

Synergistic DNA-damaging effect in multiple myeloma with the combination of zalypsis, bortezomib and dexamethasone

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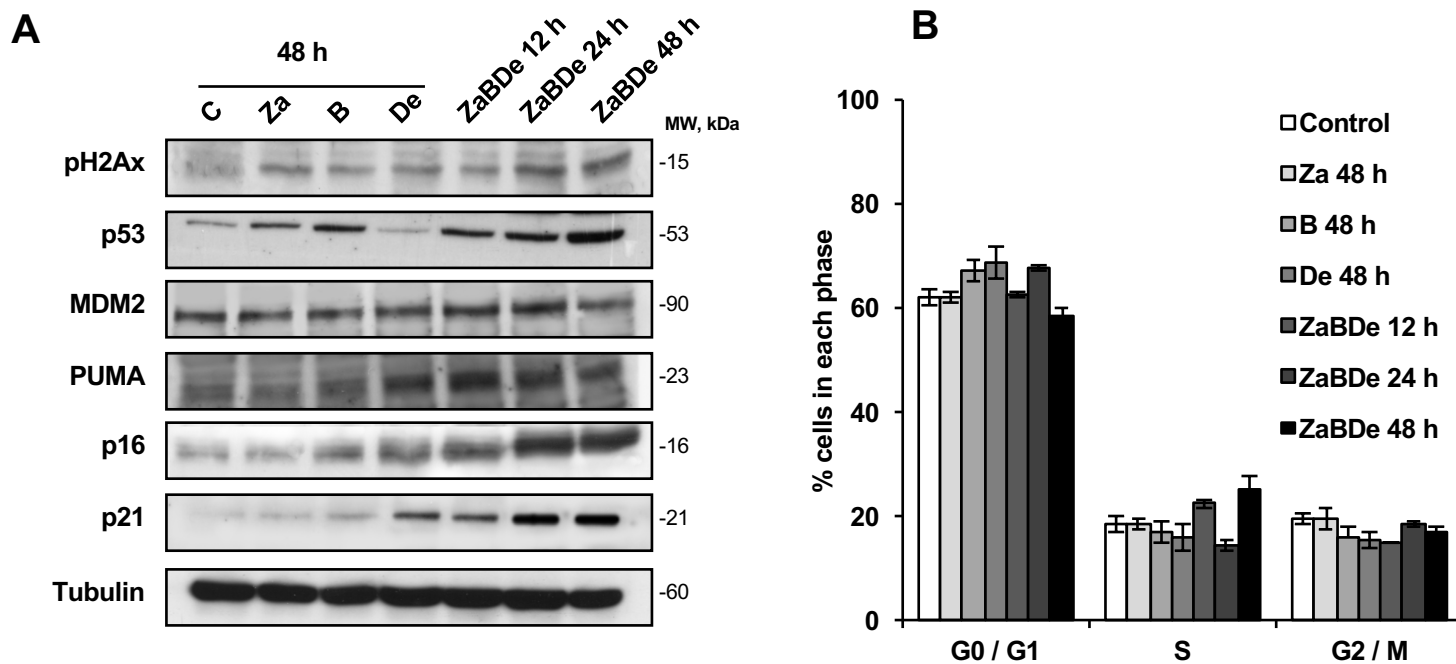
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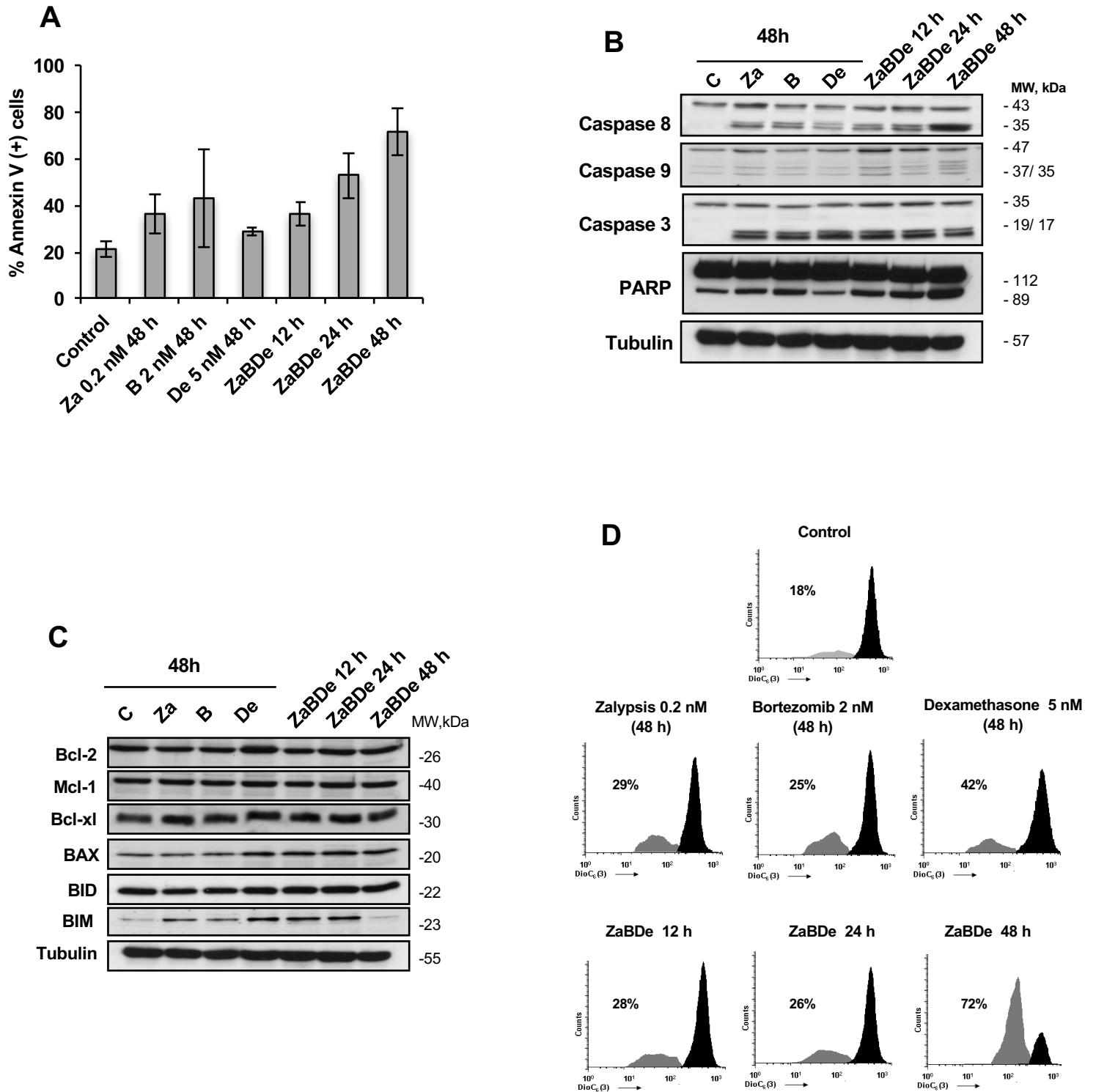
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Supplemental Figure 1



Supplemental Figure 1. ZaBDe triggers DNA damage. A) Western blot of different proteins implicated in the DNA damage response after treatment of MM.1S cells for the indicated times with vehicle (control), zalypsis (0.2 nM), bortezomib (2 nM), dexamethasone (5 nM) and the triple combination ZaBDe for different times. B) Cell cycle distribution examined by flow cytometry after propidium iodide staining of MM.1S cells treated with the same agents and conditions as above. Data represent means \pm SD of three independent experiments.

Supplemental Figure 2



Supplemental Figure 2. The triple combination ZaBDe induces apoptosis through caspase dependent and independent mechanisms. A) Apoptosis induction as evaluated by annexin V+ staining of MM.1S cells treated for the indicated times with vehicle (control), zalypsis (0.2 nM), bortezomib (2 nM), dexamethasone (5 nM) and the triple combination for different times. Data represent means \pm SD of three independent experiments. B) Western-Blot showing cleavage of caspases-8, -9, -3 and PARP in MM.1S cells after incubation with the indicated treatments and times. C) Western-Blot evaluation of Bcl-2 family members after treatment of MM.1S cells with the drugs alone and in triple combination in the same conditions as above. D) Representative examples of mitochondrial membrane potential ($\Delta\Psi_m$) changes evaluated by DioC₆ (3) staining after incubation with the indicated treatments.