



**Figure S5: Additional functional analysis of *BRCA1* VUS.** (A) Growth curve analysis of *Brca1* deficient mouse ES cells complemented by human *BRCA1* variants in different functional domains. The effects of inactivating missense variants in the RING domain (c.181T>G), the RING-bordering replication fork protection region (4) (c.397C>T), the coiled-coil domain (c.4198A>G, c.4220T>C, c.4232T>C) and the BRCT (c.4964C>T) domain on proliferation were compared with those of wild-type *BRCA1* (WT) and empty RMCE vector controls. Experiments were performed in triplicate; a representative example is shown. Error bars indicate the standard deviation between technical triplicates. (B) DR-GFP HRR assay results from *Brca1* deficient ES cells transiently complemented by human *BRCA1* variants. Experiments were repeated twice; a representative example is shown. Dots show the normalized percentage of GFP-positive transfected cells for each technical replicate, and bars show mean values and standard deviations. Horizontal lines indicate the average level of *BRCA1* wild-type (WT, green) and empty RMCE vector (EV, red) controls.