



**Supplementary Fig. 8:** Analyses of mutational hotspots with their interaction partners expressed in tumors. **A**, Fraction of hotspot-affected/unaffected interaction partners expressed in corresponding tumors. **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 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. **E**, Association of proteins in the hotspot-affected and hotspot-unaffected networks with previously known cancer proteins. **F**, Edge betweenness distributions of multi-cancer and single-cancer interactions. **G**, Average number of cancer types shared between hotspots on the same interface and between hotspots on different interfaces.