



Figure S4 Sequence - function map of the effect of missense substitutions on E3 ligase function.

The functional score for each variant is the slope of the fit curve, normalized by setting stop codons to a score of 0 and the wild-type to a score of 1. Each position in BRCA1(2-304) is arranged along the x-axes, structural features of the RING domain are diagrammed above. The amino acid substitutions, grouped by side-chain properties, are on the y-axes. The E3 ligase scores range from improved activity versus wild-type (red), equivalent to wild-type (white), to less than wild-type (blue). Yellow represents the wild-type residue and gray missing or low confidence data.