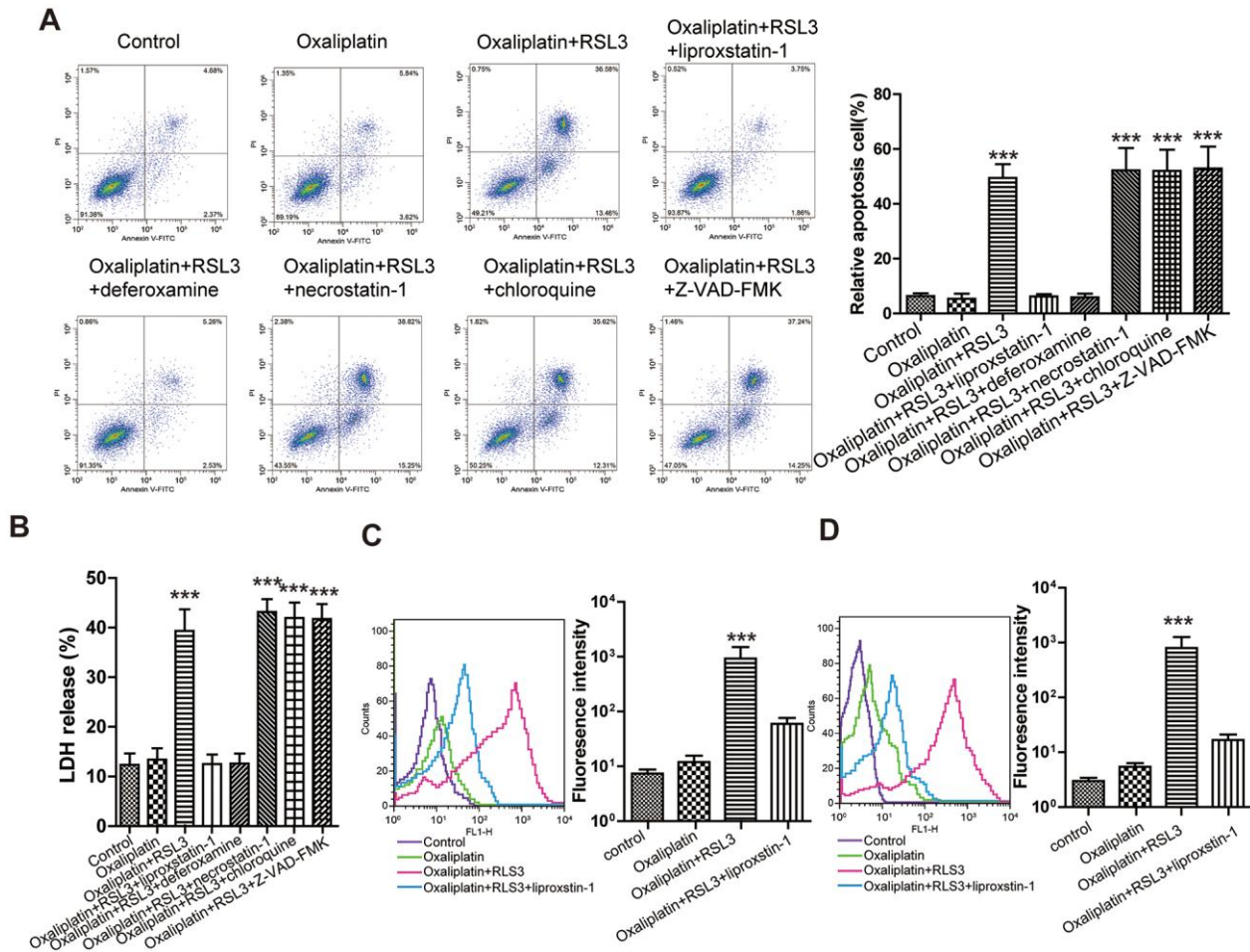
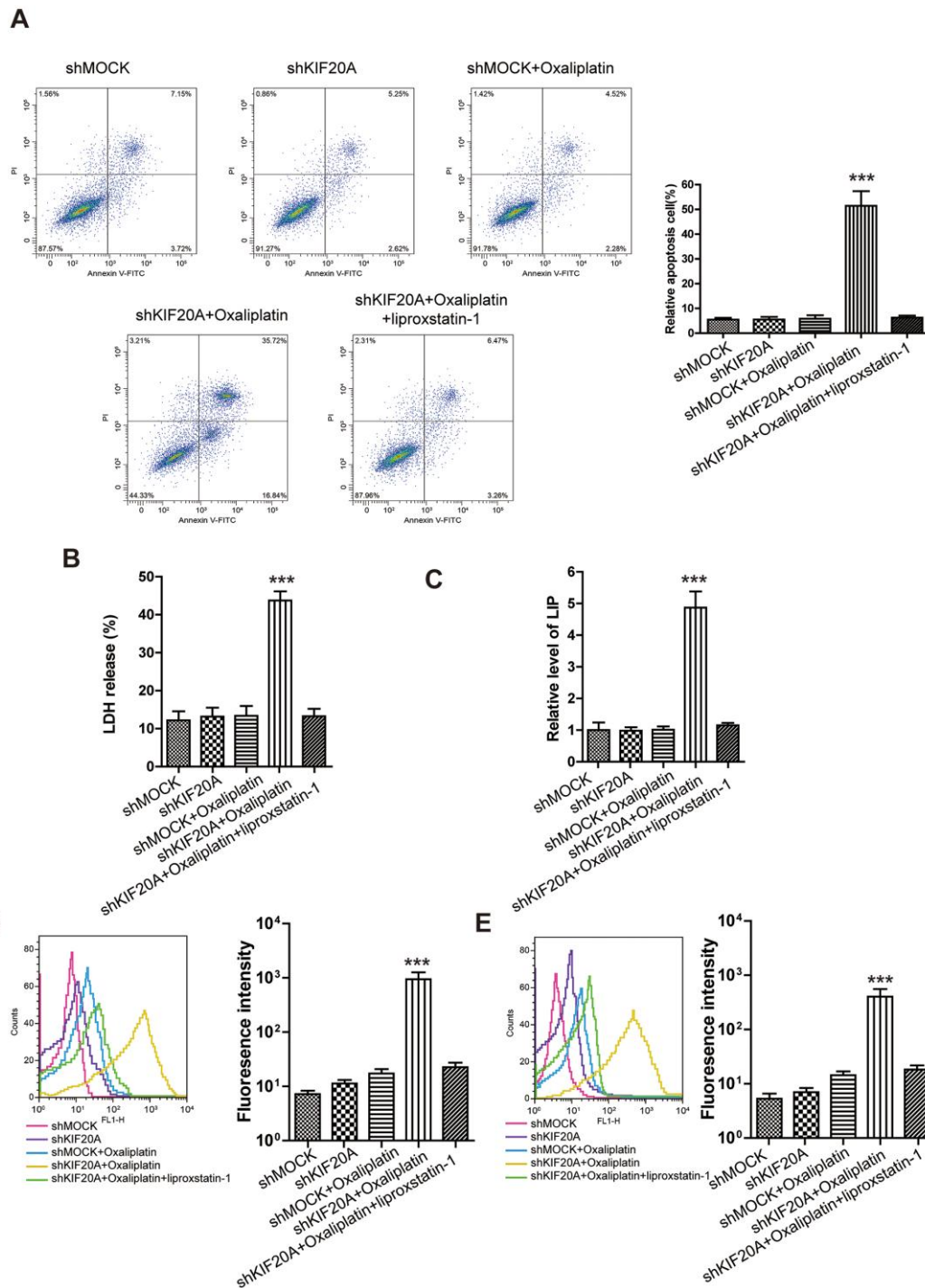


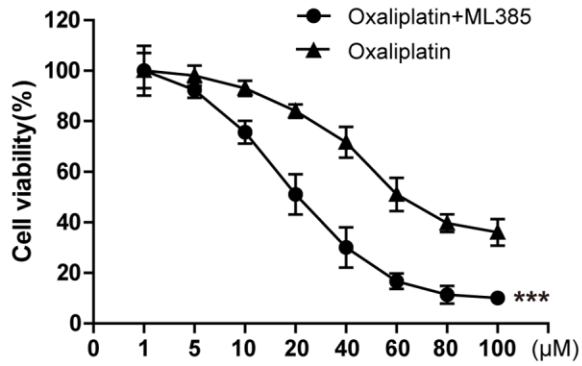
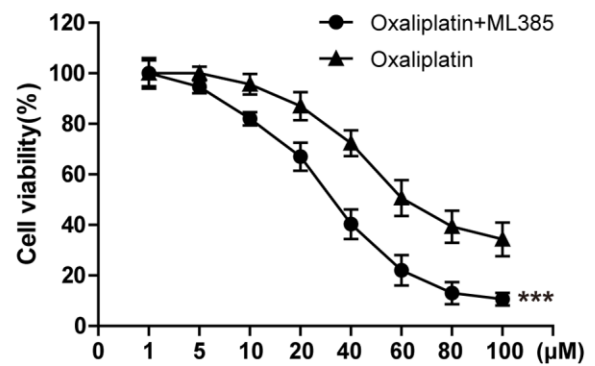
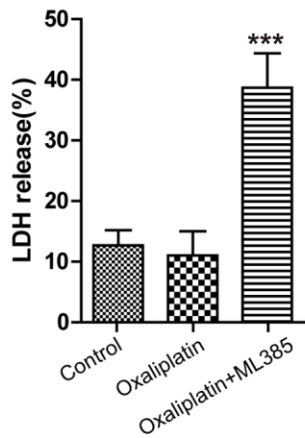
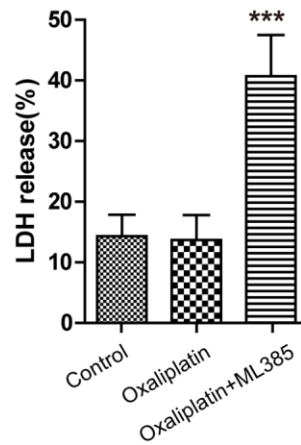
SUPPLEMENTARY FIGURES



Supplementary Figure 1. Inducing ferroptosis enhanced the sensitivity of CRC to Oxaliplatin. (A) Cell death was assessed by flow cytometry (annexin V-FITC/PI staining) to observe whether RSL3 with or without the indicated inhibitors would affect the lethal effect of oxaliplatin on H716 cells *in vitro*. Left, representative results of annexin V-FITC/PI staining. Right, quantitative analysis. The data are presented as the mean ± SD, ***p < 0.001 (versus Oxaliplatin). (B) Cell death was assessed by LDH release assay to observe whether RSL3 with or without the indicated inhibitors would affect the lethal effect of oxaliplatin on H716 cells *in vitro*. The data are presented as the mean ± SD, ***p < 0.001 (versus Oxaliplatin). (C, D) The cellular level of ROS (C) and lipid peroxidation (D) was assessed by flow cytometry to observe whether RSL3 with or without liproxstatin-1 would affect the oxidative damage induction of oxaliplatin on H716 cells. The data are presented as the mean ± SD, ***p < 0.001 (versus Oxaliplatin).



Supplementary Figure 2. High KIF20A expression in resistant CRC cell line suppressed the intracellular ferroptosis process. (A) Cell (H716) death was assessed by flow cytometry (annexin V-FITC/PI staining) to observe whether KIF20A silencing with or without liproxstatin-1 would affect the lethal effect of oxaliplatin on H716 cells *in vitro*. Left, representative results of annexin V-FITC/PI staining. Right, quantitative analysis. The data are presented as the mean \pm SD, *** p < 0.001 (versus shMOCK+Oxaliplatin). (B) Cell (H716) death was assessed by LDH release assay to observe whether KIF20A silencing with or without liproxstatin-1 would affect the lethal effect of oxaliplatin on colorectal cancer *in vitro*. The data are presented as the mean \pm SD, *** p < 0.001 (versus shMOCK+Oxaliplatin). (C) The cellular LIP was analyzed with a flow cytometer to observe whether KIF20A silencing with or without liproxstatin-1 would affect the LIP induction of oxaliplatin on H716 cells. The data are presented as the mean \pm SD, *** p < 0.001 (versus shMOCK+Oxaliplatin). (D, E) The cellular level of ROS (D) and lipid peroxidation (E) was assessed by flow cytometry to observe whether KIF20A silencing with or without liproxstatin-1 would affect the oxidative damage induction of oxaliplatin on H716 cells. The data are presented as the mean \pm SD, *** p < 0.001 (versus shMOCK+Oxaliplatin).

A**B****C****D**

Supplementary Figure 3. The sensitivities of HCT116-Or and H716 to Oxaliplatin could be induced by the application of ML385. (A, B) The cell (HCT116-Or (A) and H716 (B)) viability was measured to observe whether ML385 would affect the suppression of oxaliplatin on resistant cancer cells *in vitro*. The data are presented as the mean \pm SD, *** p < 0.001 (versus Oxaliplatin). (C, D) Cell death was assessed by LDH release assay to observe whether ML385 would affect the lethal effect of oxaliplatin on resistant cancer cells (HCT116-Or (C) and H716 (D)) *in vitro*. The data are presented as the mean \pm SD, *** p < 0.001 (versus Oxaliplatin).