Supplemental Material

Supplemental Figure Legends

Figure S1. Nutlin inhibits γH2AX foci formation and prolongs resolution. (A) *p53*$^{-/-}$ and (B) *p53*$^{-/-}$*Mdm2*$^{-/-}$ MEFs were treated with Nutlin (10 μM) or vehicle control (DMSO). MEFs with ectopic Mdm2 overexpression served as a positive control. Following exposure to 5 Gy of γIR, MEFs were fixed at the indicated intervals and immunofluorescence for γH2AX was performed. DAPI was used to visualize the nucleus. Representative images are shown.

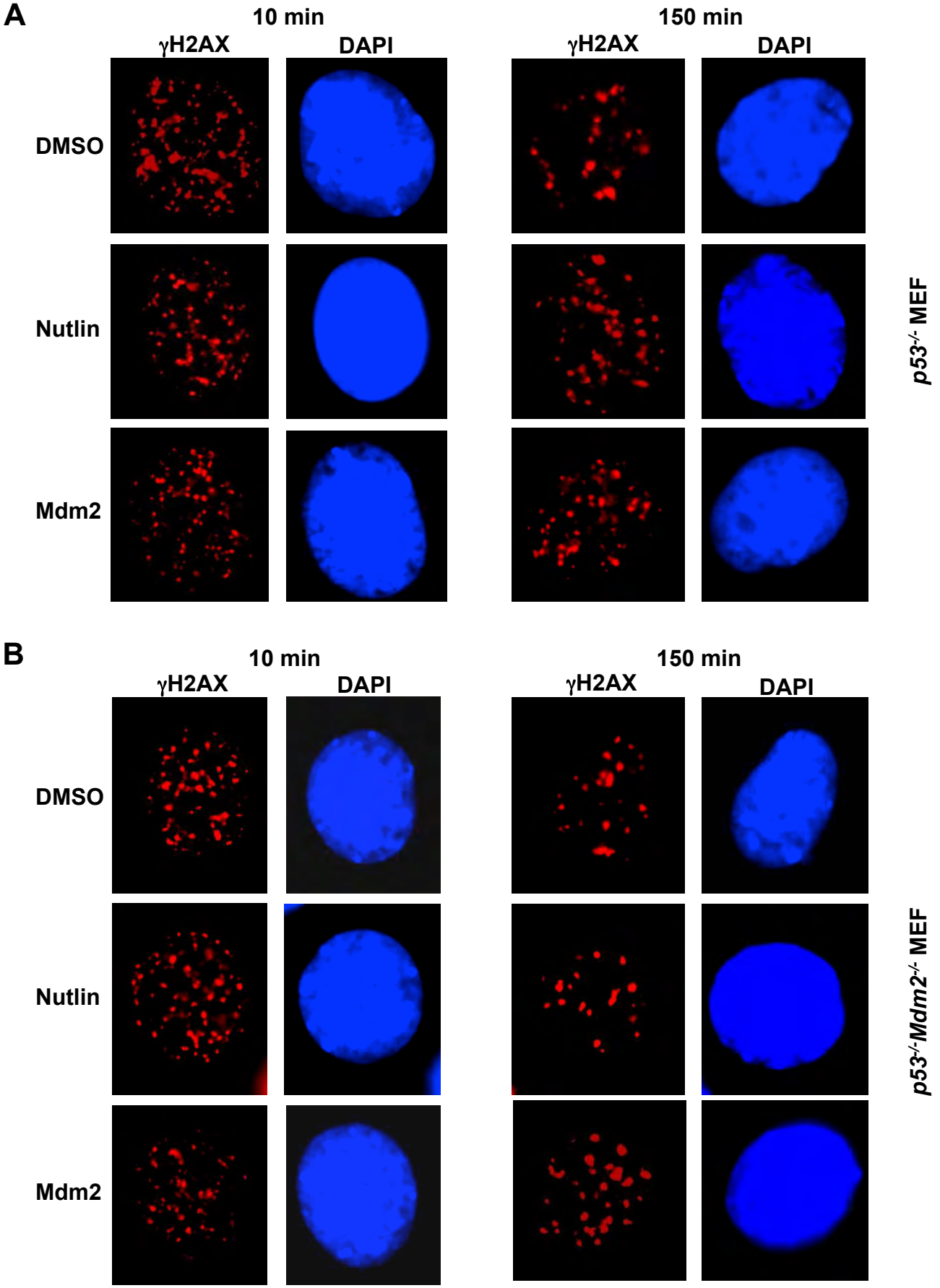
Figure S2. Inhibition of pS/TQ foci formation and resolution by Nutlin. (A) *p53*$^{-/-}$ and (B) *p53*$^{-/-}$*Mdm2*$^{-/-}$ MEFs were treated with Nutlin (10μM) or vehicle control (DMSO). MEFs with ectopic Mdm2 overexpression served as a positive control. Following exposure to 5 Gy of γIR, cells were fixed at the indicated intervals and immunofluorescence for pS/TQ was performed. DAPI was used to visualize the nucleus. Representative images are shown.

Figure S3. Nutlin inhibits γH2AX foci formation and resolution in ovarian cancer cells. SKOV-3 (A), OVCAR-5 (B) and OVCAR-8 (C) ovarian cancer cells were treated with Nutlin (10μM) or vehicle control (DMSO). Following exposure to 5 Gy of γIR, cells were fixed at the indicated intervals and immunofluorescence for γH2AX was performed. DAPI was used to visualize the nucleus. Representative images are shown.

Figure S4. Nutlin cooperates with genotoxic agents in p53-inactivated ovarian cancer cells. The indicated ovarian cancer cell lines were treated with the indicated drug(s) or vehicle control

(DMSO). Nutlin was always at 10 μM. Cisplatin (A) or etoposide (B) was at 1 or 10 μM. MTT assays were performed at intervals. Representative graphs of 3 independent experiments are shown. Error bars are SEM.

Figure S5. Nutlin and DNA damaging drugs combine to kill ovarian cancer cells that harbor mutant p53. OVCAR-5 (A) and OVCAR-8 (B) ovarian cancer cell lines were treated with vehicle control (DMSO) or 10 μM Nutlin, 5 μM cisplatin, 5 μM etoposide or a combination of Nutlin with cisplatin or etoposide. After 48 hours, microscopic representative pictures were taken of each.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γH2AX
DAPI
150 min
γH2AX
DAPI
DMSO
Nutlin
Mdm2
p53-/- MEF
B
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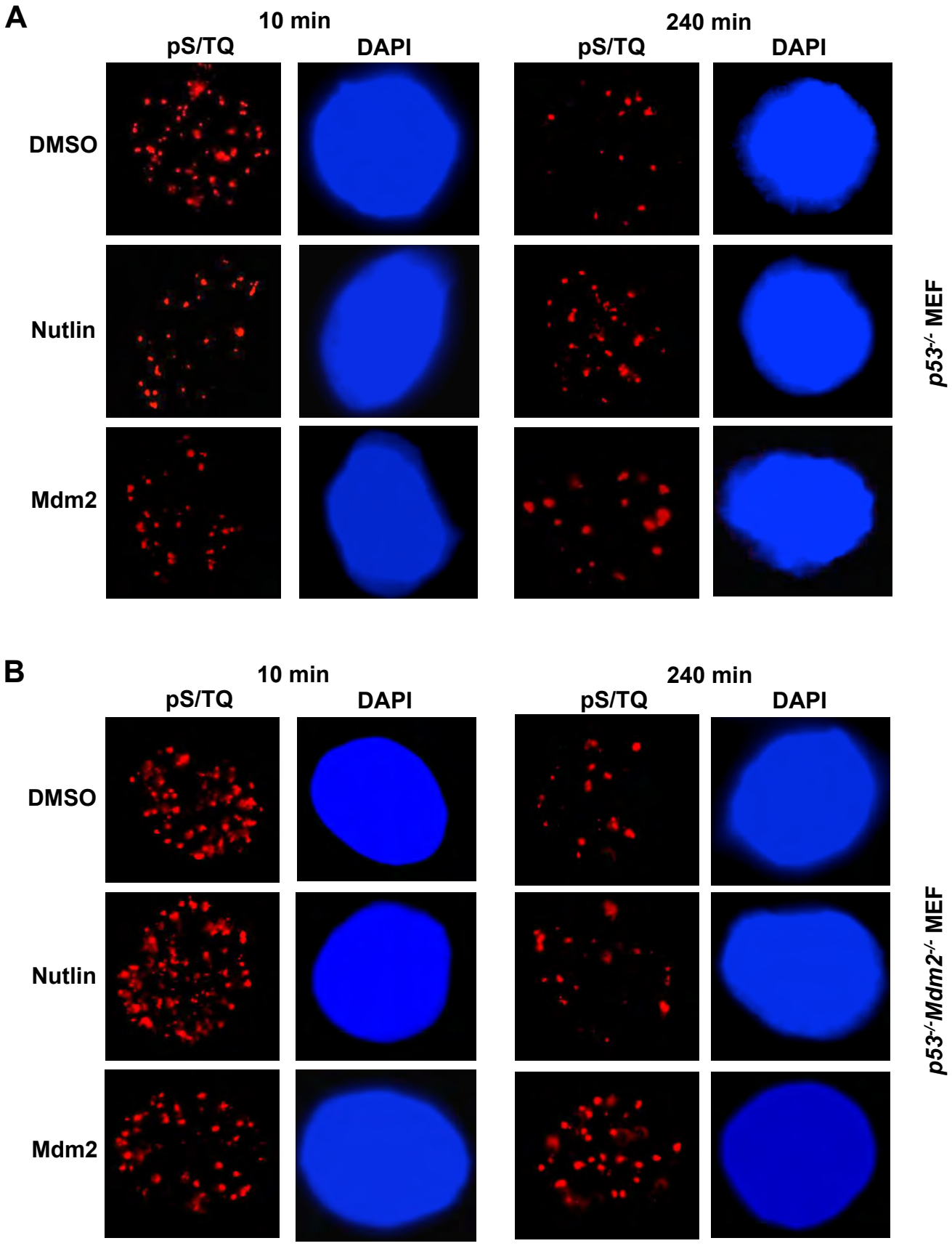
γH2AX
DAPI
150 min
γH2AX
DAPI
DMSO
Nutlin
Mdm2
p53-/-Mdm2-/- MEF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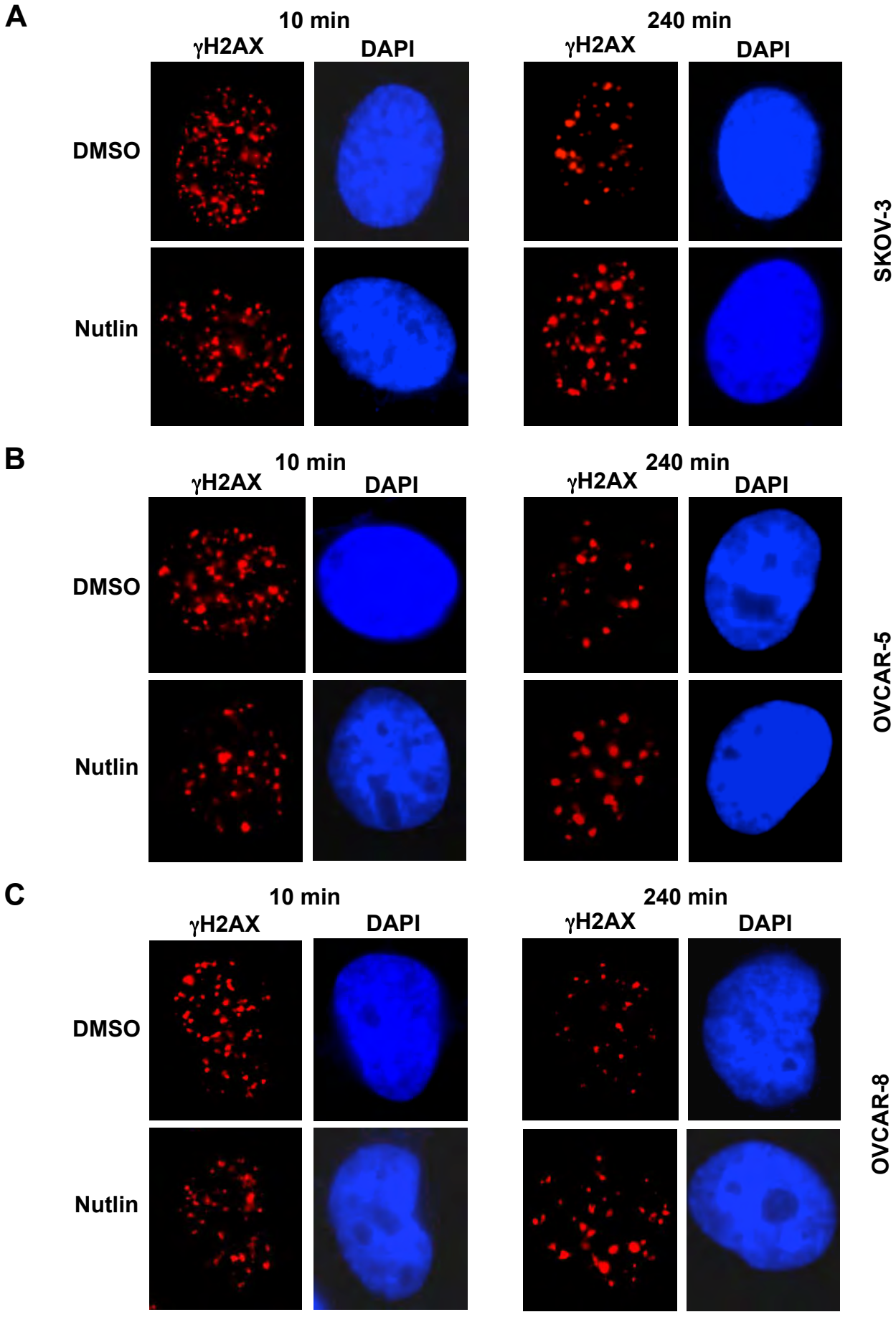
240 min
pS/TQ
DAPI
pS/TQ
DAPI
DMSO
Nutlin
Mdm2
p53-/- MEF
B
10 min
240 min
pS/TQ
DAPI
pS/TQ
DAPI
DMSO
Nutlin
Mdm2
p53-/-Mdm2-/- MEF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DAPI
240 min
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DAPI
DMSO
Nutlin
SKOV-3
B
10 min
γH2AX
DAPI
240 min
γH2AX
DAPI
DMSO
Nutlin
OVCAR-5
C
10 min
γH2AX
DAPI
240 min
γH2AX
DAPI
DMSO
Nutlin
OVCAR-8

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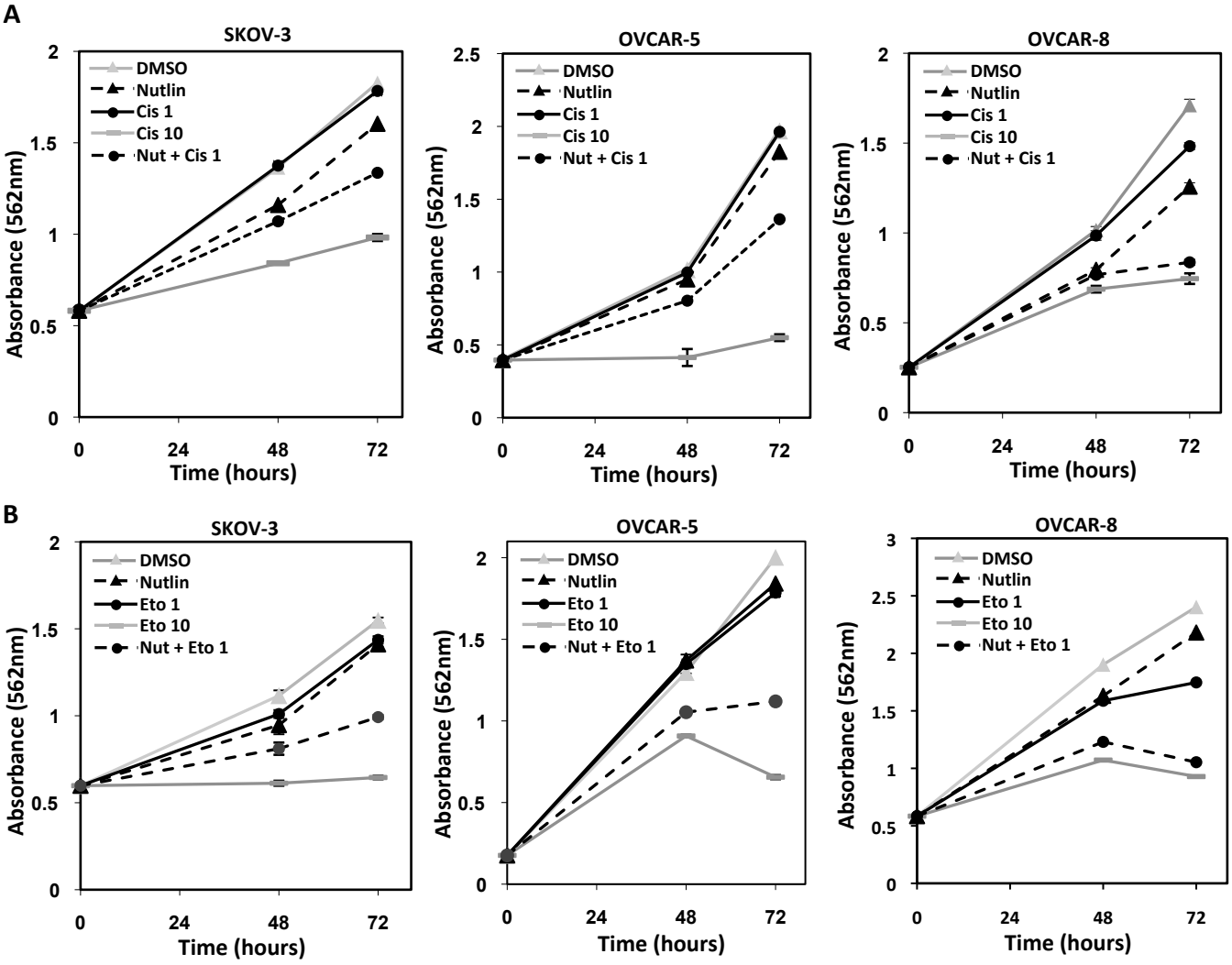

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