## SUPPLEMENTARY FIGURE LEGENDS

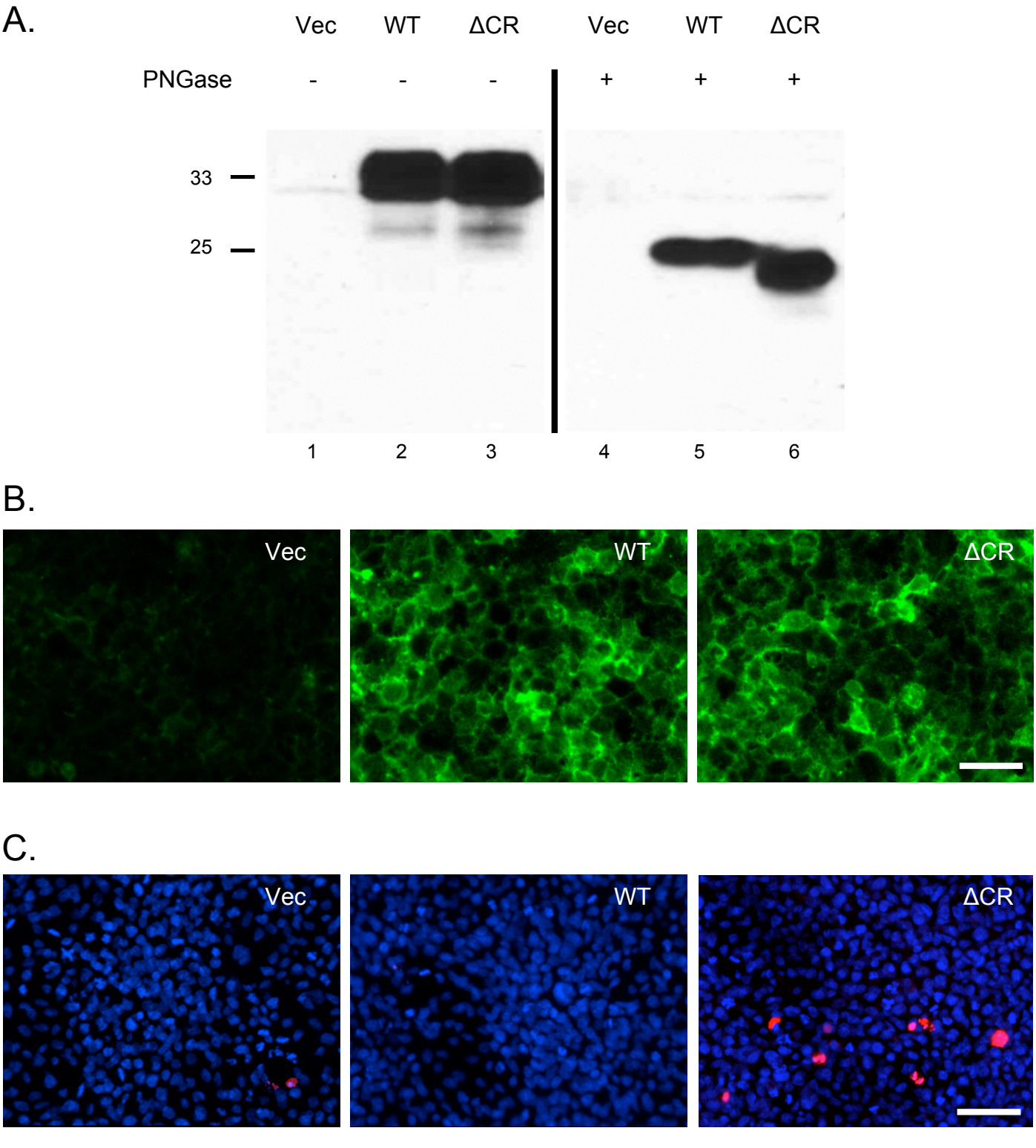
SUPPL. FIGURE S1: *Both WT and ΔCR PrP are glycosylated and expressed on the surface of HEK cells; ΔCR PrP causes a small reduction in cell viability.* **(A)** PrP expression was analyzed by Western blotting lysates of HEK cells stably transfected with empty vector (Vec), or with vector encoding WT or ΔCR PrP. Samples in lanes 4-6 were subjected to enzymatic deglycosylation with PNGase F prior to analysis. PrP was detected using anti-PrP antibody SA65. **(B)** Live cells of the indicated lines were stained for surface PrP with SA65 antibody. **(C)** Cells of the indicated lines were stained by TUNEL (red) to reveal fragmented DNA and with DAPI (blue) to reveal nuclei. Scale bars in B and C = 50 μm.

SUPPL. FIGURE S2: *Drug structures.* Structures of G418, hygromycin B, Zeocin, and bleomycin are taken from the Pubchem database (http://pubchem.ncbi.nlm.nih.gov).

SUPPL. FIGURE S3: *HEK cells expressing ΔCR PrP are hypersensitive to G418 and Zeocin, as measured by TUNEL.* **(A)** Cells expressing empty vector, WT PrP, or ΔCR PrP were treated with the indicated concentrations of drug for 3 days, and were then stained by TUNEL (red) to reveal fragmented DNA and with DAPI (blue) to reveal nuclei. (**B, C)** Cells of the indicated lines were treated for 3 days with different concentrations of G418 **(B)** or Zeocin **(C)**. The number of TUNEL-positive cells, expressed as a percentage of the number of DAPI-stained cells, was determined in 5 fields for each sample group. Bars shown means ± SEM (n = 3 independent experiments).

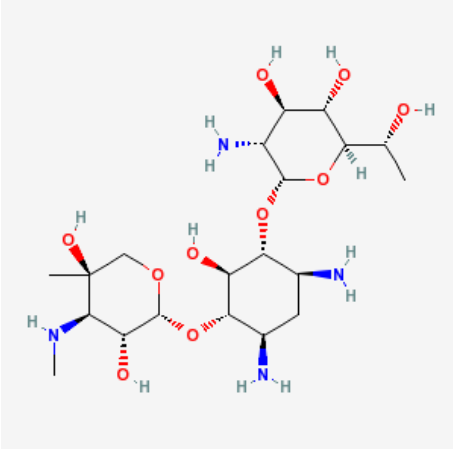
SUPPL. FIGURE S4: *CHO cells expressing ΔCR PrP are hypersensitive to G418 and Zeocin, as measured by TUNEL.* **(A)** CHO cells transiently transfected with empty vector (Vec), or with vector encoding WT or ΔCR PrP, were treated with the indicated concentrations of drug for 3 days, and were then stained by TUNEL (red) to reveal fragmented DNA and with DAPI (blue) to reveal nuclei. (**B, C)** Cells transfected with the indicated plasmids were treated for 3 days with the indicated concentrations of G418 **(B)** or Zeocin **(C)**. The number of TUNEL-positive cells, expressed as a percentage of the number of DAPI-stained cells, was determined in 5 fields for each sample group. Bars show means ± SEM (n = 3 independent experiments).

SUPPL. FIGURE S5: *Co-expression of WT PrP suppresses Zeocin-induced DNA damage in cells expressing ΔCR PrP.* **(A)** HEK cells expressing WT or ΔCR PrP were mock-transduced, or transduced with a recombinant lentiviruses encoding WT PrP or EGFP. Forty-eight hrs later, cells were incubated with or without Zeocin (500 μg/ml) for 60 min, after which cells were lysed, and γ-H2AX and PrP detected by Western blotting. The relative amount of PrP is given below each set of lanes. **(B)** Levels of γ-H2AX induced by Zeocin were determined by Odyssey analysis of blots like those shown in panel A, normalized to actin levels (not shown), and expressed as a percentage of γ-H2AX levels in the absence of drug. Bars represent means ± SEM from 3 independent experiments. Asterisks indicate values that are significantly different from mock-transduced ΔCR or EGFP-transduced ΔCR ($p<0.01$).

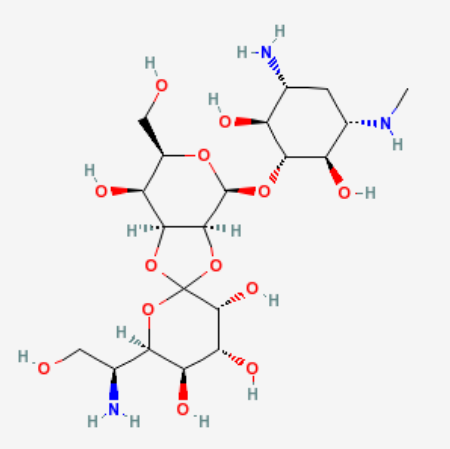



SUPPL. FIGURE S1

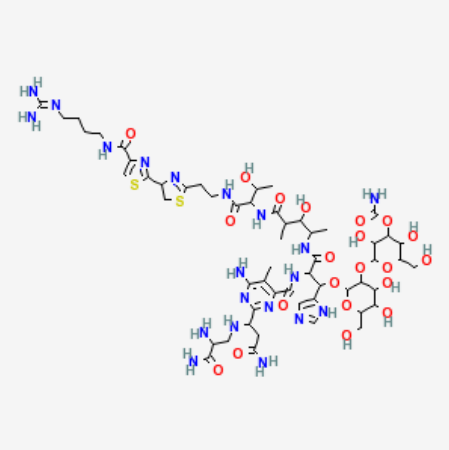
G418 (MW=496)
(Geneticin)



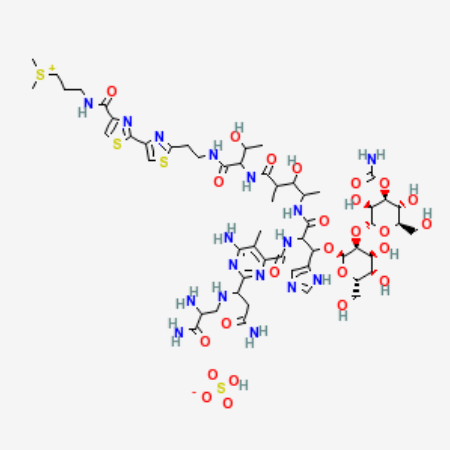
Hygromycin B (MW=528)



Zeocin (MW=1,428)
(Phleomycin D1)

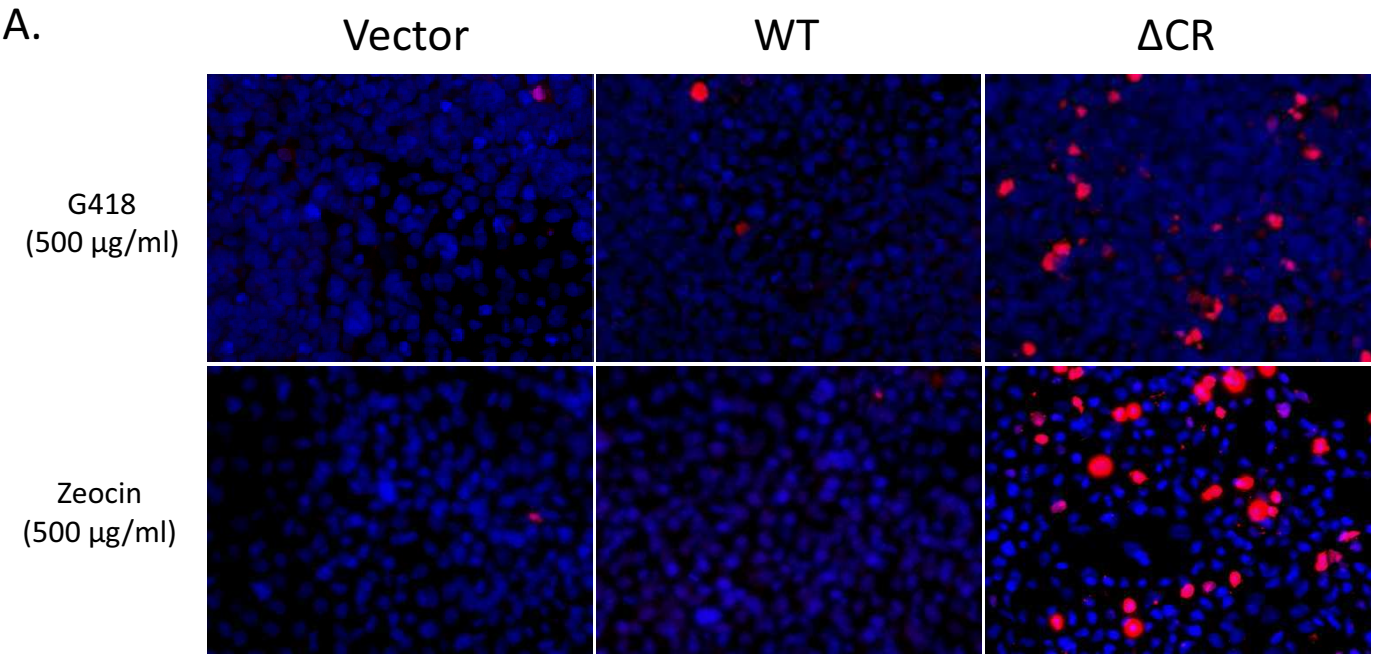


Bleomycin (MW=1,416)

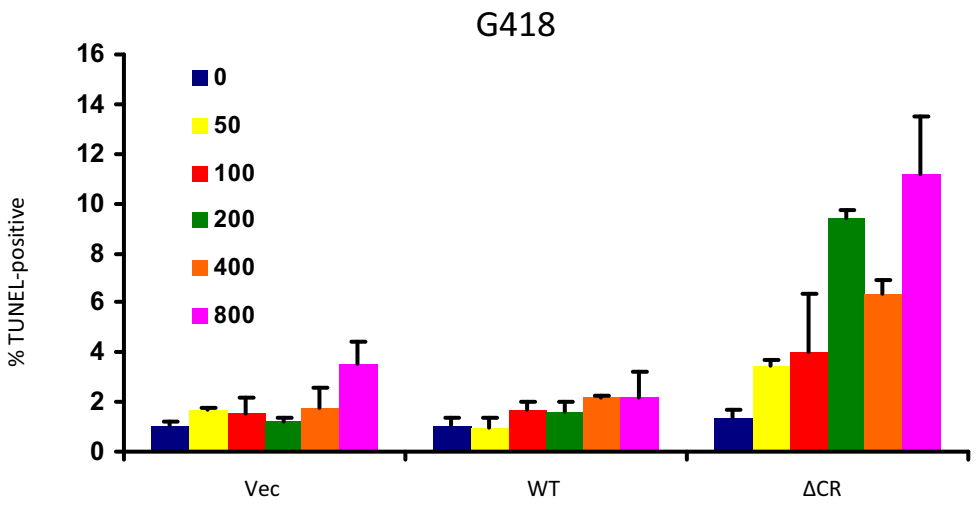


SUPPL. FIGURE S2

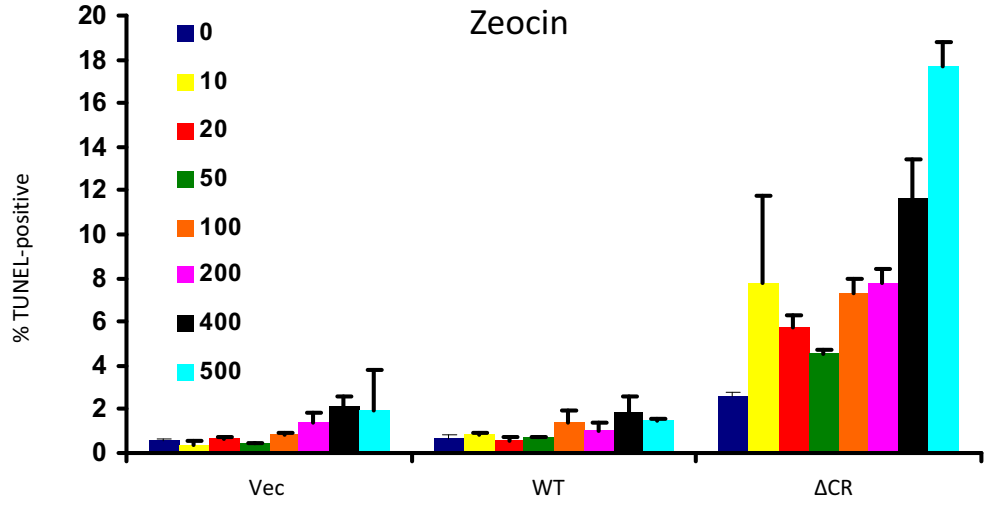
A.




B.

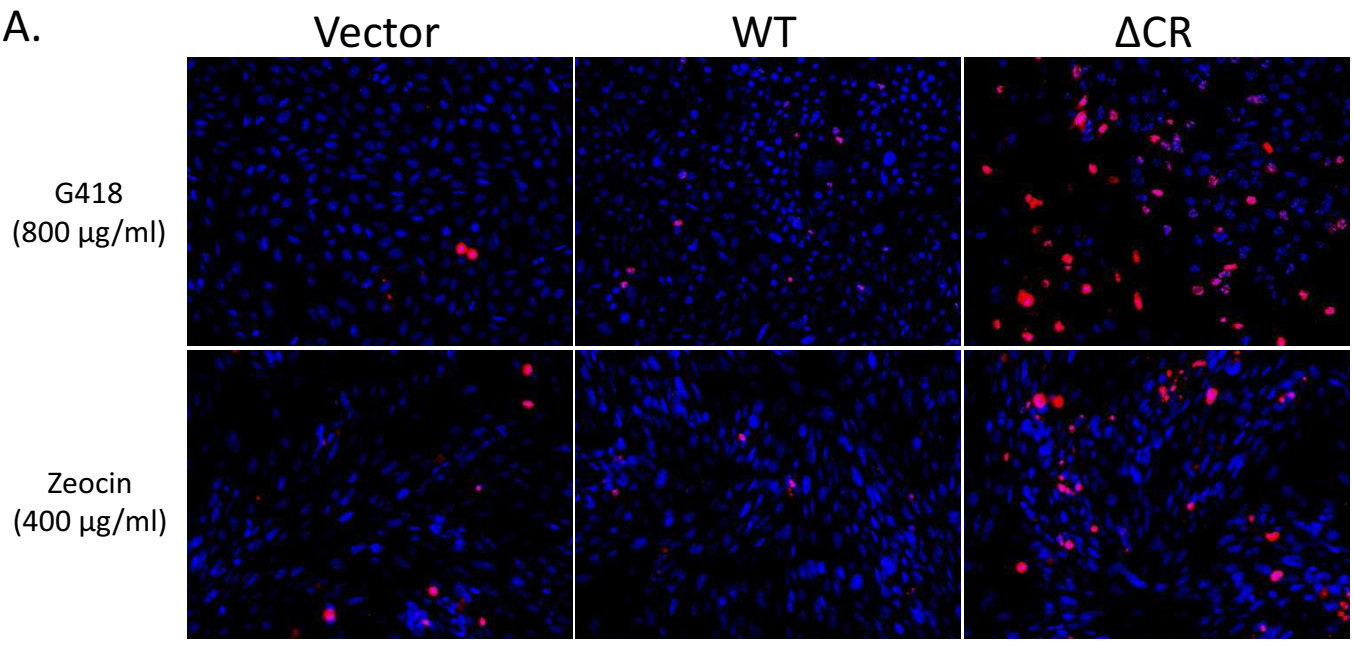



C.




SUPPL. FIGURE S3

A.

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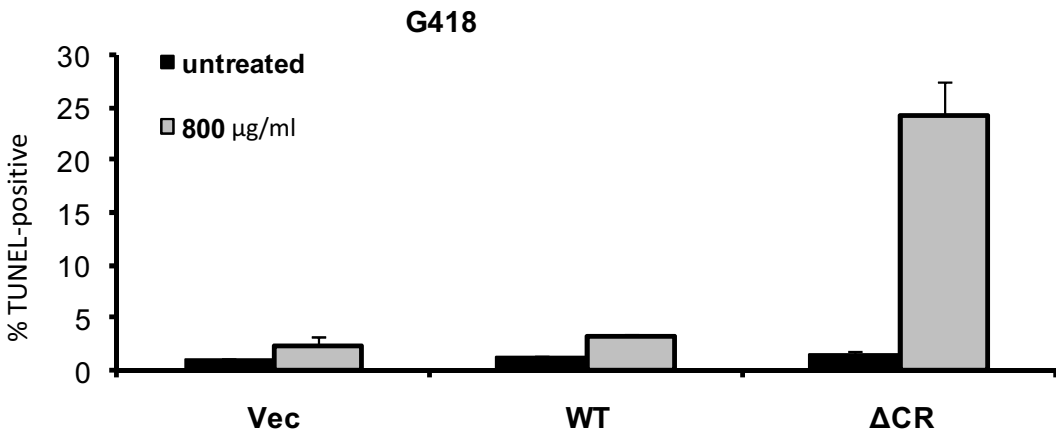


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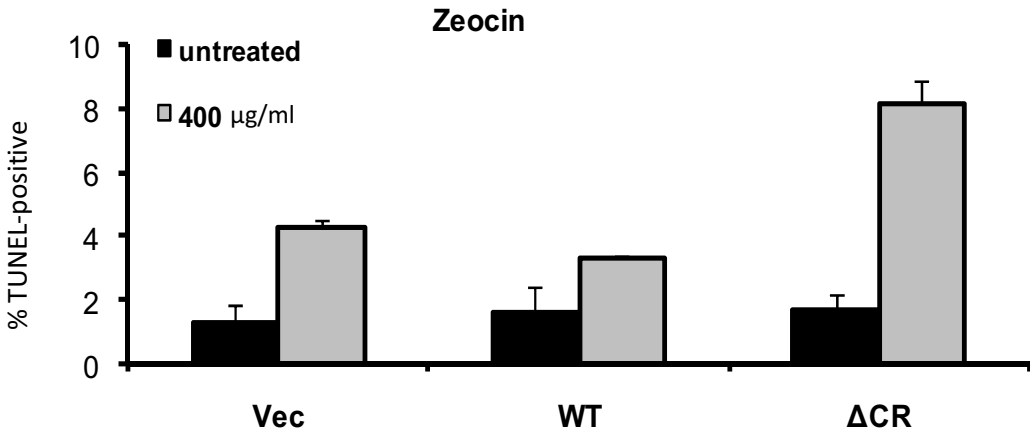
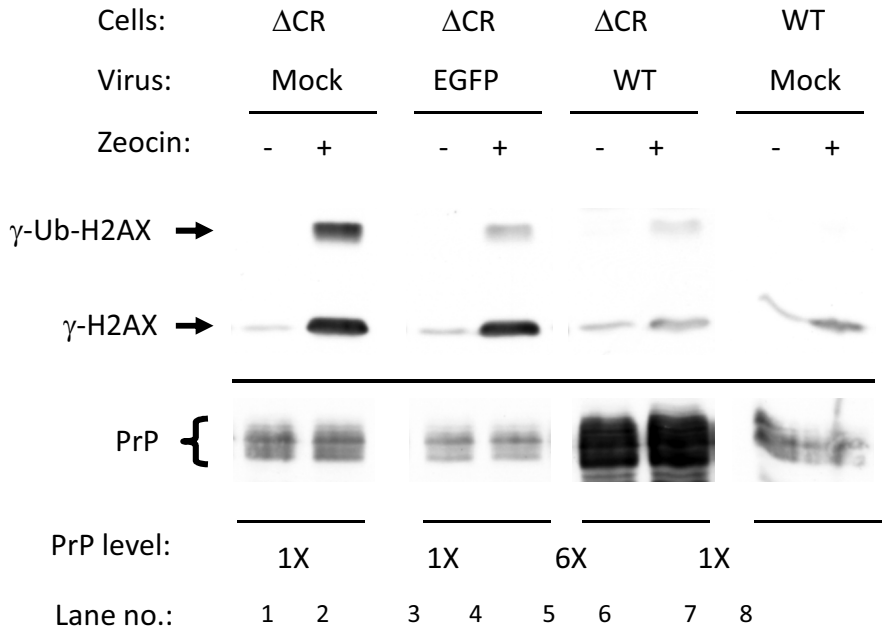



SUPPL. FIGURE S4

A.

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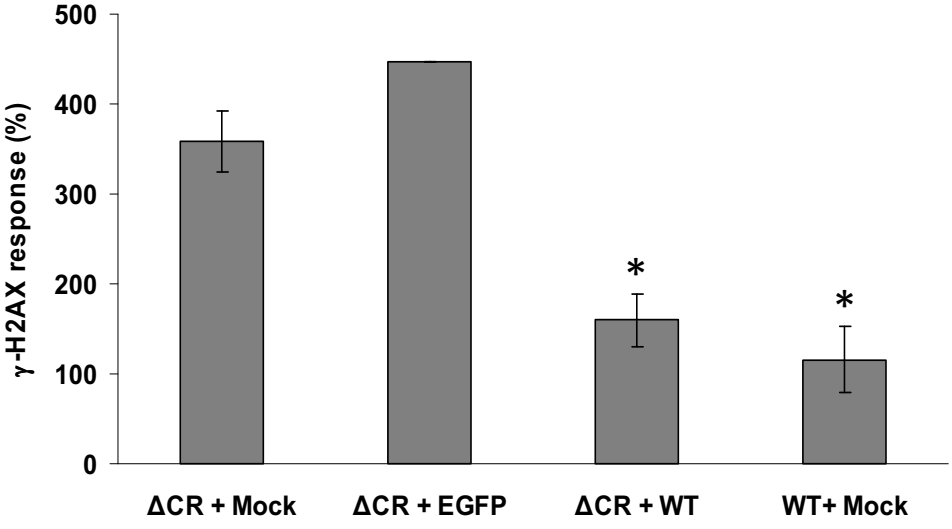


SUPPL. FIGURE S5