



**Supplementary Fig. 7:** Network properties of mutational hotspots in a high-throughput-derived human interactome. **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.