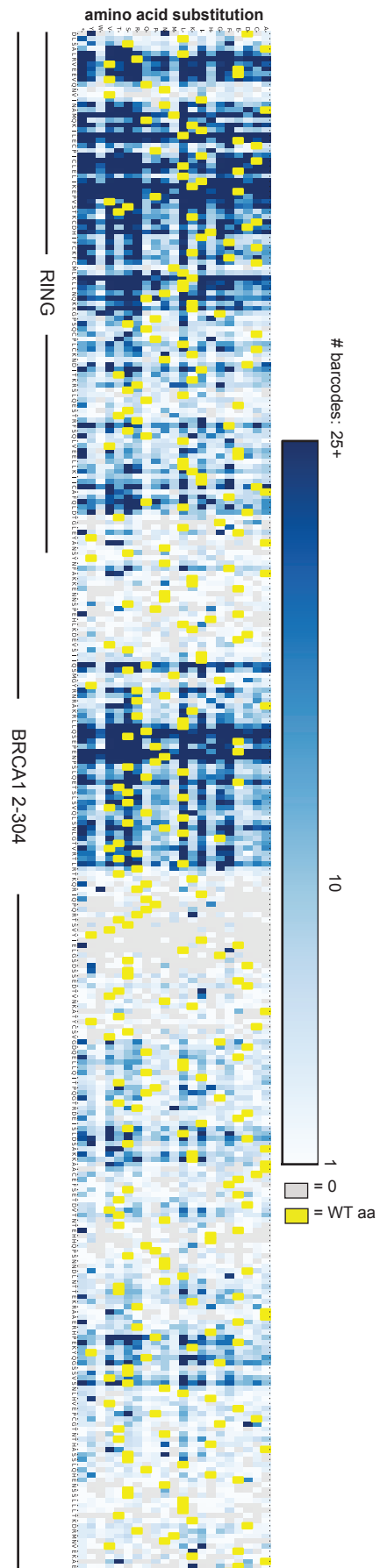


**C**



**Figure S1** Construction of the BRCA1(2-304) allelic series.

**(A)** We created an allelic series of variants within BRCA1(2-304) with single amino acid substitutions by the method known as Programmed Allelic Series (Kitzman et al. 2015), which uses mutagenic oligonucleotides synthesized on a programmed microarray to create a pool of variants with single codon changes by overlap-extension PCR. **(B)** Each variant was barcoded with a random 16-nucleotide tag that we associated with the mutation present in the BRCA1 domain. We assembled 128,237 barcoded variants, of which 60,256 corresponded to 5,156 single amino acid changes out of the possible 5,757 (89% of the 19 substitutions x 303 codons) in BRCA1(2-304). **(C)** The number of barcodes per assembled BRCA1(2-304) variant is represented in a heatmap. Shades of blue represent the number of barcodes per variant with the maximum color fill set to 25 barcodes. There were many variants that had more than 25 barcodes. Yellow represents wild-type residues and gray potential variants for which there was not a full length BRCA1(2-304) assembly.