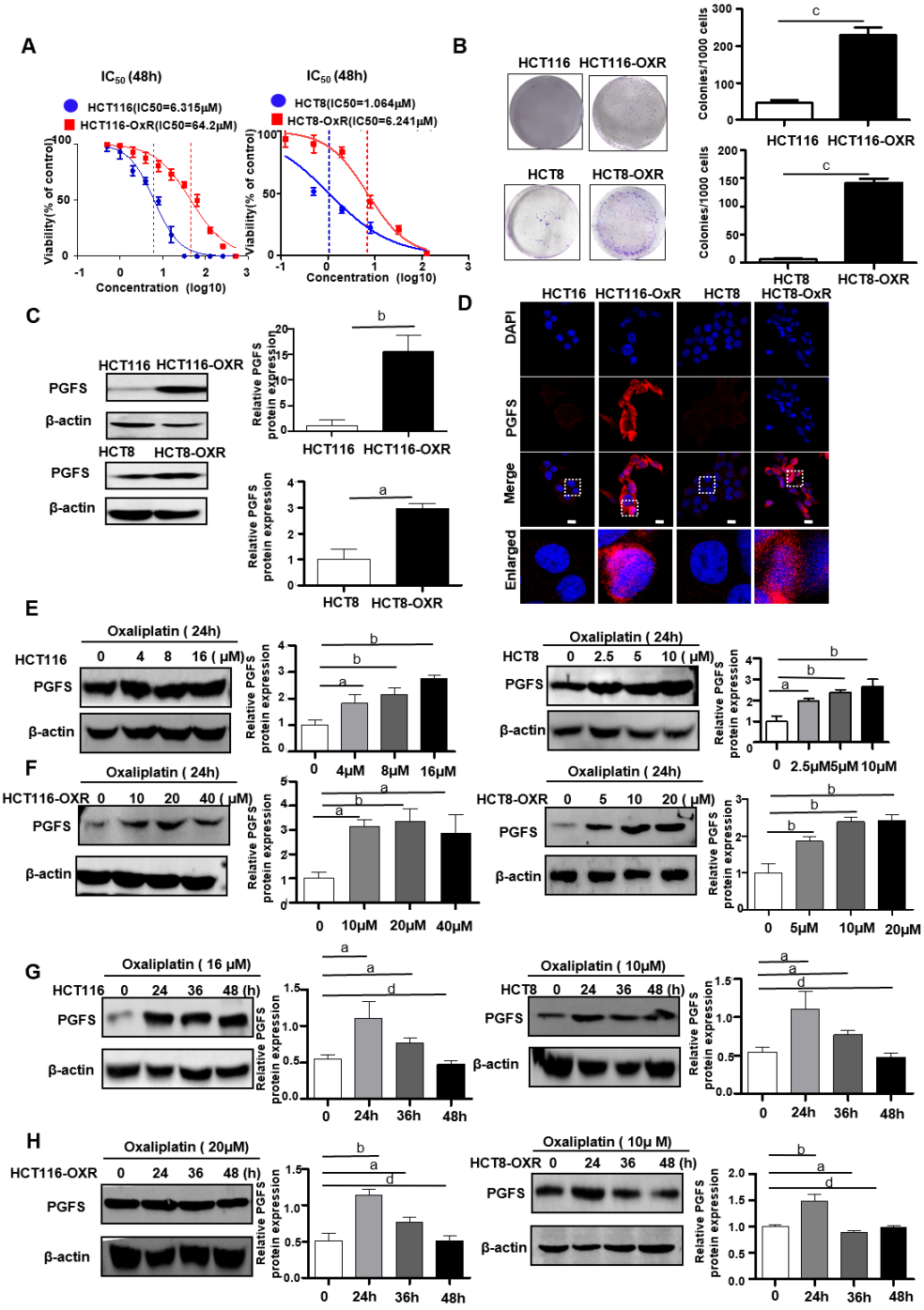
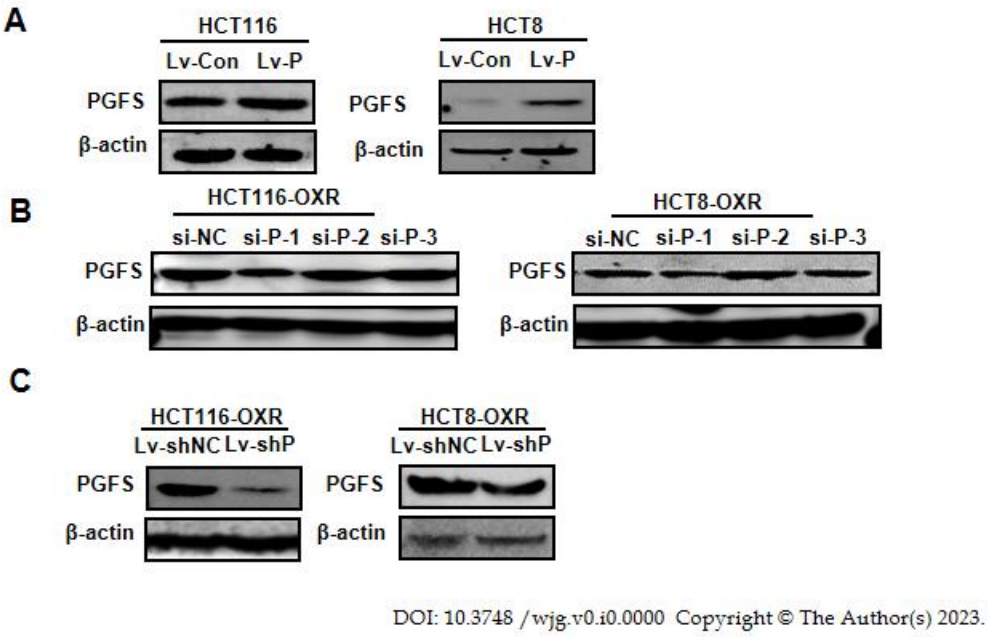


Supplementary Figure 1 Evaluation of the sensitivity of colorectal cancer cells to oxaliplatin. A: The half-inhibitory concentration values of oxaliplatin in the parent and drug-resistant colorectal cancer (CRC) cells were detected by the cell counting kit-8 assay; B: Plate colony formation assay in the parent and drug-resistant CRC cells; C and D: Prostaglandin $F_{2\alpha}$ synthase (PGFS) expression in parent and drug-resistant cells was detected using western blot and immunofluorescence (scale bar, 10 μm); E-H: Western blot analysis shows the PGFS expressions in CRC cells treated with oxaliplatin at different concentrations and different incubation times. $^{a}P < 0.05$, $^{b}P < 0.01$, $^{c}P < 0.001$,

[d]*P* No significance. PGFS: Prostaglandin $F_{2\alpha}$ synthase; IC_{50}: half-inhibitory concentration.



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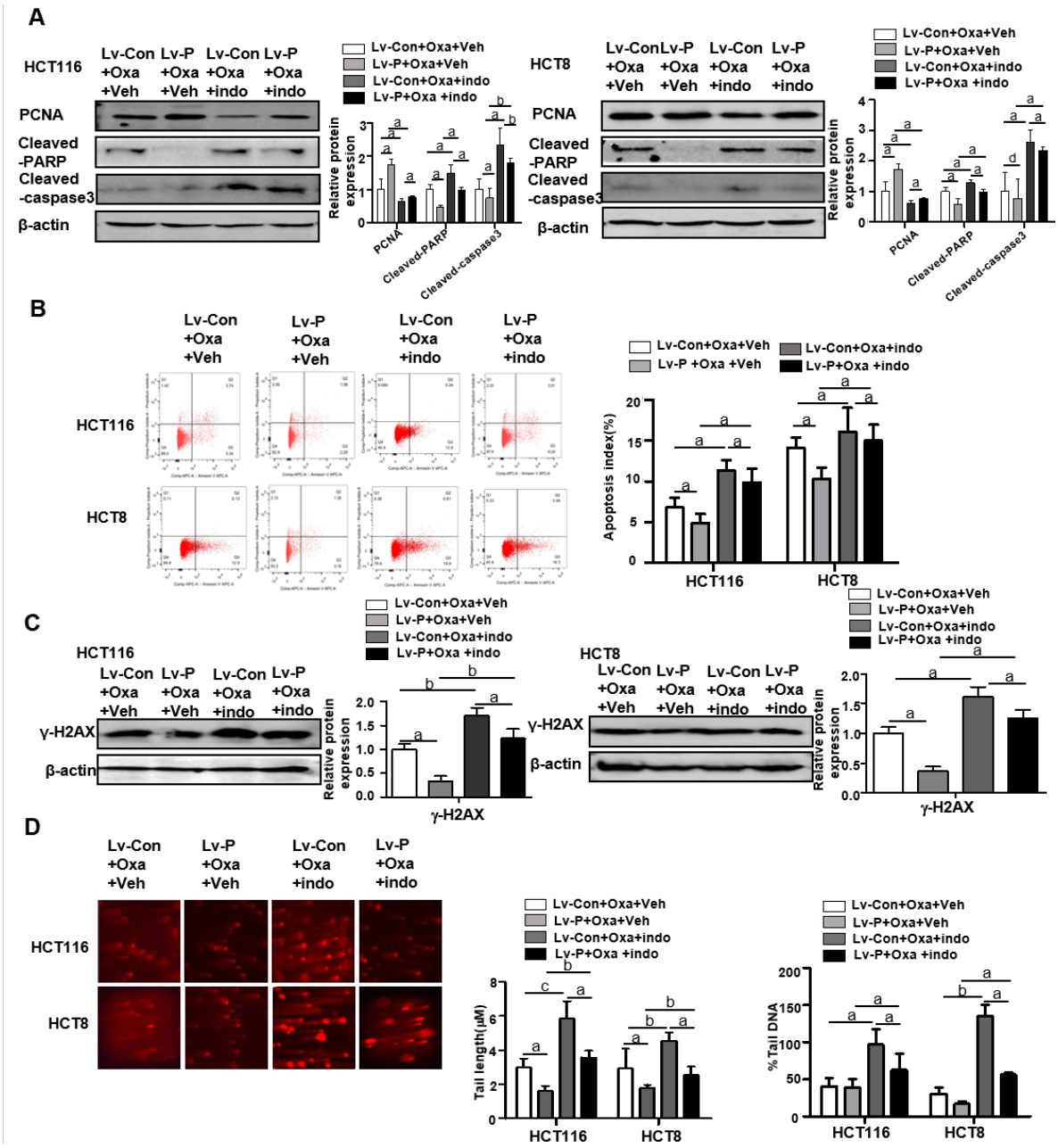
Supplementary Figure 2 Overexpression or knockdown of prostaglandin $F_{2\alpha}$ synthase was confirmed. A: The overexpression efficiency of prostaglandin $F_{2\alpha}$ synthase (PGFS) in HCT116 and HCT8 cells was confirmed using western blot; B: PGFS knockdown with small interfering RNAs was confirmed by immunoblotting; C: Lentiviral short hairpin RNA-mediated knockdown of PGFS was confirmed by western blot in HCT116-OxR and HCT8-OxR cells. PGFS: Prostaglandin $F_{2\alpha}$ synthase.



Supplementary Figure 3 The inhibitor indomethacin suppressed the effect of Prostaglandin $F_{2\alpha}$ synthase in oxaliplatin-resistance. A: Western blot analysis showed the levels of proliferating cell nuclear antigen, cleaved-poly ADP-ribose polymerase, and cleaved-caspase 3 in HCT116 and HCT8 cells; B: The apoptosis analysis was conducted using flow cytometry in HCT116 and HCT8 cells; C: The cleavage of γ-H2A histone family member X protein expressions was assessed using western blot in HCT116 and HCT8 cells; D: DNA damage effects were evaluated using the comet assay (scale bar 50 μm). $^{a}P < 0.05$, $^{b}P < 0.01$, $^{c}P < 0.001$, ^{d}P No significance. PCNA: Proliferating

cell nuclear antigen; γ-H2AX: γ-H2A histone family member X; PARP: Poly ADP-ribose polymerase; Oxa: Oxaliplatin.