



$\Delta G$ / kcal/mol	Stage 1	Stage 2	Stage 3
Protein	31.6	1.0	2.7
Water	30.2	0.9	2.8

Figure S11. Convergence of the free energy of the T08A mutation in the RAD51-BRC4A complex using thermodynamic integration in three stages. Stage 1: Removal of partial charges from T08, stage 2: transformation of vdW parameters of T08 to A08 using soft-core potentials, stage 3: introduction of partial charges to A08.  $\Delta\Delta G = \Delta G(\text{protein}) - \Delta G(\text{water})$ . T08 does not form any direct hydrogen bonds with RAD51, yet the majority of the free energy change is due to the removal of charge in stage 1.