Figure legends for supplemental materials:

Fig. S1. MLN4924 induces accumulation of CDT1 and WEE1: Cells were treated with MLN4924 at 100 nM for 6 or 12 hrs, followed by IB with β-actin as loading control.

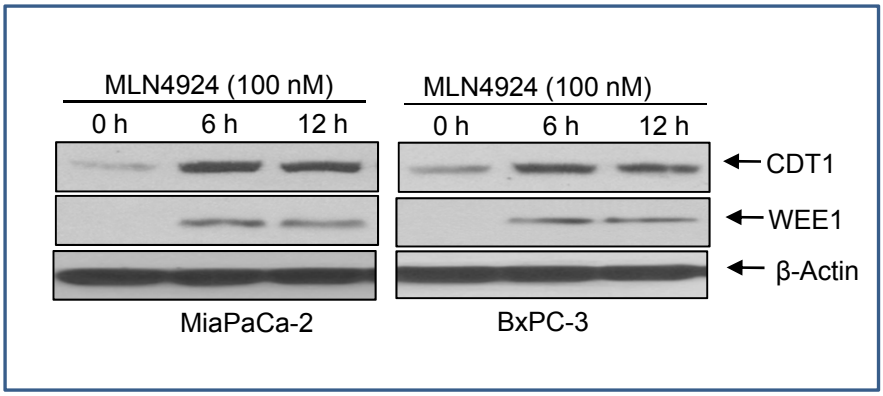
Fig. S2. MLN4924 inhibits cullin-1 neddylation and sensitizes pancreatic cancer cells to radiation: (**A**) Cells were treated with MLN4924 at 20 nM (for MiaPaCa-2) or 25 nM (BxPC-3) for indicated time periods, followed by IB analysis. (**B**) Cells were seeded in 60-mm dish in duplicate and subjected to MLN4924 and radiation treatment as indicated. (**C**) MiaPaCa-2 cells were transfected with siRNA oligonucleotides targeting CDT1 or WEE1. Forty-eight hrs later, cells were plated for clonogenic assay. The colonies with more than 50 cells were counted after 6-11 days. Surviving fraction was calculated as the proportion of seeded cells following irradiation to form colonies relative to that of untreated cells (mean ± SEM, n = 3).

Fig. S3. MLN4924 inhibits cullin-1 neddylation, cell growth and survival and promotes radiosensitization, selectively in lung cancer cells: (**A**) Subconfluent cells were treated with MLN4924 (100 nM) for 24 hrs, followed by IB. (**B&C**) Cells were seeded in 96-well plates in triplicates (B) or 60-mm dishes in duplicates (C), and treated with various concentrations of MLN4924 for 72 hrs (B) or 7-9 days (C). Cells were then lysed for ATPlite assay (B, mean ± SEM, n = 3) or the colonies with more than 50 cells were counted (C, mean ± SEM, n = 3). (**D**) Radiosensitization by MLN4924: Cells were seeded in 60-mm dishes in duplicate and treated with MLN4924 and radiation as indicated. The colonies with more than 50 cells were counted after 9 days. Surviving fraction was calculated as the proportion of seeded cells following irradiation to form colonies relative to that of untreated cells (mean ± SEM, n = 3).

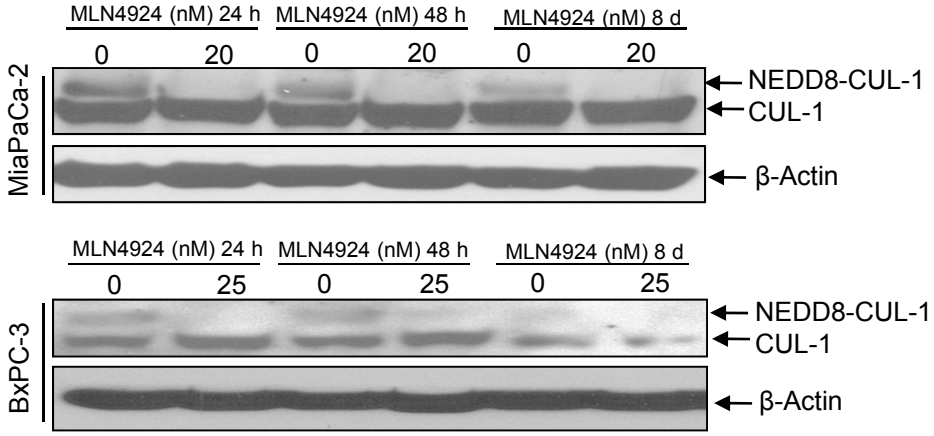
Fig. S4. MLN4924 induces DNA damage: Cells were treated with MLN4924 (100 nM) alone or in combination with radiation (6 Gy) for 24 hr, followed by IB analysis with β-actin as loading control.

Figure S5. Radiation-enhancing activity of MLN4924 is inhibited at least in part by siRNA knockdown of CDT1 or WEE1. MiaPaCa-2 cells were transfected with siRNA oligonucleotides targeting CDT1 or WEE1. Forty-eight hrs later, one portion of cells was subjected for IB analysis (**A**), the other portion was for FACS analysis (**B&C**), and still other portion was plated for clonogenic assay (**D**). Shown (B-D) is mean ± SD (n = 2).

Wei et al., Fig. S1



A



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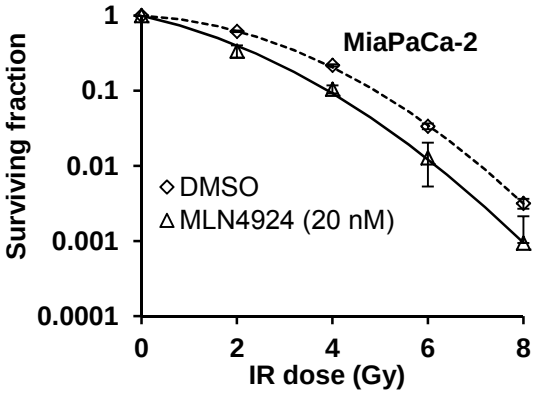
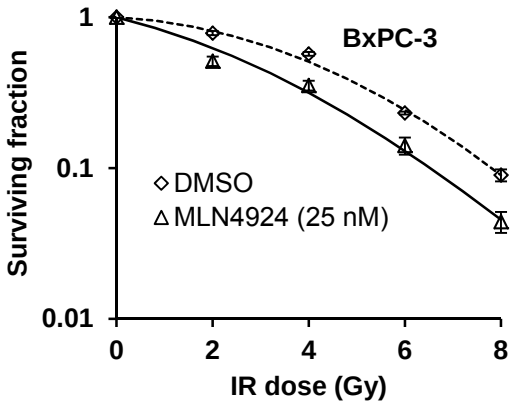
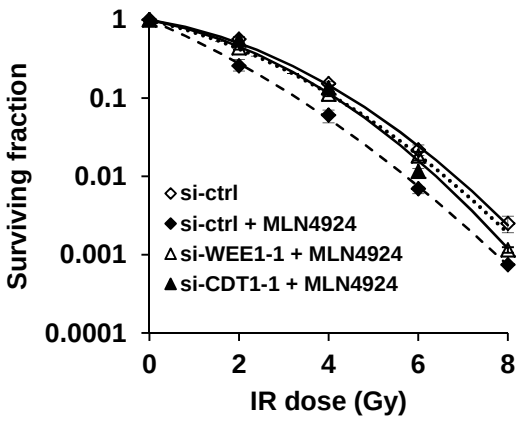


Treatment	SER	PE
DMSO	1	0.62 ± 0.03
MLN4924	1.43 ± 0.05	0.4 ± 0.07



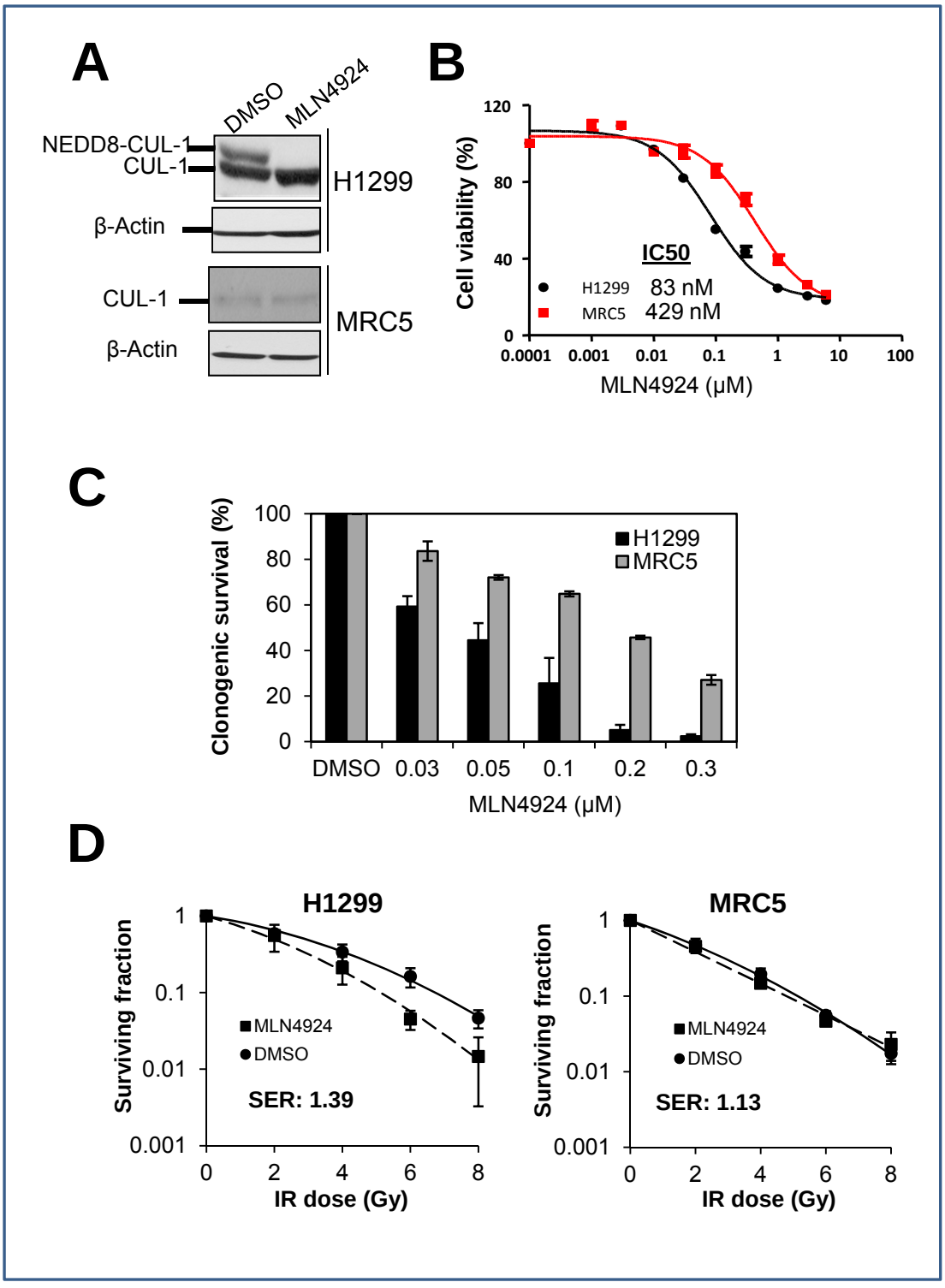
Treatment	SER	PE
DMSO	1	0.2 ± 0.03
MLN4924	1.36 ± 0.13	0.16 ± 0.01

C

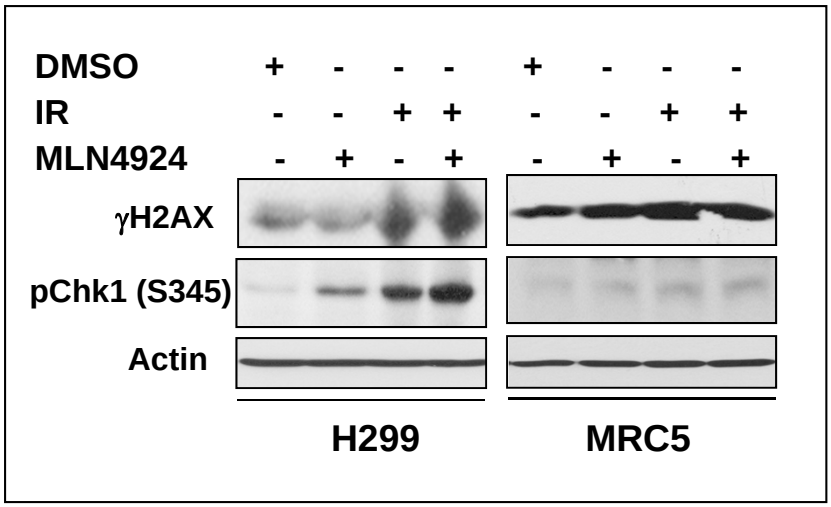


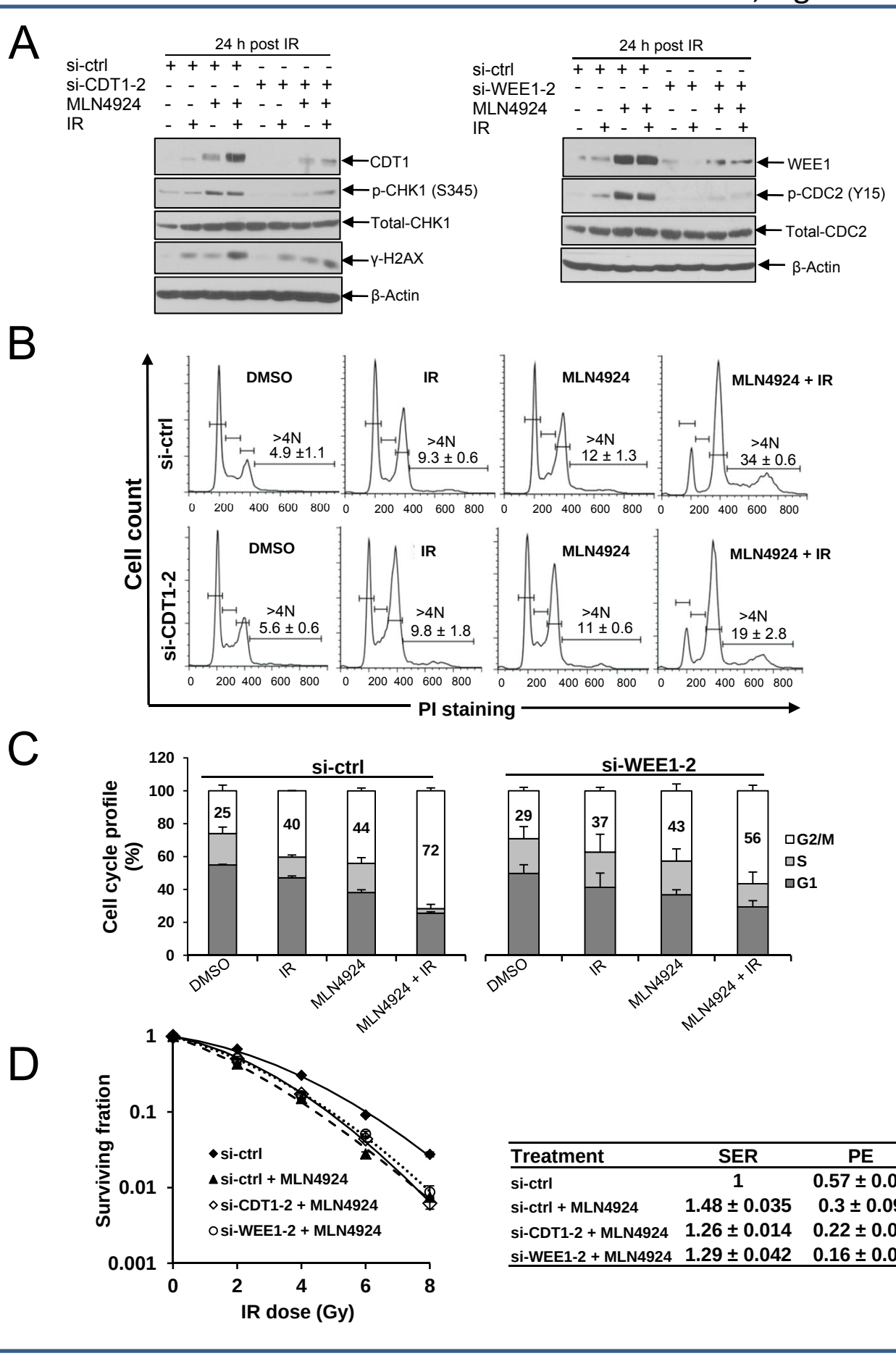
Treatment	SER	PE
si-ctrl	1	0.35 ± 0.03
si-ctrl + MLN4924	1.34 ± 0.07	0.29 ± 0.04
si-CDT1-2 + MLN4924	1.10 ± 0.02	0.11 ± 0.02
si-WEE1-2 + MLN4924	1.12 ± 0.04	0.13 ± 0.03

Wei et al., Fig. S3



Wei et al., Fig. S4





Treatment	SER	PE
si-ctrl	1	0.57 ± 0.03
si-ctrl + MLN4924	1.48 ± 0.035	0.3 ± 0.09
si-CDT1-2 + MLN4924	1.26 ± 0.014	0.22 ± 0.09
si-WEE1-2 + MLN4924	1.29 ± 0.042	0.16 ± 0.04

Supplemental Table 1.

Posterior estimates from the BHC model, with 90% high probability density (HPD) intervals.**

Treatment:	**Control**	**MLN4924**
Regression time (days)	No*	No
Growth rate	0.06 (0.04, 0.09)	0.06 (0.04, 0.09)
Treatment:	**IR**	**MLN4924+IR**
Regression time (days)	24 (21,27)	22 (14,31)
Nadir volume (mm^3)	71 (39,101)	24 (6,40) $^{\pi}$
Regression rate †	0.01 (0,0.02)	0.05 (0.01,0.09)$^{\pi}$
Regrowth rate‡	0.08 (0.06,0.09)	0.06 (0.04,0.08)

******BHC model using the WinBUGS code of Treat1.txt

*"No" means no tumor regression, that occurs when the lower bound of the 90% HPD interval of the regression period is less than 0.

†Regression rate is the number of times tumor halves per day, and its reciprocal is the tumor halving time.

‡Regrowth rate is the number of times tumor doubles per day, and its reciprocal is the tumor doubling time.

$^{\pi}$Statistically significant difference versus IR.