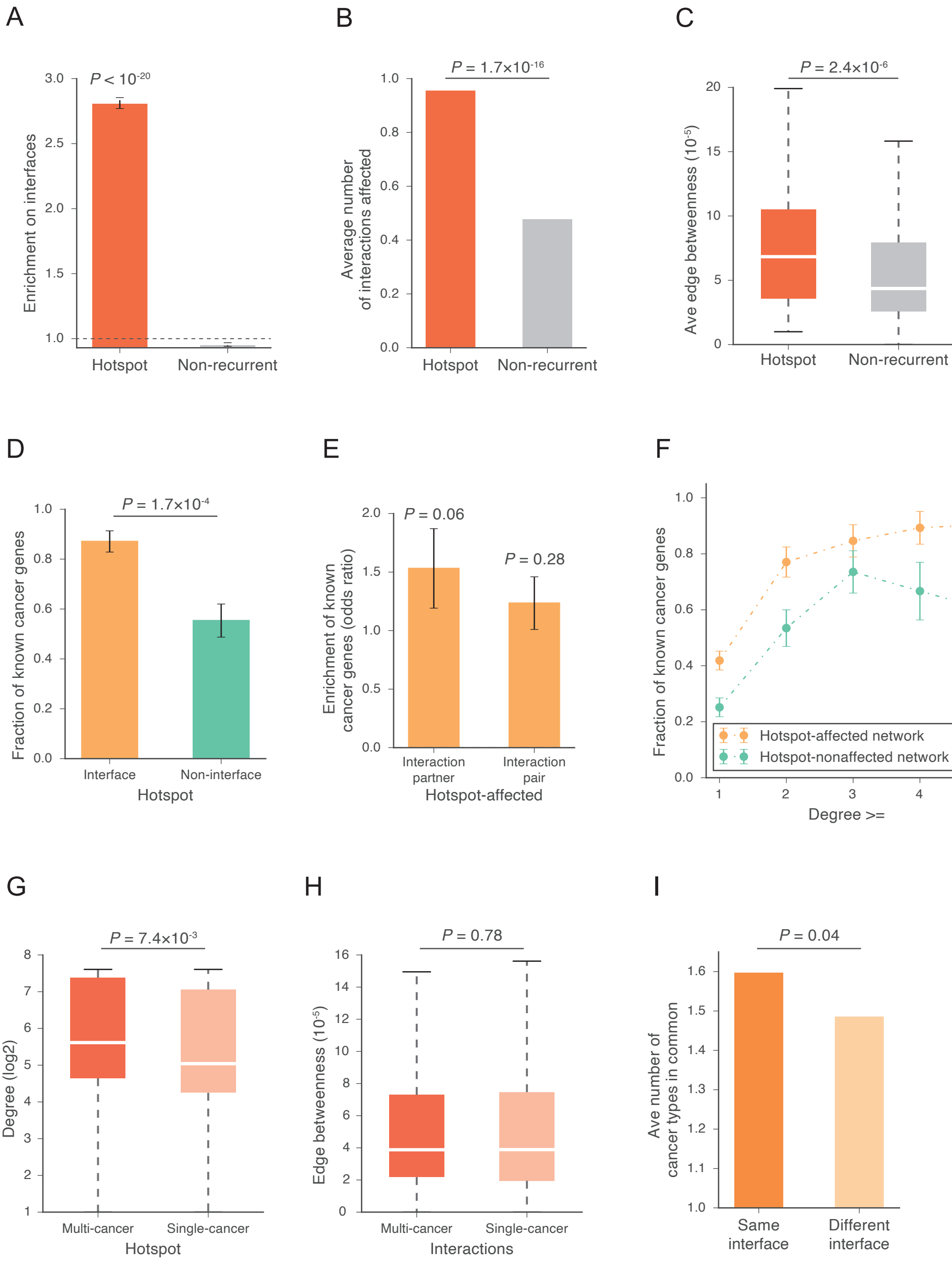

Supplementary Fig. 6: Analyses of mutational hotspots using protein interfaces resolved from cocrystal structures and homology models. **A**, Distribution of hotspots and non-recurrent variants on proteins with regard to protein interaction interfaces. Enrichment was calculated as the ratio of the observed fraction of hotspots/variants that occur on interaction interfaces over the fraction of interface residues on corresponding proteins (expected fraction). **B**, Average number of protein interactions affected by hotspots and non-recurrent variants. **C**, Average edge betweenness of interactions affected by hotspots and non-recurrent variants. **D**, Association of genes harboring interface and non-interface hotspots with previously known cancer genes. **E**, Association of hotspot-affected interaction partners and interaction pairs with known cancer genes. An interaction pair was counted when both the gene carrying hotspot and its interaction partner are known cancer genes. **F**, Association of proteins in the hotspot-affected and hotspot-unaffected networks with previously known cancer proteins. **G**, Degree distributions of proteins harboring multi-cancer and single-cancer hotspots. Degree values are transformed by log2 for presentation purposes. **H**, Edge betweenness distributions of multi-cancer and single-cancer interactions. **I**, Average number of cancer types shared between hotspots on the same interface and between hotspots on different interfaces.