Supplmenetary Figure S3

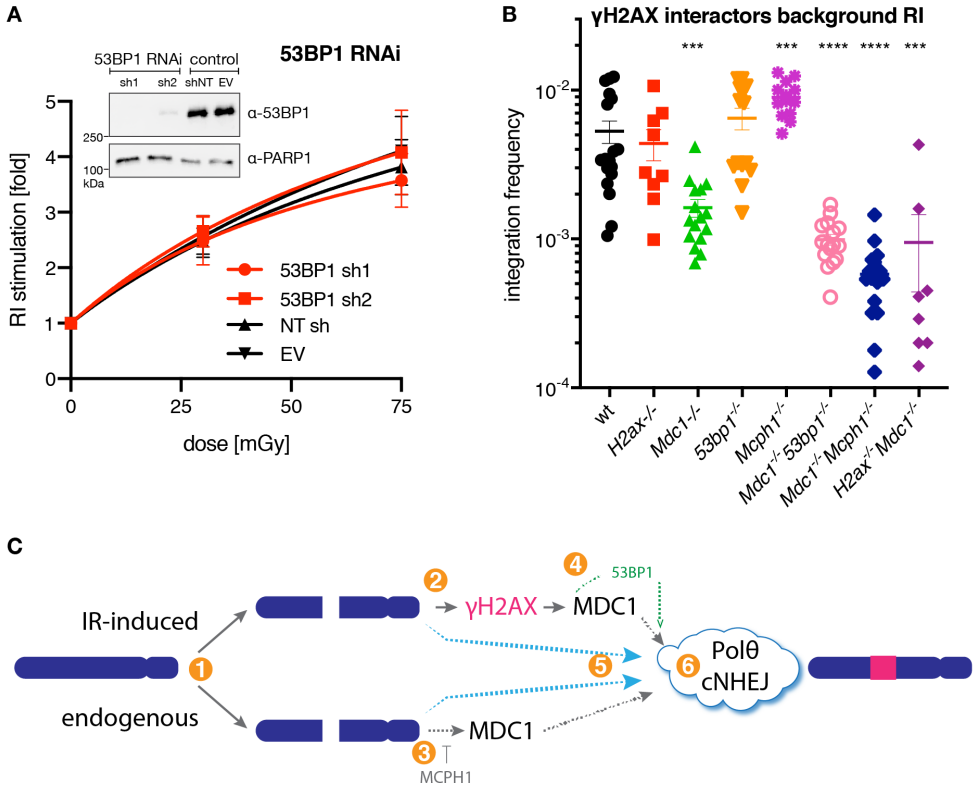

Figure S3 (related to Figure 3) (**A**) 53BP1 knock-down does not affect S-RI efficiency. Means of four independent puromycin-resistant colony formation S-RI assays (two with linearized, two with circular plasmid DNA) are plotted. Immunoblot on total cell lysates with the indicated antibodies confirming the efficiency of knock-down is shown as an inset. (**B**) Background RI efficiency in mES cell lines deficient for γH2AX interacting proteins. Data is plotted as in **(Fig S2A)**. (**C**) A model of RI and S-RI, based on the supposition that the initial stages of the two processes are mechanistically distinct 1, to account for the observation that S-RI is γH2AX-dependent 2, while RI is not 3; MCPH1 competes with MDC1 for γH2AX binding, and its removal results in elevated RI 3. MDC1 contributes to both RI and S-RI 4, and 53BP1 can provide a backup mechanism for S-RI in the absence of MDC1, but does not contribute to the RI process 4. Since neither RI nor S-RI are completely abolished by the deletion of the proteins listed in the scheme, alternative pathways must exist 5. The final ligation steps are mediated by Pol θ or cNHEJ 6, as we previously showed that all integration events in ES cells are abolished when both these end joining mechanisms are inactivated, however the relative contribution of Pol θ and cNHEJ to RI and S-RI may be different.