

Figure S1. The distributions of the number of the mutated genes in mutation profiles. (a) The violin-plot for the number of mutated gene in a cell line across 1741 cell lines. The ACH-000999 cell line contains 9698 (the most) mutated gene, and the ACH-001150 cell line contains 12 (the fewest) mutated gene among 18K gene. (b) The histogram of the data presented in (a). (c) The violin-plot for the number of cells involving a mutated gene across 18K genes. The TTN gene is mutated in 1109 (the most) cell lines, and the RPL41 gene is mutated in 1 (the fewest) cell line among 1741 cell lines. The genes mutated in more than 52 (i.e. 3% of 1741) cell lines were only analyzed in this study, allowing 4339 genes (genes above the red line). (d) The histogram of the data presented in (c).

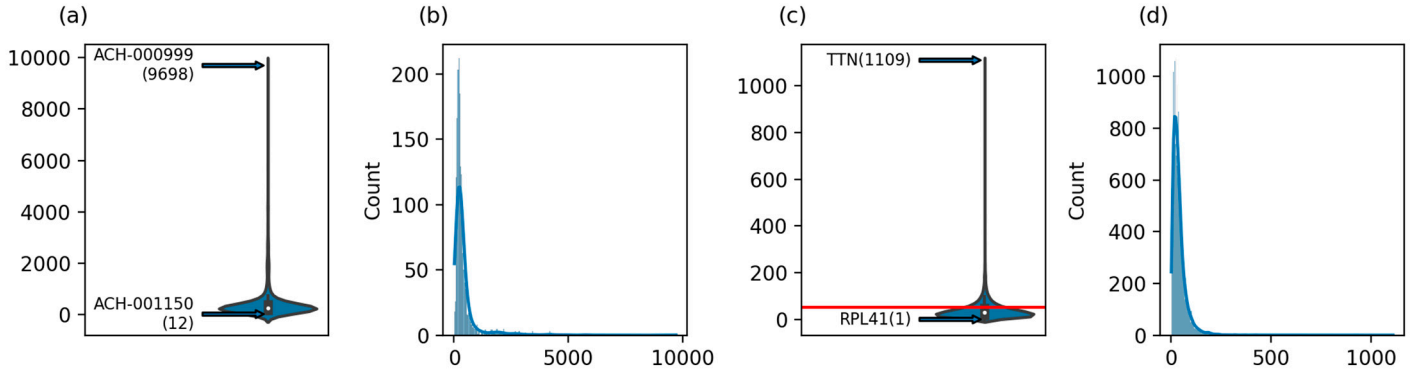


Figure S2. The distributions of the number of the depleted genes in CRISPR screening. (a) The violin-plot for the number of depleted gene in a cell line across 1741 cell lines. Here, for simplicity, gene whose depletion score is lower than 0 is regarded as depleted gene (depletion scores are ranged from -4.01 to 6.37). The ACH-001517 cell line contains 10647 (the most) depleted gene, and the ACH-000459 cell line contains 8512 (the fewest) depleted gene among 16K gene. (b) The histogram of the data presented in (a). (c) The violin-plot for the number of cells involving a depleted gene across 16K genes. The U2SURP gene is depleted in all 769 (the most) cell lines, and the IGFL1 gene is not depleted in any cell line among 769 cell lines. (d) The histogram of the data presented in (c).

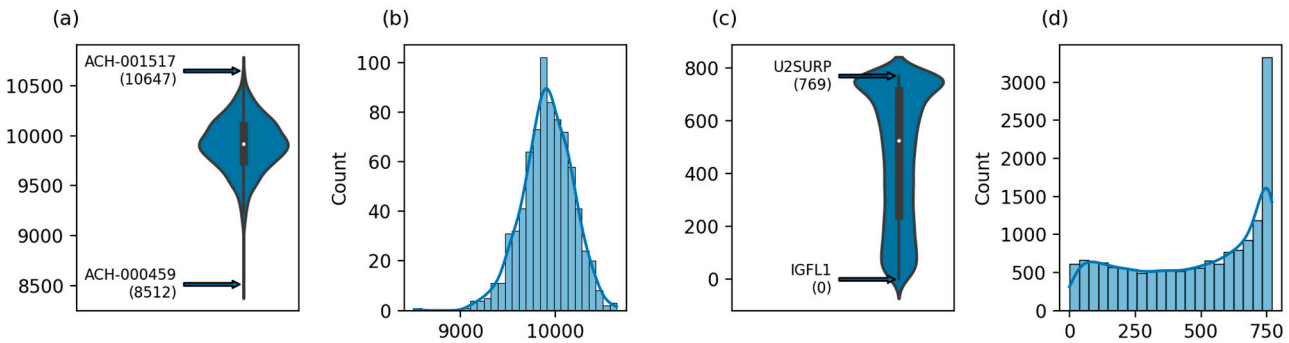


Figure S3. The distributions of the number of the depleted genes in shRNA screening. (a) The violin-p lot for *the number of depleted gene in a cell line* across 702 cell lines. Here, for simplicity, gene whose d epletion score is lower than 0 is regarded as depleted gene (depletion scores are ranged from -5.93 to 2.77) . The ACH-001441 cell line contains 3207 (the most) depleted gene, and the ACH-000869 cell line contains 1340 (the fewest) depleted gene among 6K gene. (b) The histogram of the data presented in (a). (c) The violin-plot for *the number of cells involving a depleted gene* across 16K genes. The CDC23 gene is depleted in all 702 (the most) cell lines, and the RGPDP8 gene is not depleted in any cell line among 702 cell lines. (d) The histogram of the data presented in (c).

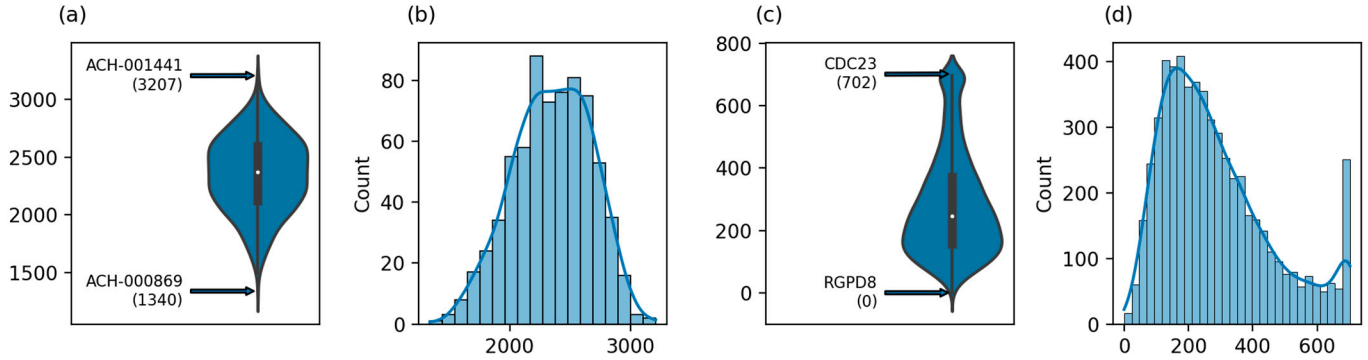


Figure S4. The distributions of the number of the non-expressed genes in expression profiles. (a) The violin-plot for *the number of non-expressed gene in a cell line* across 1305 cell lines. The ACH-001097 cell line contains 6298 (the most) non-expressed gene, and the ACH-000682 cell line contains 647 (the fewest) non-expressed gene among 19K genes. (b) The histogram of the data presented in (a). (c) The violin-plot for *the number of cells involving a non-expressed gene* across 19K genes. The CT47A8 gene is non-expressed in all 1305 (the most) cell lines, and the MPRIP gene is expressed in all 1305 cell lines. (d) The histogram of the data presented in (c).

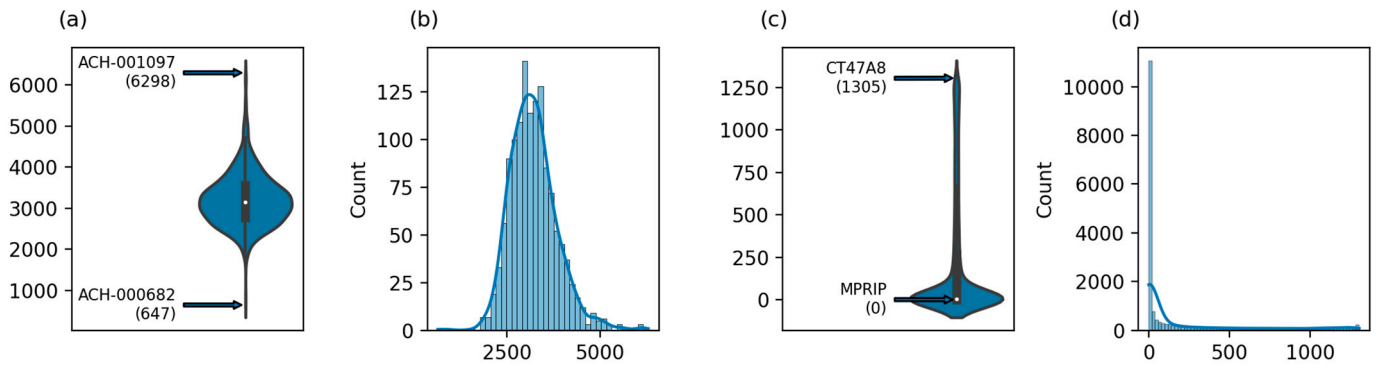
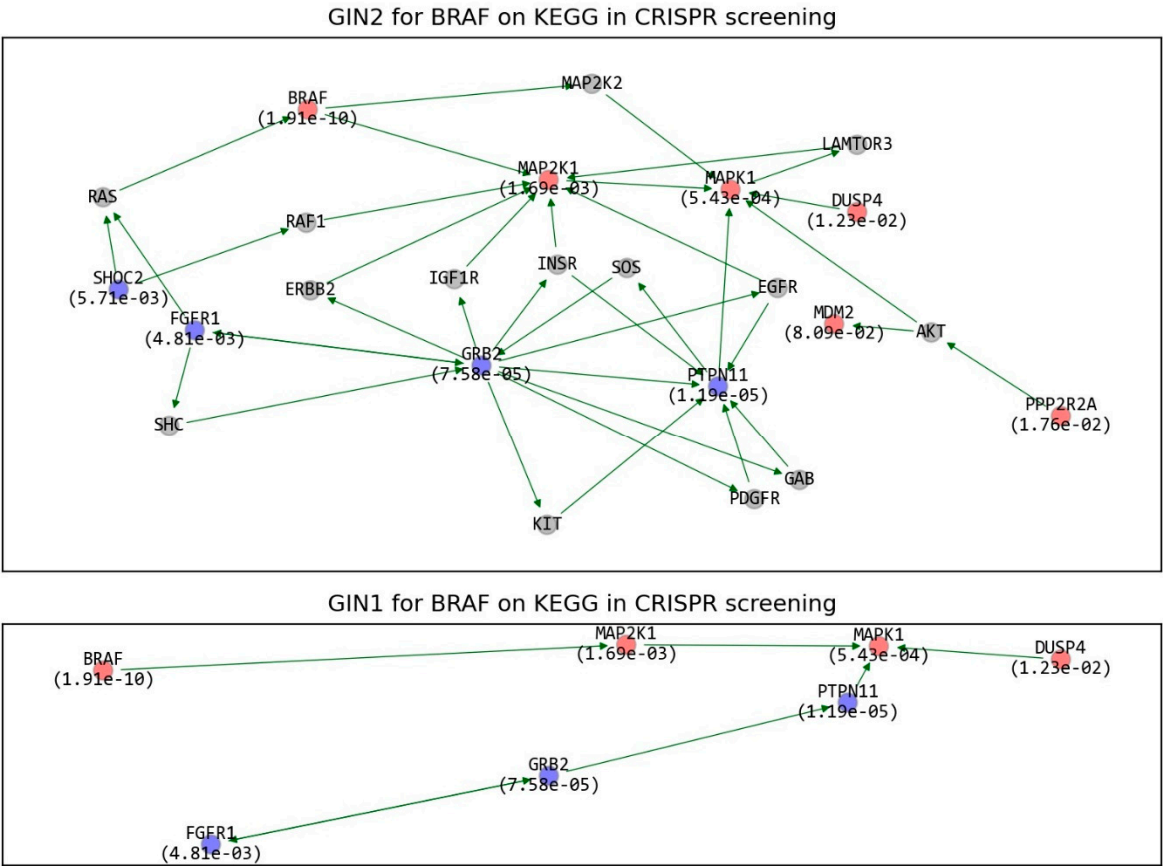
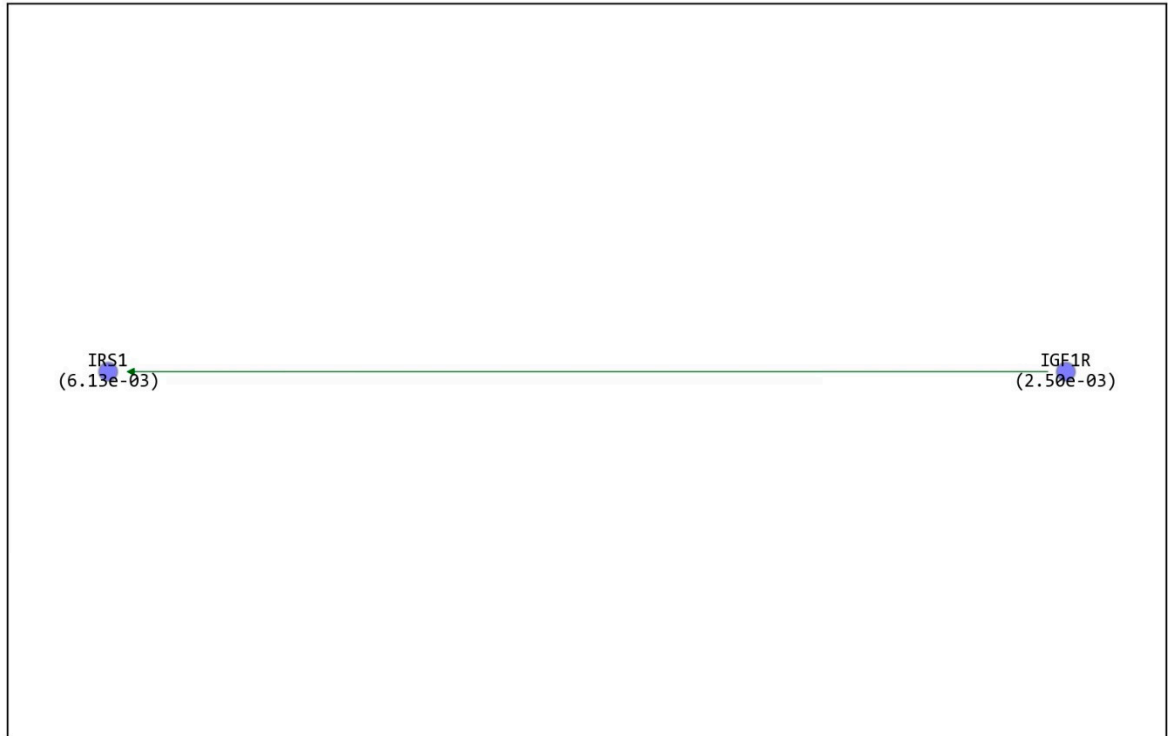


Figure S5. SPNs on KEGG networks from (a) CRISPR and (b) shRNA screenings for the mutated genes in Figure 3.

1. SPNs based on KEGG networks from CRISPR screening



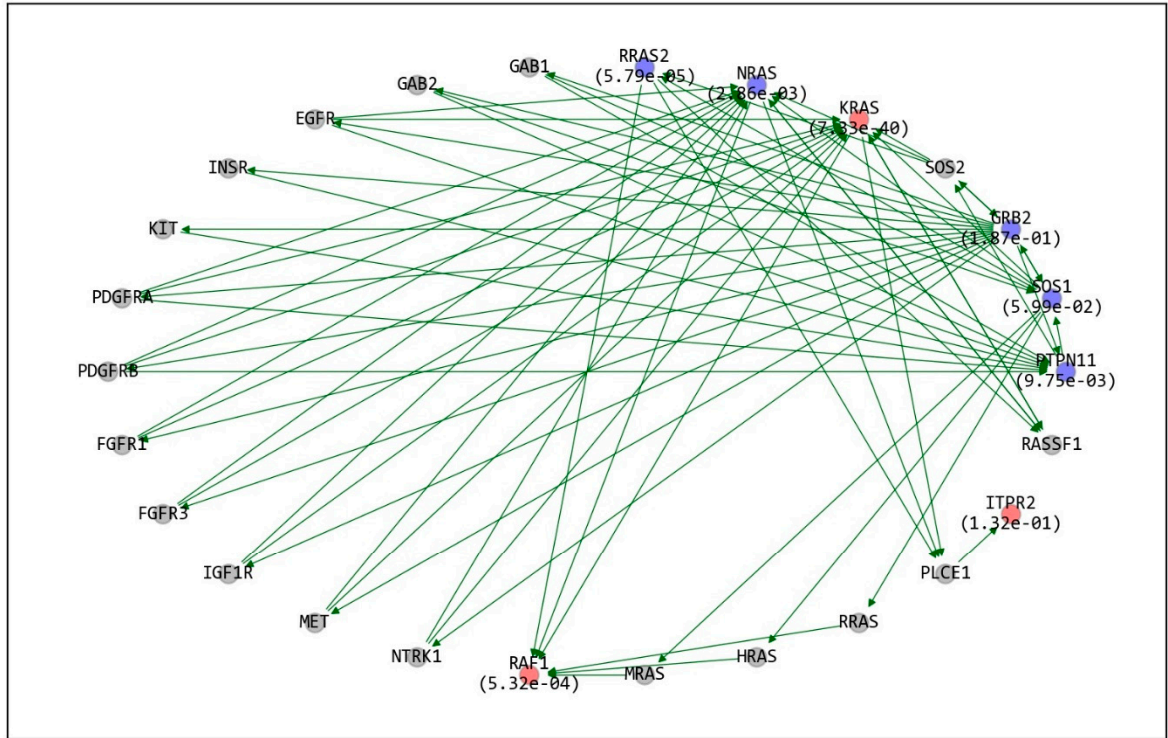
GIN2 for CTCF on KEGG in CRISPR screening



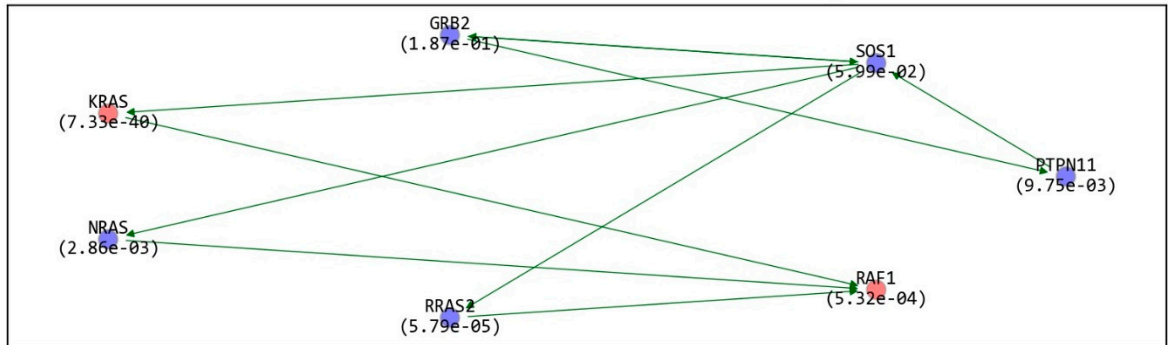
GIN1 for CTCF on KEGG in CRISPR screening



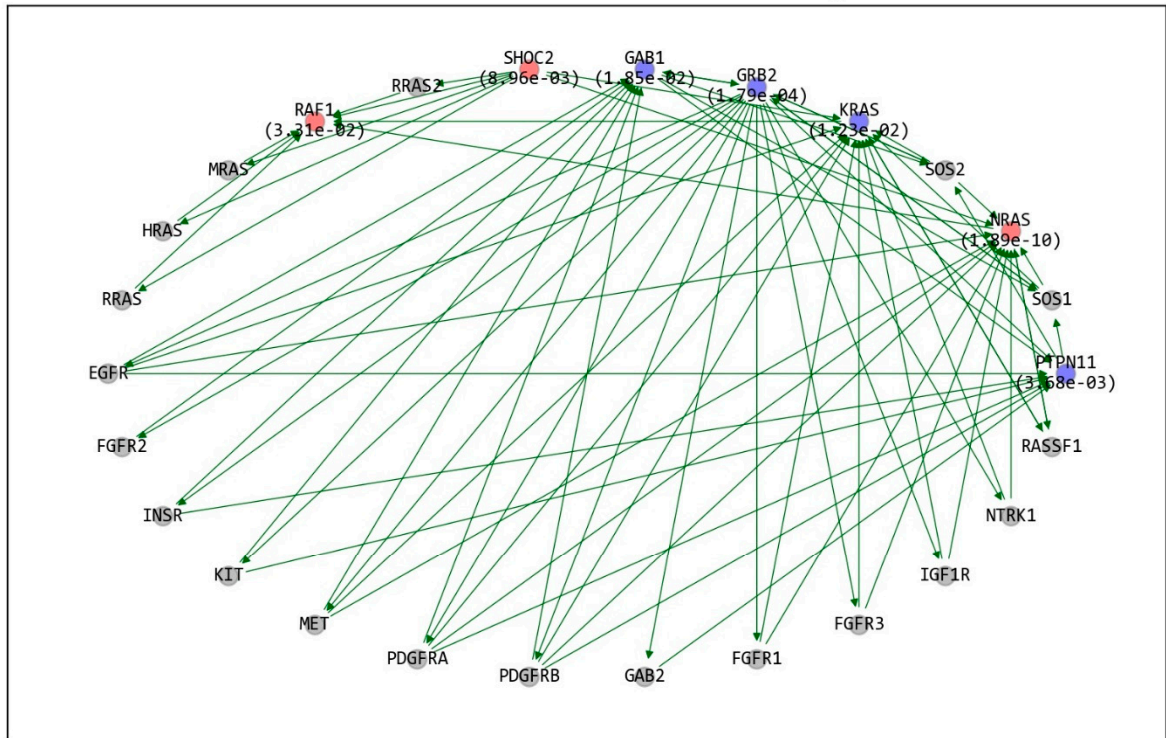
GIN2 for KRAS on KEGG in CRISPR screening



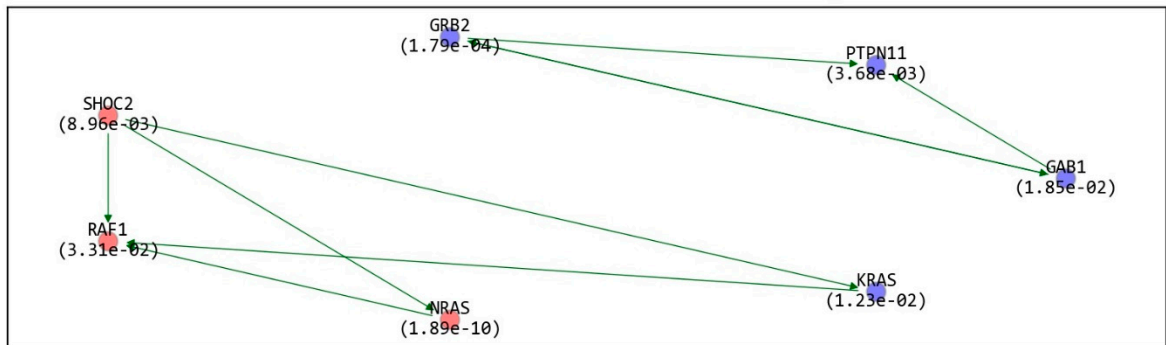
GIN1 for KRAS on KEGG in CRISPR screening



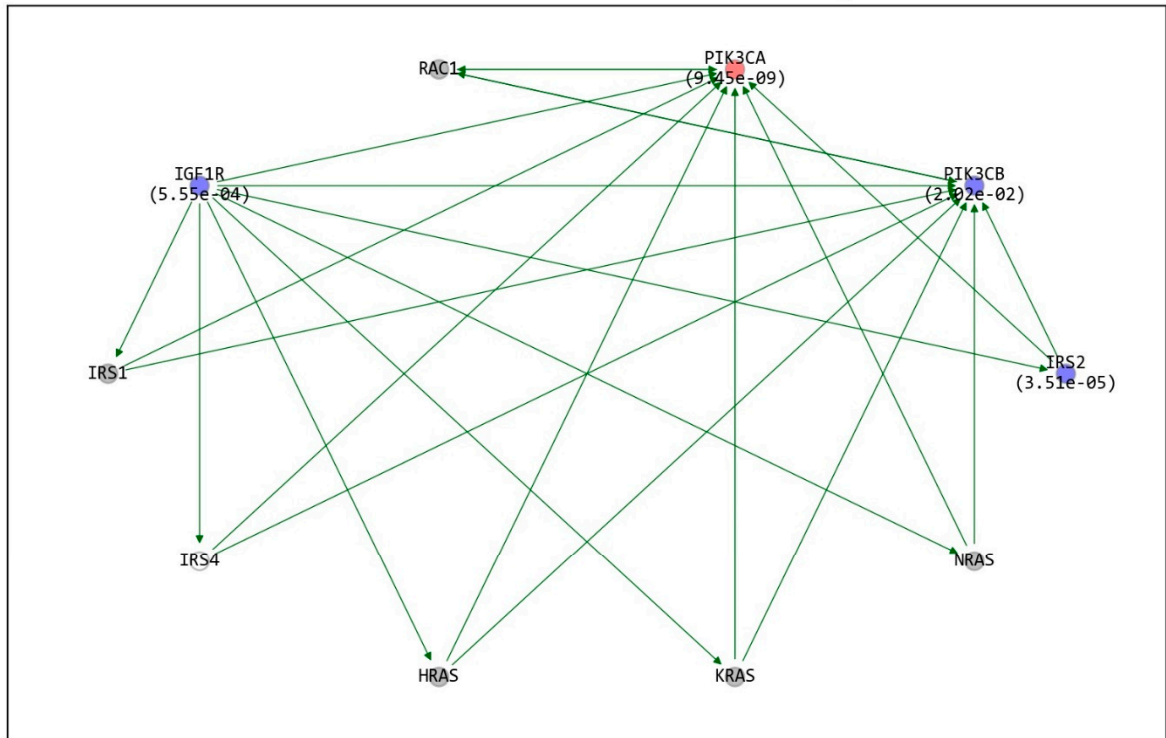
GIN2 for NRAS on KEGG in CRISPR screening



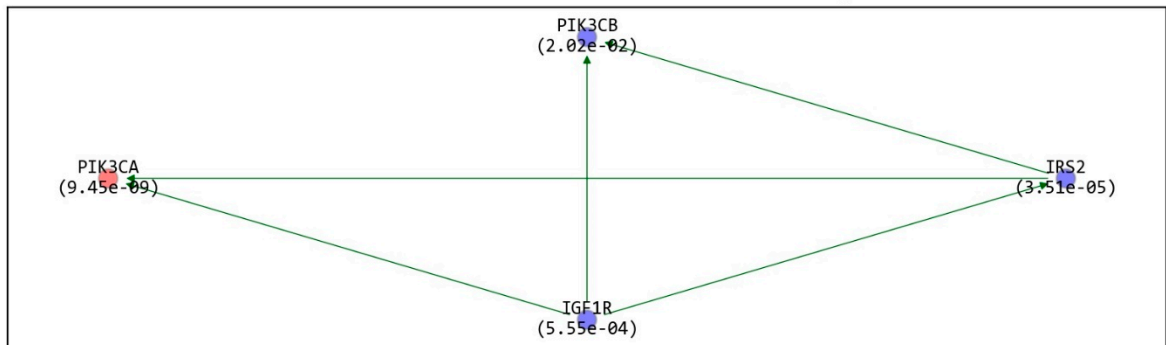
GIN1 for NRAS on KEGG in CRISPR screening



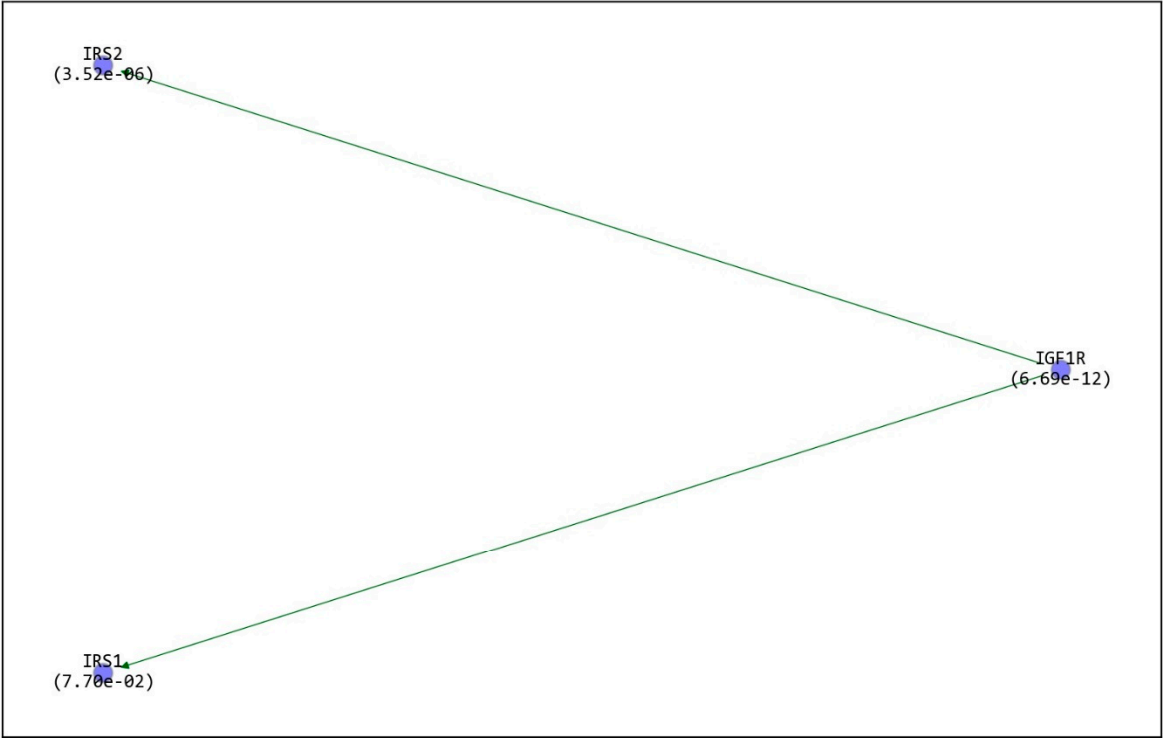
GIN2 for PIK3CA on KEGG in CRISPR screening



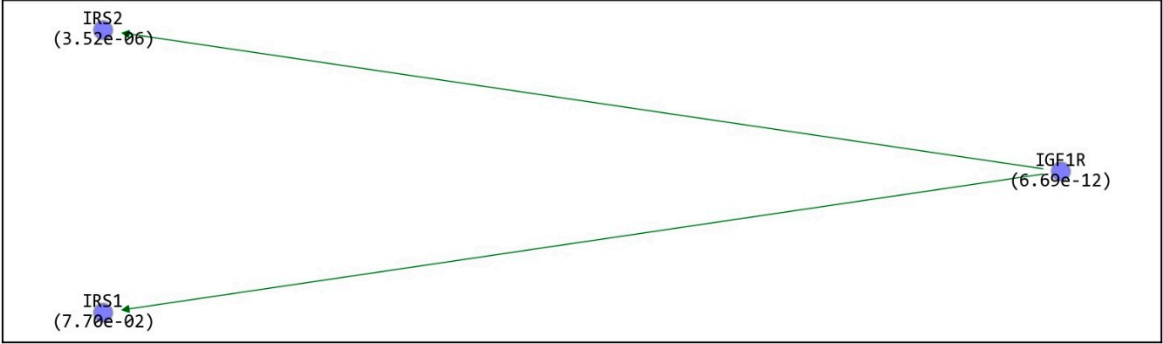
GIN1 for PIK3CA on KEGG in CRISPR screening



GIN2 for PTEN on KEGG in CRISPR screening



GIN1 for PTEN on KEGG in CRISPR screening



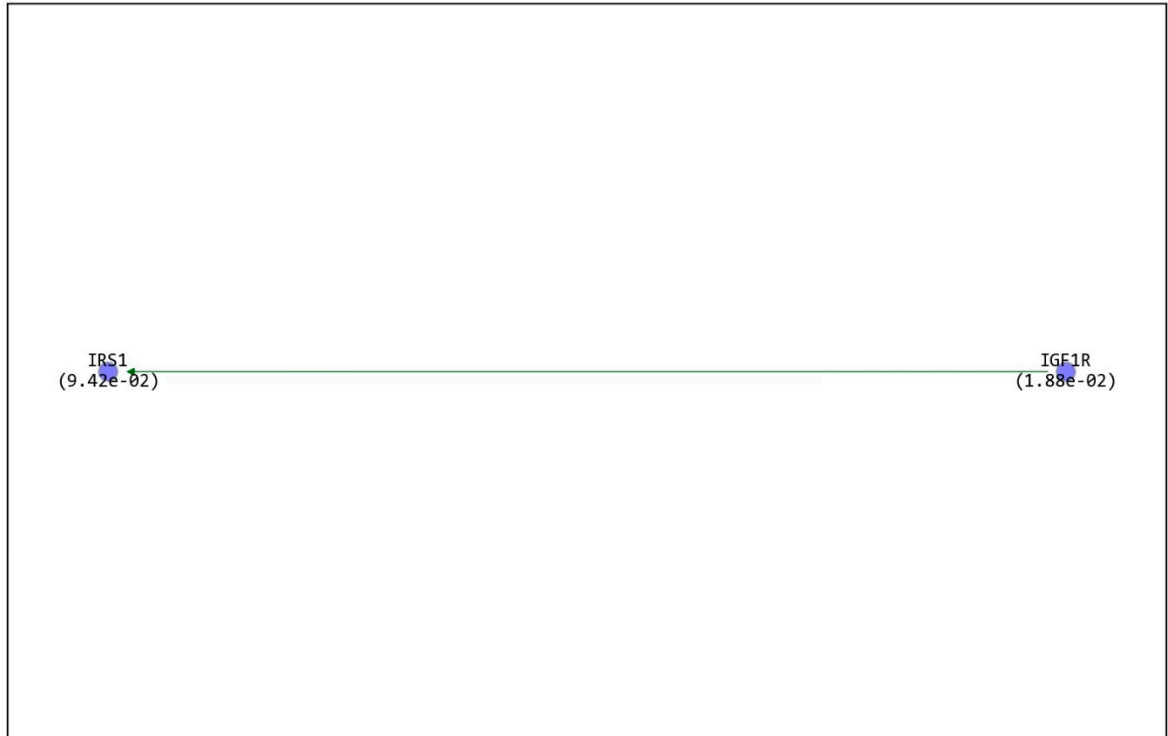
GIN2 for RB1 on KEGG in CRISPR screening



GIN1 for RB1 on KEGG in CRISPR screening



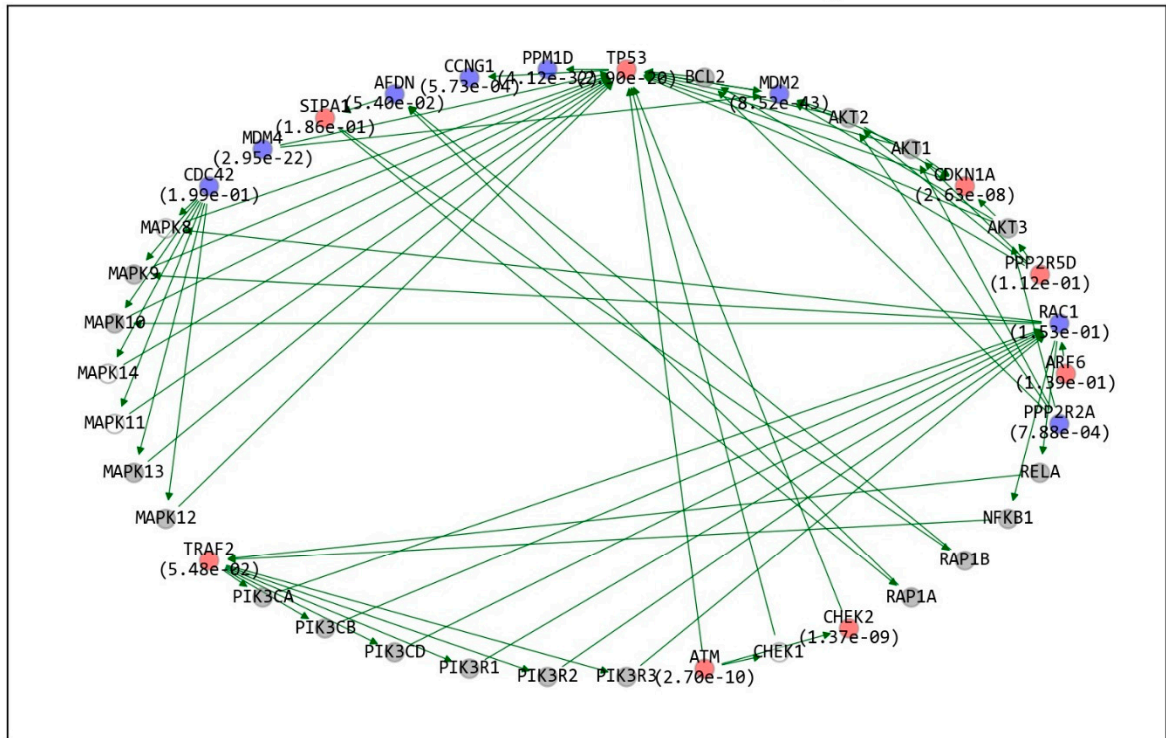
GIN2 for RPL22 on KEGG in CRISPR screening



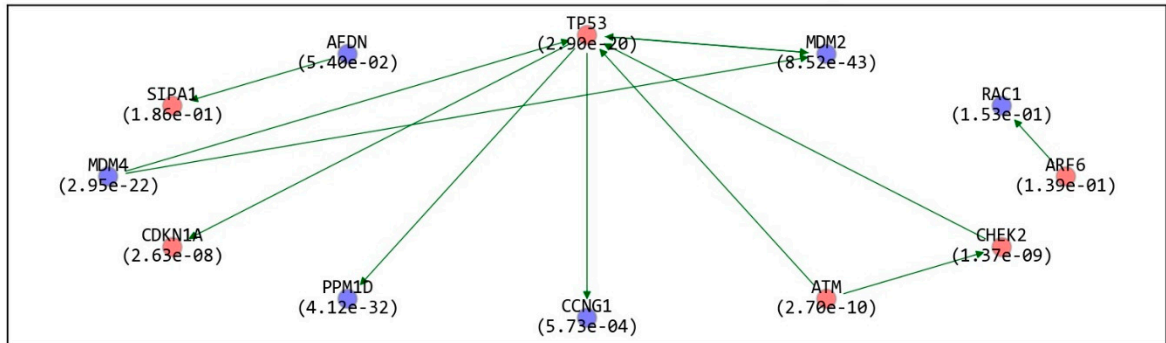
GIN1 for RPL22 on KEGG in CRISPR screening



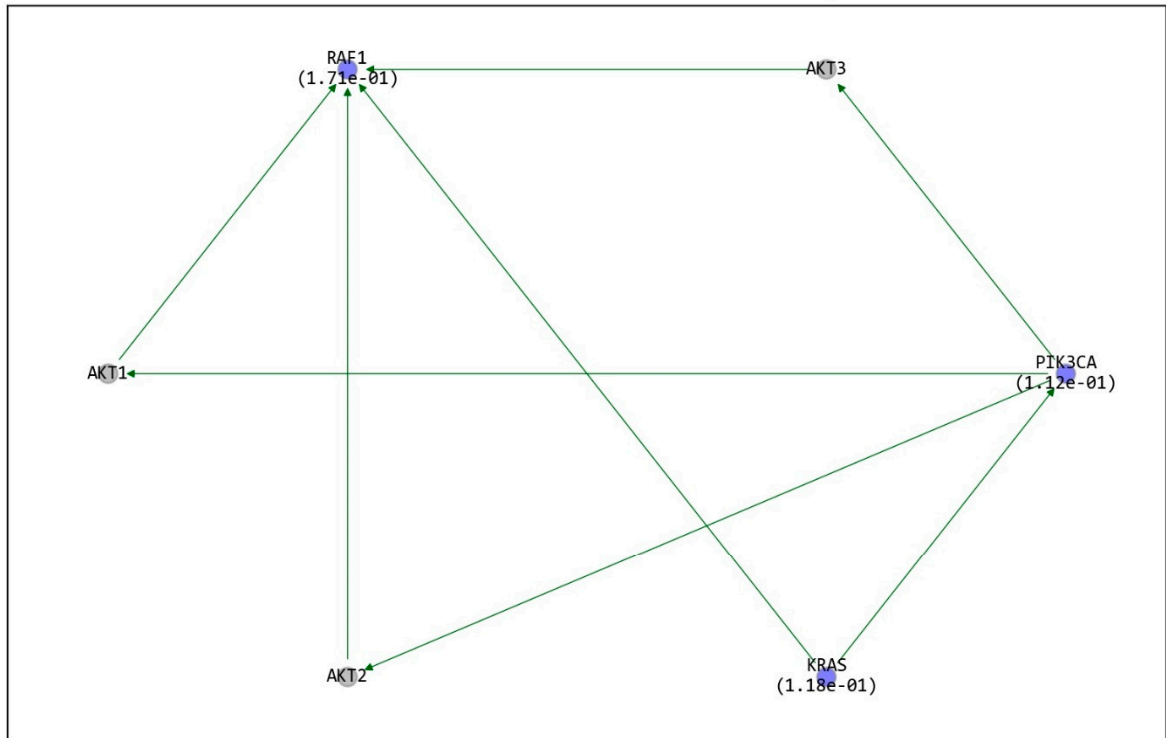
GIN2 for TP53 on KEGG in CRISPR screening



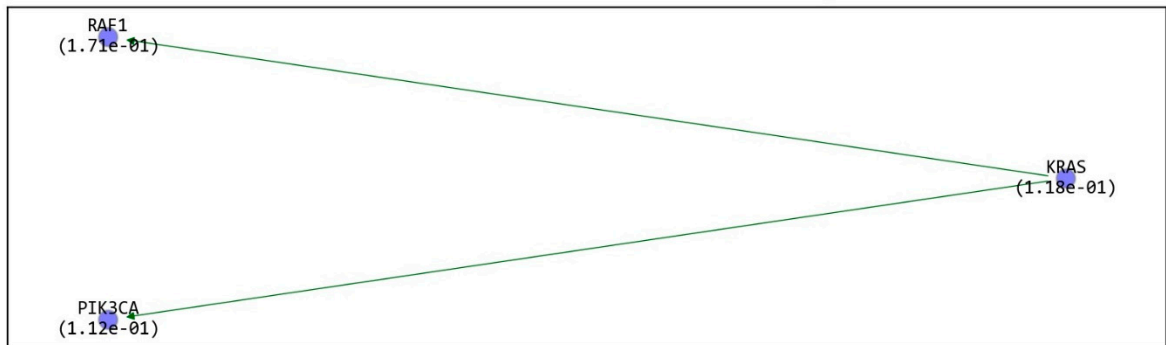
GIN1 for TP53 on KEGG in CRISPR screening



GIN2 for VHL on KEGG in CRISPR screening

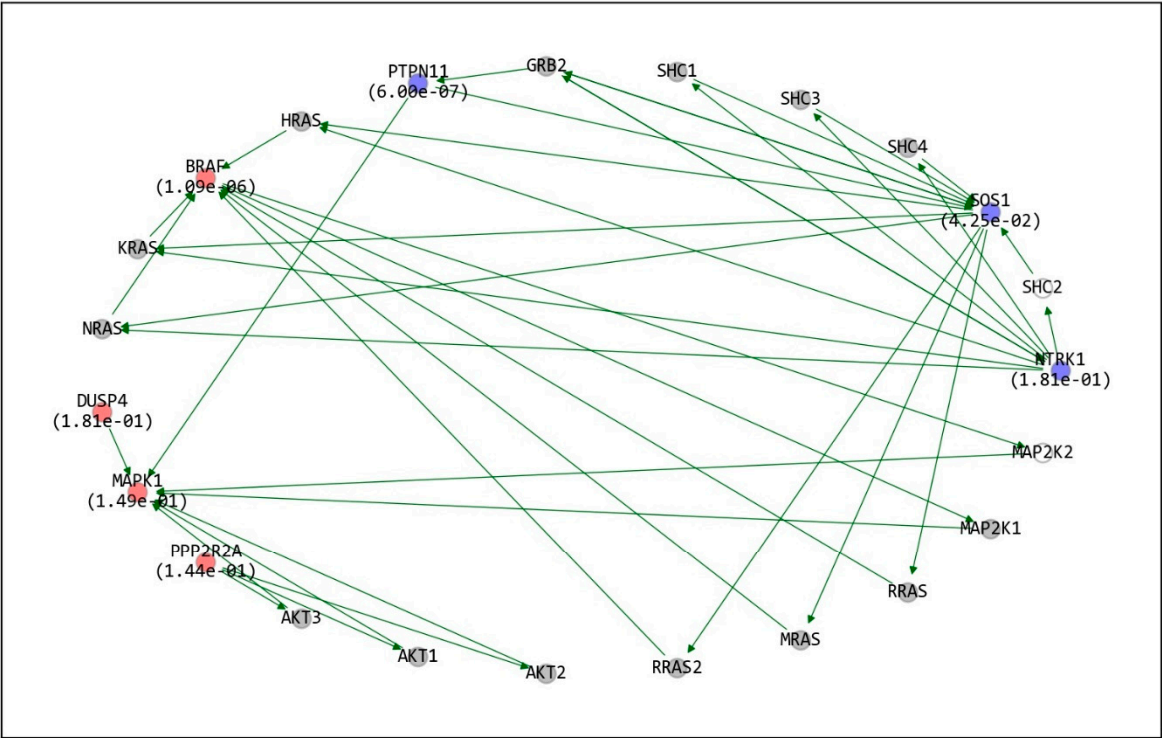


GIN1 for VHL on KEGG in CRISPR screening

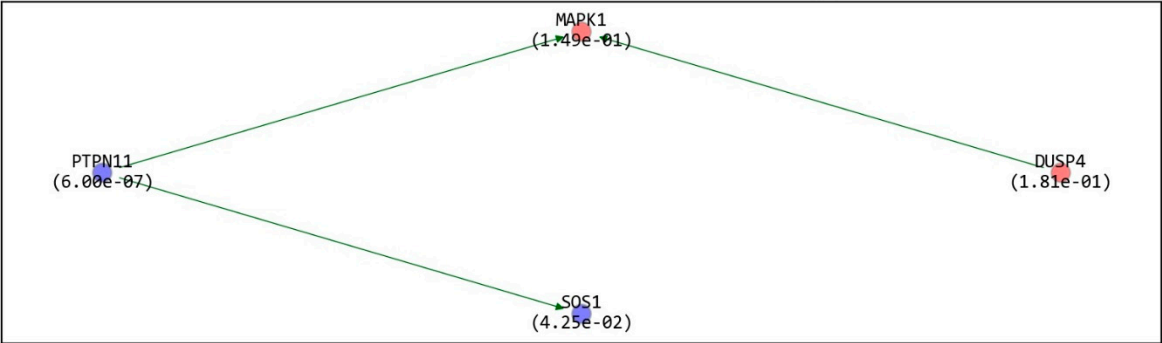


2. SPNs based on KEGG networks from shRNA screening

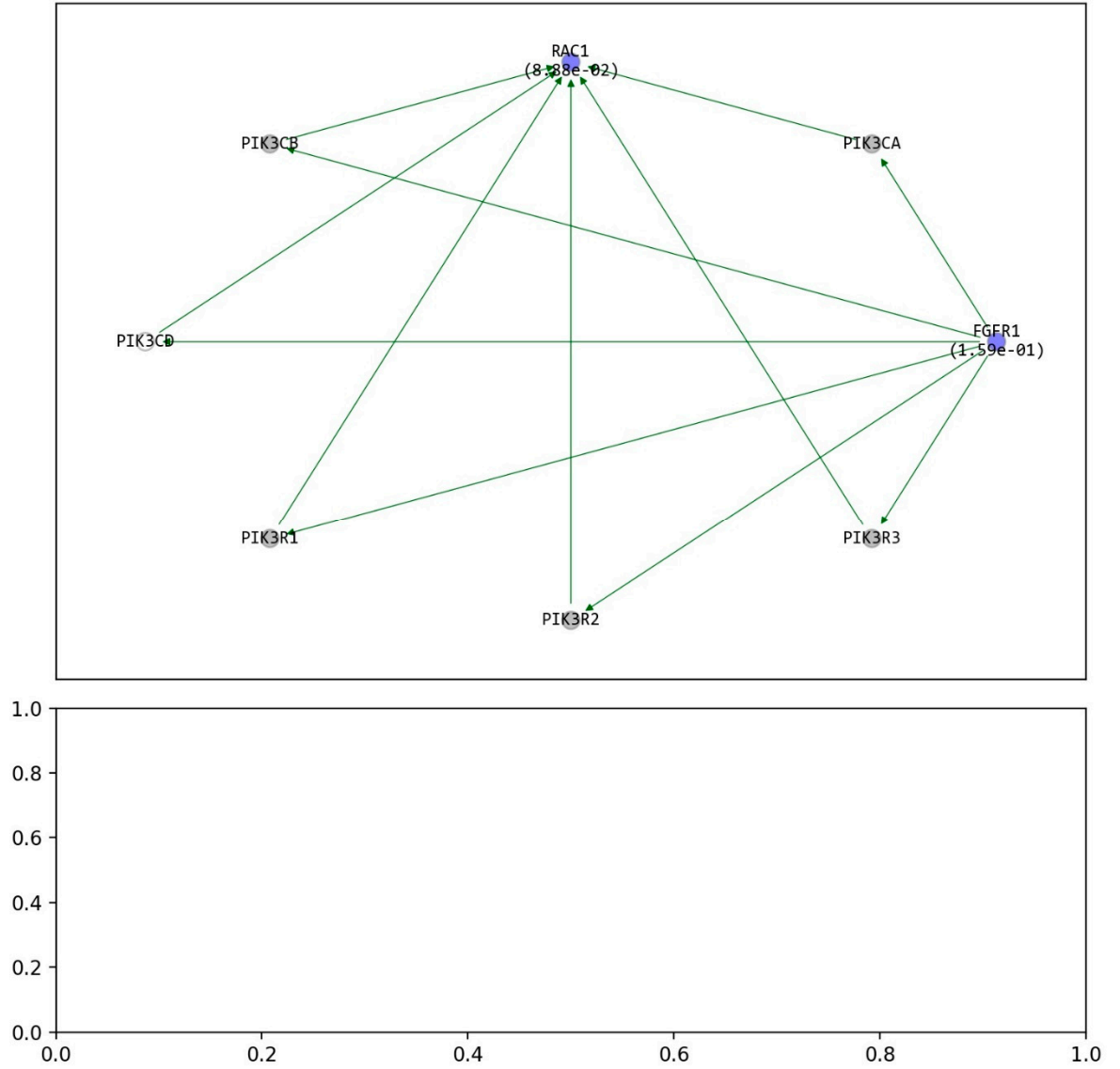
GIN2 for BRAF on KEGG in shRNA screening



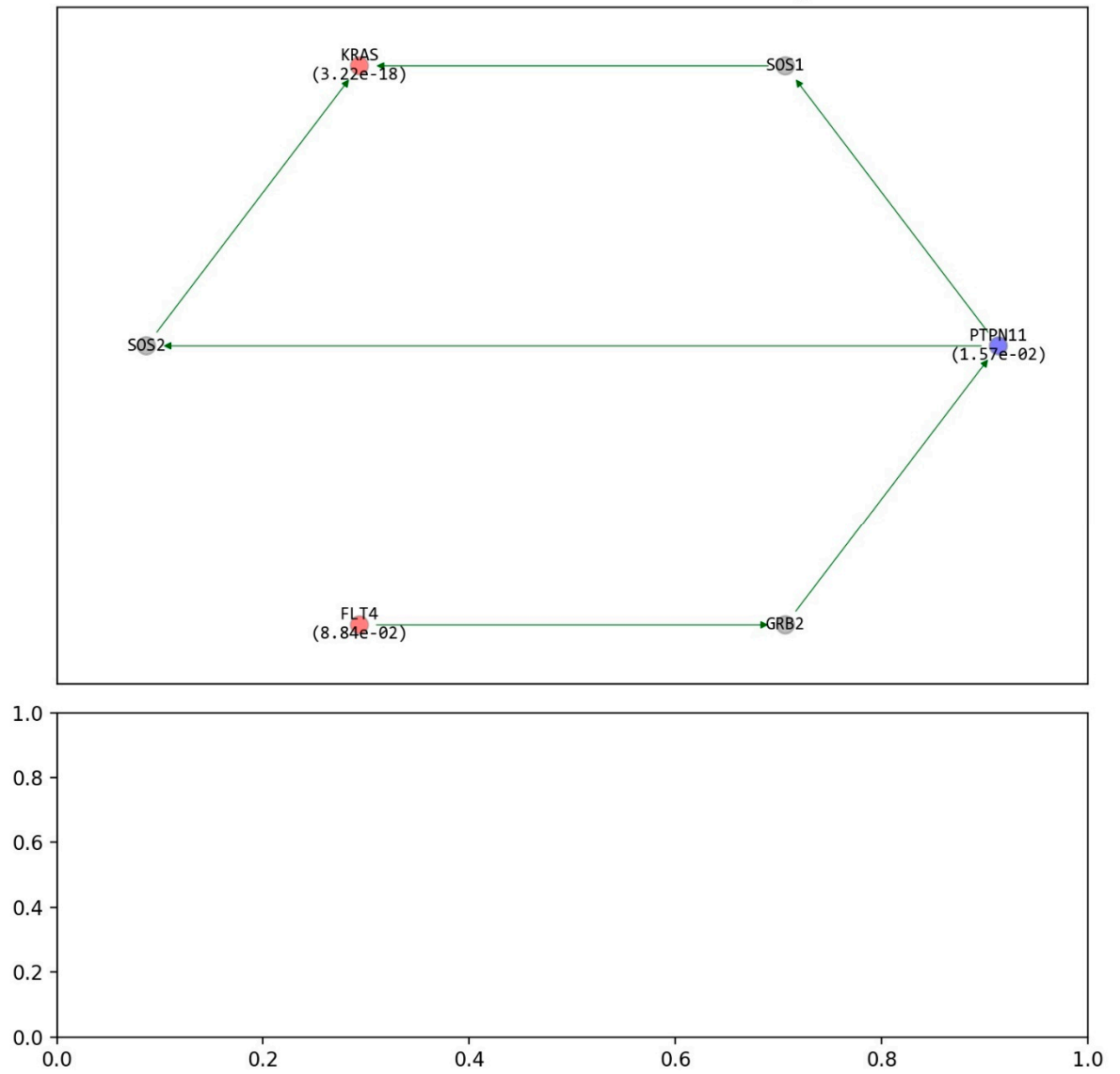
GIN1 for BRAF on KEGG in shRNA screening



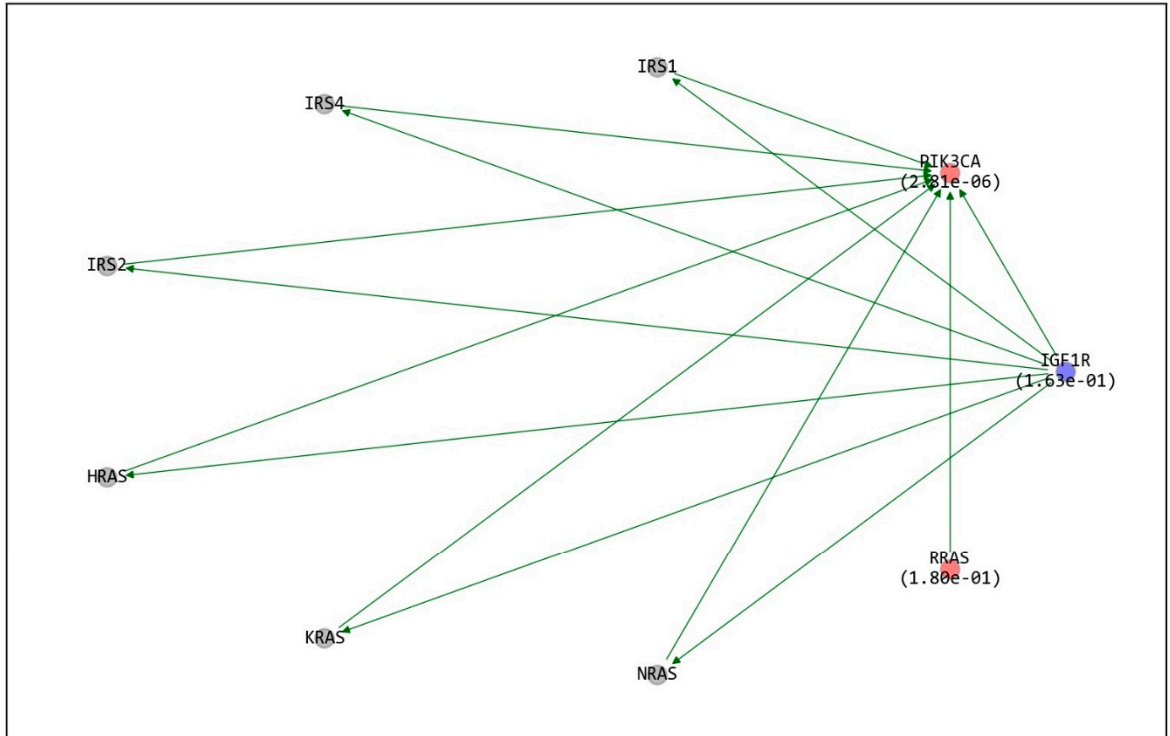
GIN2 for FBXW10 on KEGG in shRNA screening



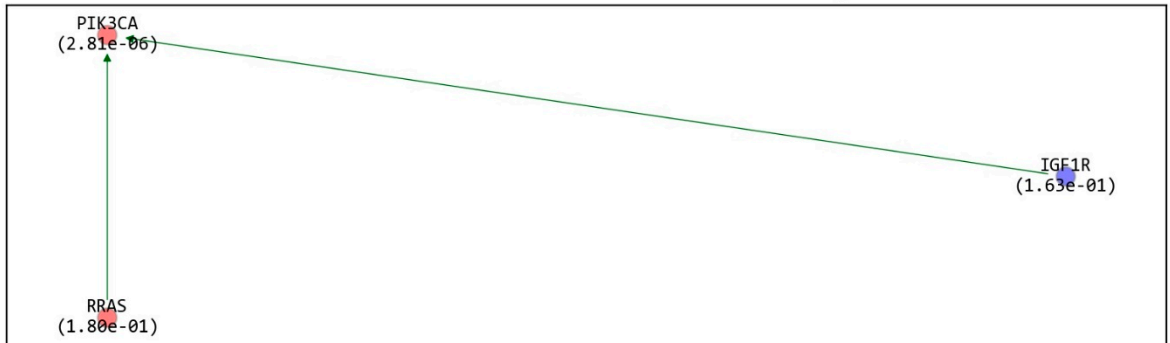
GIN2 for KRAS on KEGG in shRNA screening



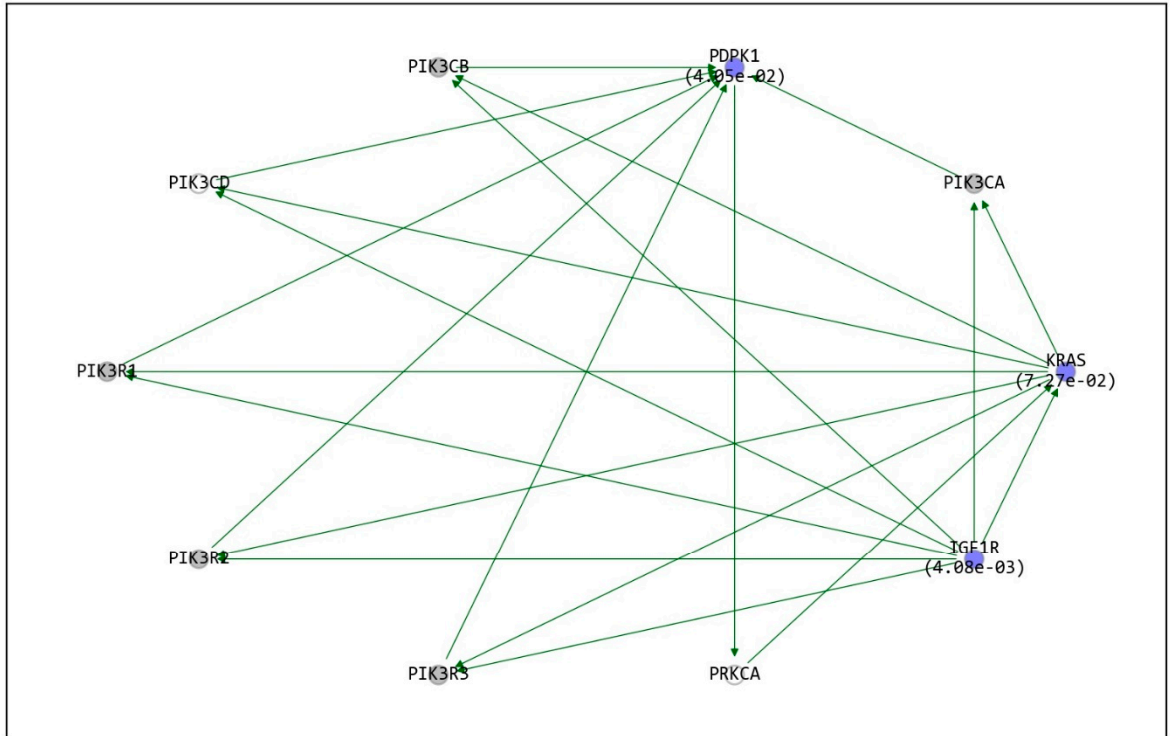
GIN2 for PIK3CA on KEGG in shRNA screening



GIN1 for PIK3CA on KEGG in shRNA screening



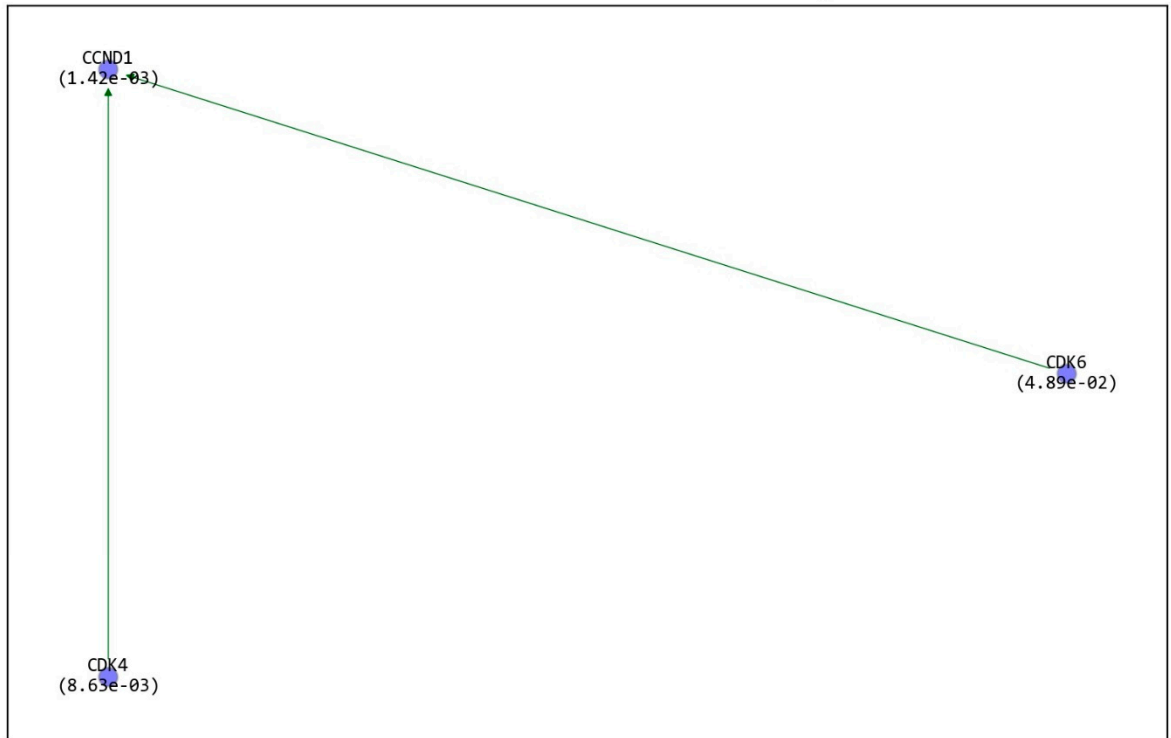
GIN2 for PTEN on KEGG in shRNA screening



GIN1 for PTEN on KEGG in shRNA screening



GIN2 for RB1 on KEGG in shRNA screening



GIN1 for RB1 on KEGG in shRNA screening

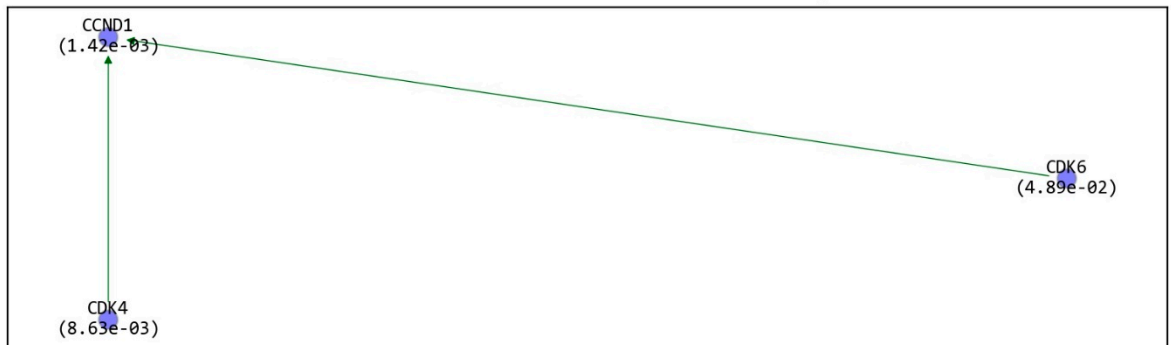


Figure 2: A network diagram showing interactions between various proteins. The nodes are labeled with protein names and their corresponding p-values in parentheses. The network is highly interconnected, with many lines connecting different proteins. The proteins are color-coded: red (e.g., ATM, GADD45, ACDKN2D, PLK1, MDM2, PPM1D, YWHAE, PPP2R2A, AKT3, AKT1, AKT2, BCL2, CREB3L4, JUN, FOS, DAPK3, MAPK1, MAPK3, GRK2, CSNK1A1L, CSNK1A1, CHEK2, NBNB1, DUSP2, MAPK14, MAPK11, MAPK13, MAPK12, MAPK8, MAPK9, MAPK10, CHEK1, MDM4, CAMK2A, CREBBP, TP53, EP300, USP7, FOXO6, FOXO1, FOXO3, FOXO4), blue (e.g., GADD45, ACDKN2D, PLK1, MDM2, PPM1D, YWHAE, PPP2R2A, AKT3, AKT1, AKT2, BCL2, CREB3L4, JUN, FOS, DAPK3, MAPK1, MAPK3, GRK2, CSNK1A1L, CSNK1A1, CHEK2, NBNB1, DUSP2, MAPK14, MAPK11, MAPK13, MAPK12, MAPK8, MAPK9, MAPK10, CHEK1, MDM4, CAMK2A, CREBBP, TP53, EP300, USP7, FOXO6, FOXO1, FOXO3, FOXO4), green (e.g., GADD45, ACDKN2D, PLK1, MDM2, PPM1D, YWHAE, PPP2R2A, AKT3, AKT1, AKT2, BCL2, CREB3L4, JUN, FOS, DAPK3, MAPK1, MAPK3, GRK2, CSNK1A1L, CSNK1A1, CHEK2, NBNB1, DUSP2, MAPK14, MAPK11, MAPK13, MAPK12, MAPK8, MAPK9, MAPK10, CHEK1, MDM4, CAMK2A, CREBBP, TP53, EP300, USP7, FOXO6, FOXO1, FOXO3, FOXO4), and grey (e.g., GADD45, ACDKN2D, PLK1, MDM2, PPM1D, YWHAE, PPP2R2A, AKT3, AKT1, AKT2, BCL2, CREB3L4, JUN, FOS, DAPK3, MAPK1, MAPK3, GRK2, CSNK1A1L, CSNK1A1, CHEK2, NBNB1, DUSP2, MAPK14, MAPK11, MAPK13, MAPK12, MAPK8, MAPK9, MAPK10, CHEK1, MDM4, CAMK2A, CREBBP, TP53, EP300, USP7, FOXO6, FOXO1, FOXO3, FOXO4).

Network diagram showing interactions between various proteins. The nodes and their associated p-values are:

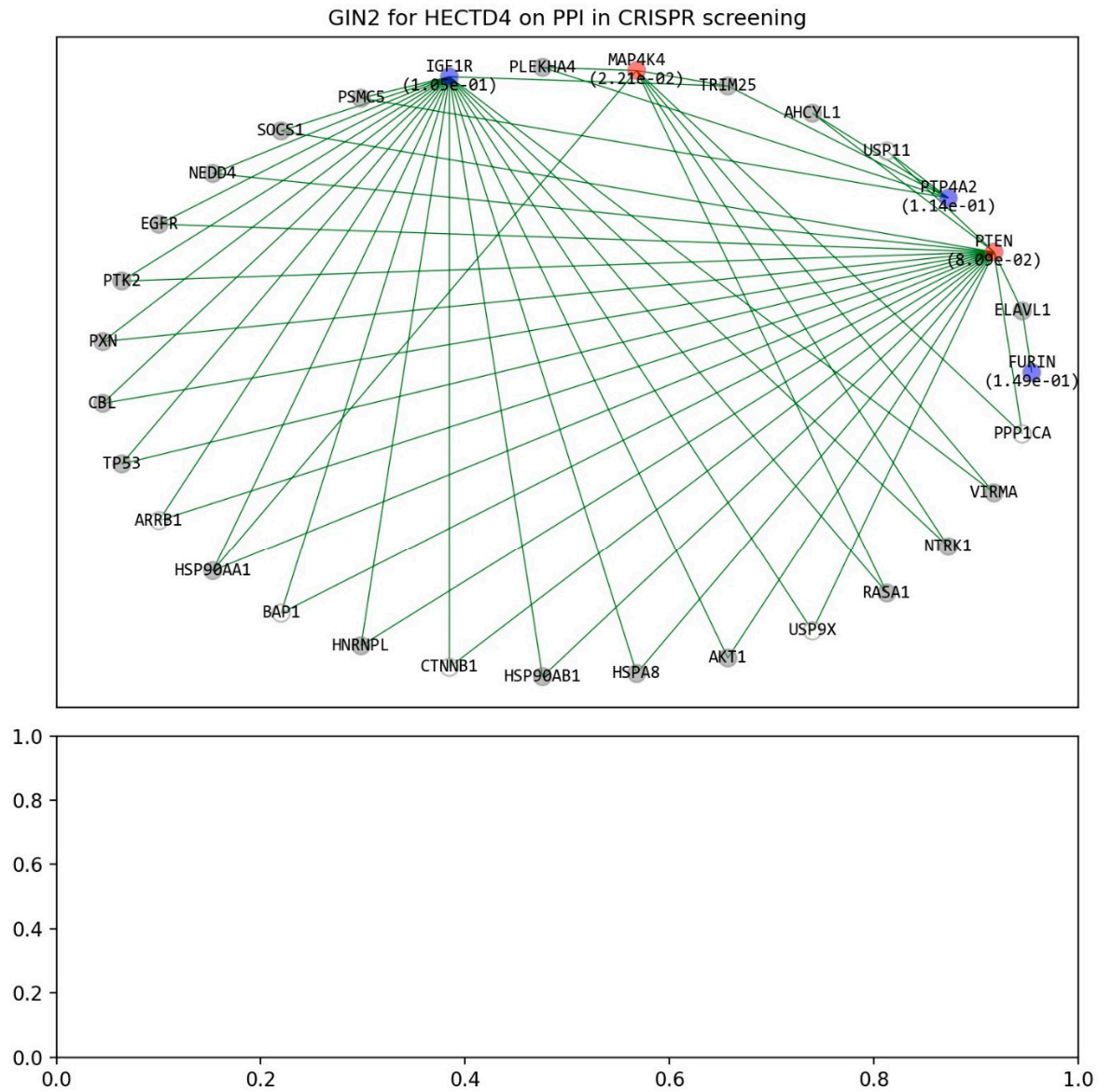
- TP53 (5.44e-23)
- CDKN1A (6.34e-05)
- GADD45A (1.61e-01)
- PPM1D (1.48e-09)
- MDM2 (1.33e-28)
- MDM4 (2.22e-17)
- ATM (1.80e-07)
- CHEK2 (9.04e-14)
- CSNK1A1 (1.15e-01)
- CSNK1A1L (2.64e-03)
- GRK2 (2.90e-02)

Interactions (edges) are shown between the following pairs of proteins:

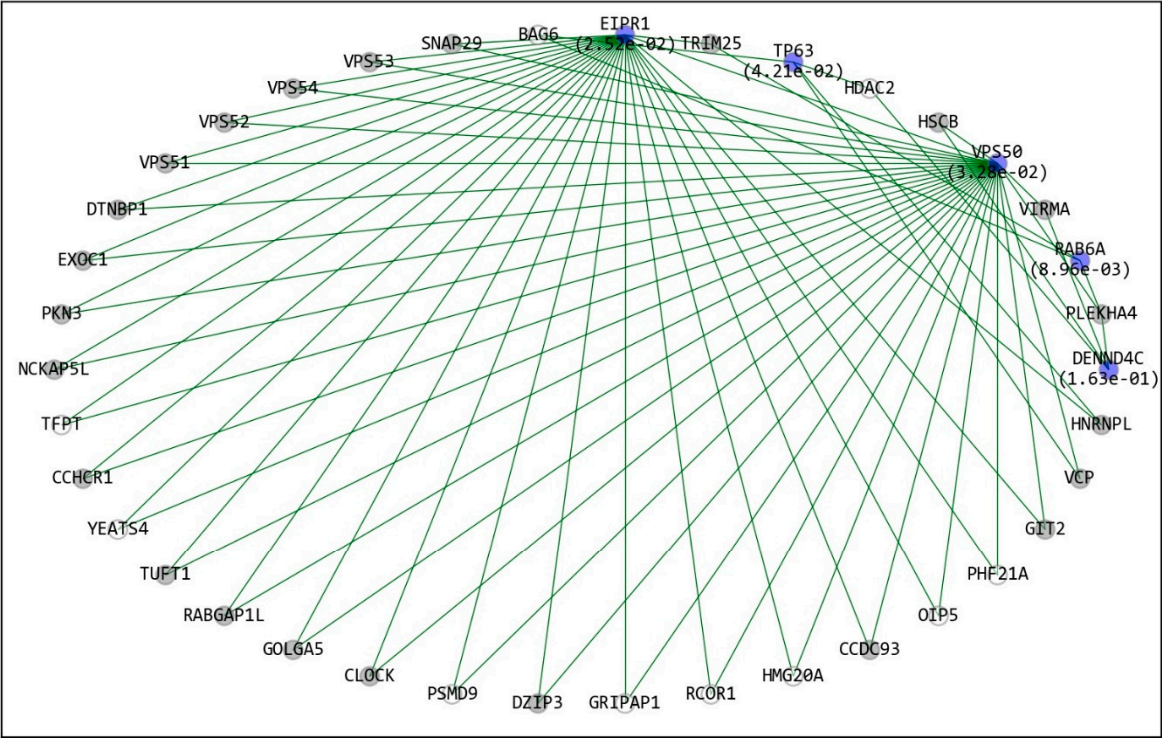
- TP53 and CDKN1A
- TP53 and GADD45A
- TP53 and PPM1D
- TP53 and MDM2
- TP53 and MDM4
- TP53 and ATM
- TP53 and CHEK2
- CDKN1A and TP53
- GADD45A and TP53
- PPM1D and TP53
- MDM2 and TP53
- MDM4 and TP53
- ATM and TP53
- CHEK2 and TP53
- CSNK1A1 and CSNK1A1L
- GRK2 and CSNK1A1L

Figure S6. SPNs on PPI networks from (a) CRISPR and (b) shRNA screenings for the mutated genes in Figure 5.

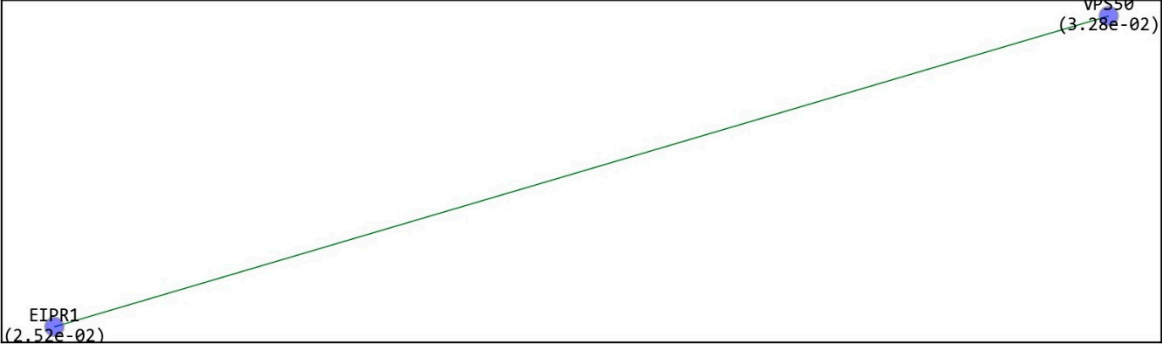
1. SPNs based on PPI networks from CRISPR screening



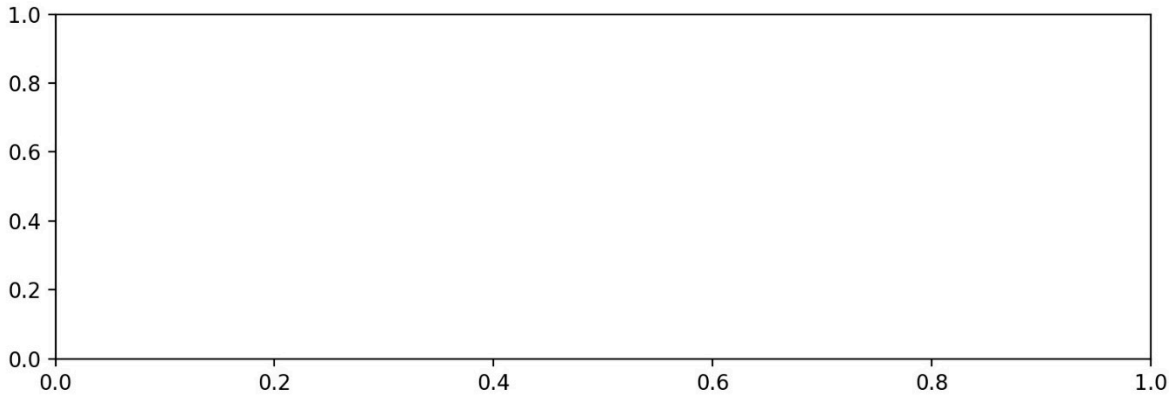
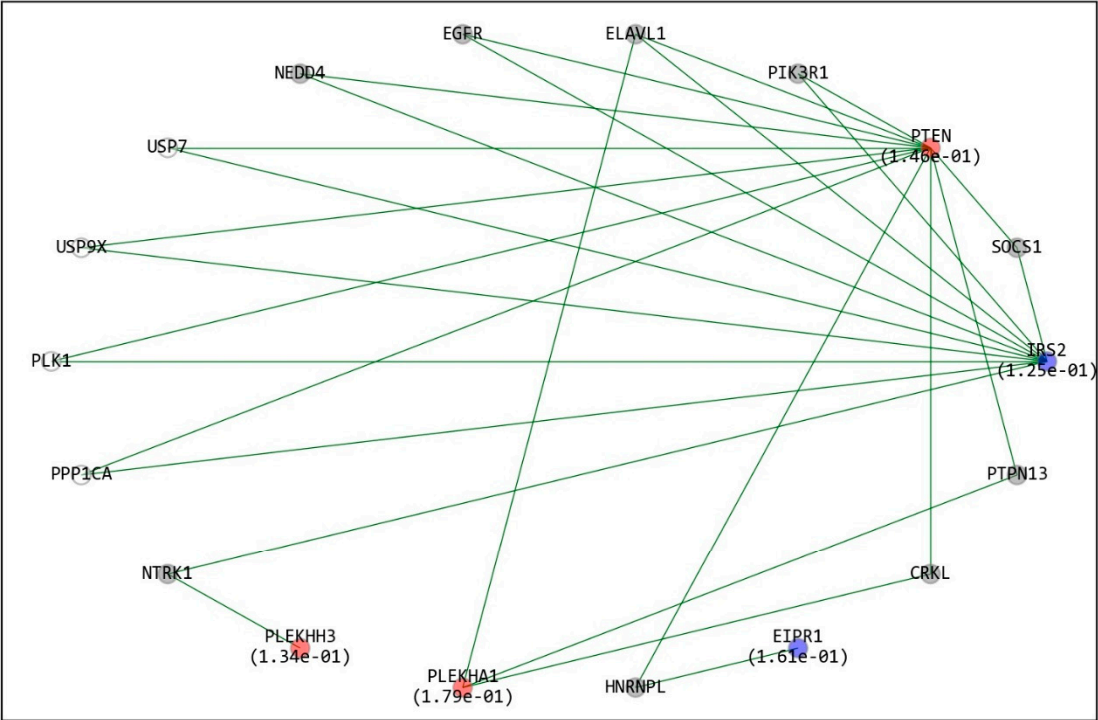
GIN2 for MAGEA2 on PPI in CRISPR screening



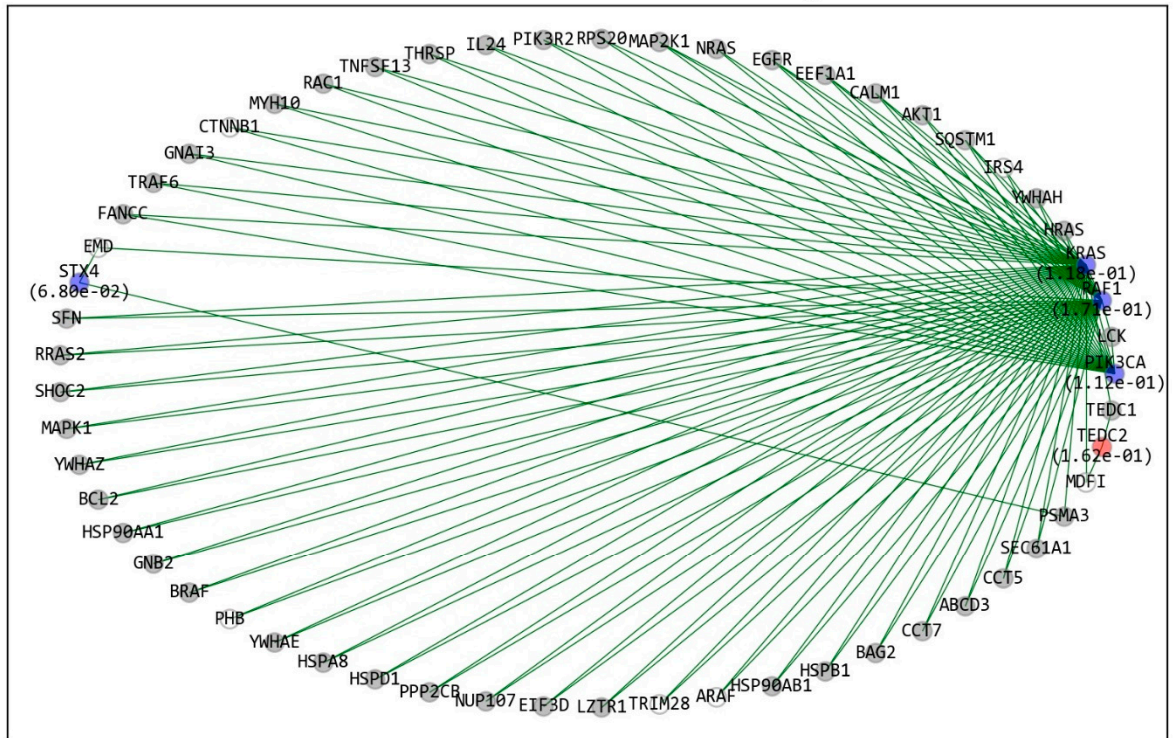
GIN1 for MAGEA2 on PPI in CRISPR screening



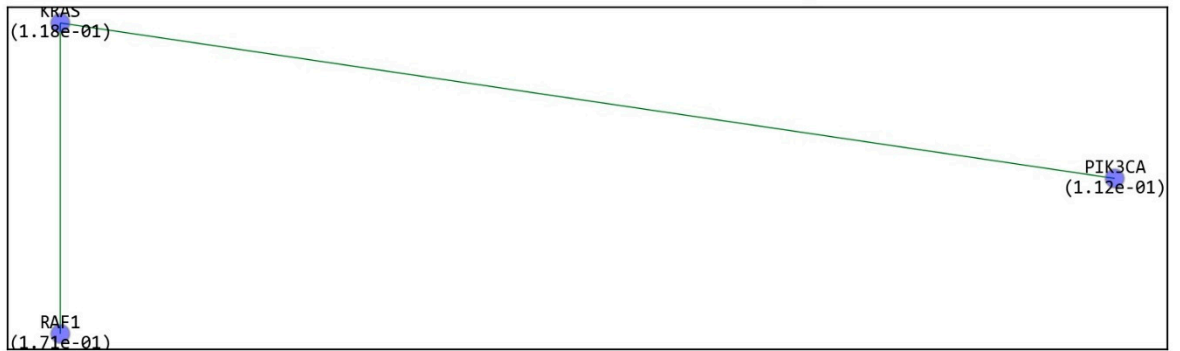
GIN2 for CCDC57 on PPI in CRISPR screening



GIN2 for VHL on PPI in CRISPR screening

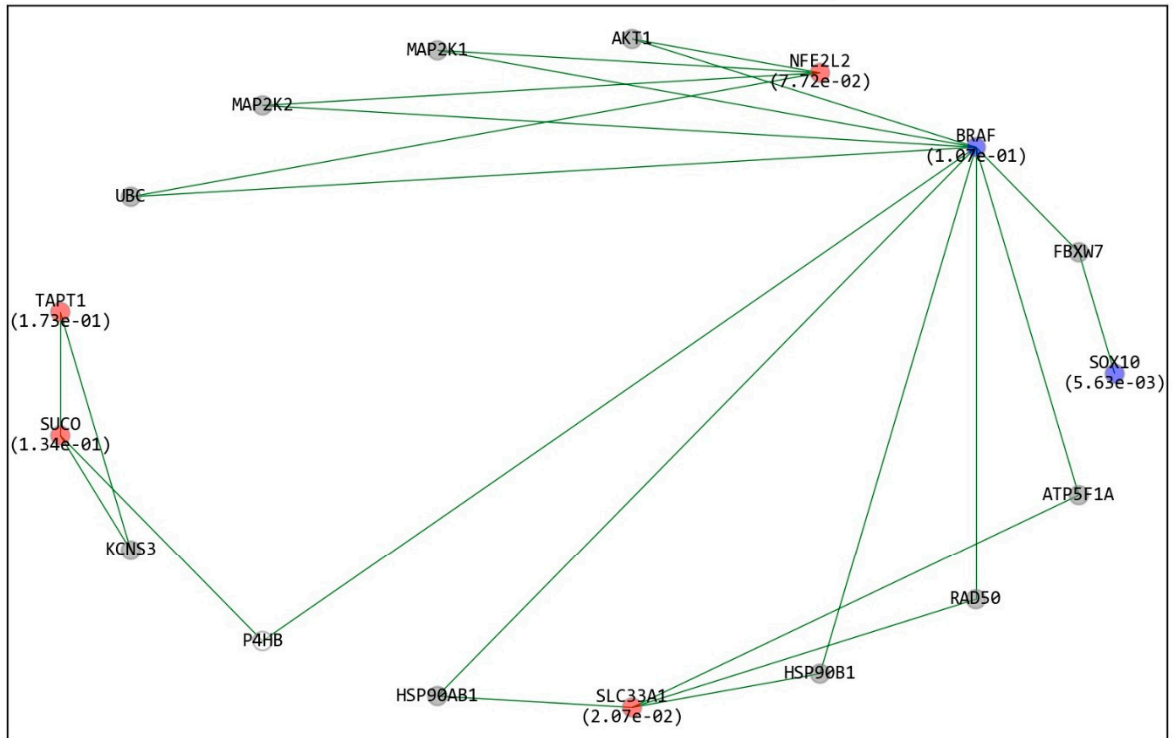


GIN1 for VHL on PPI in CRISPR screening

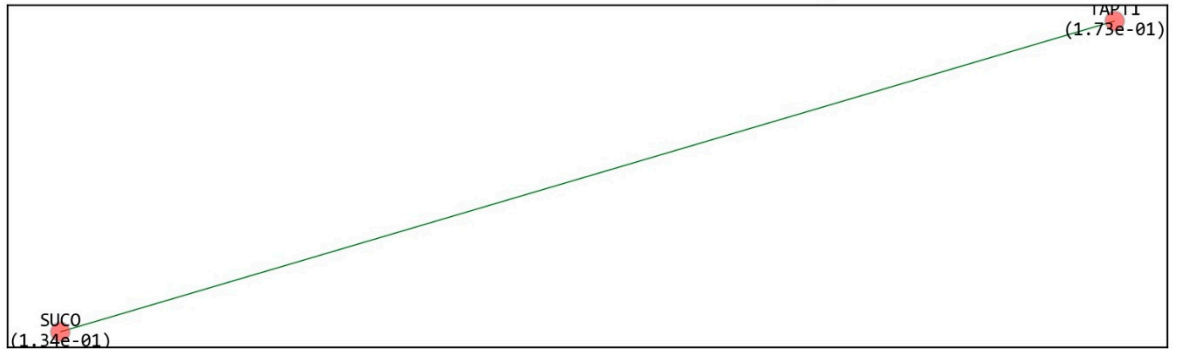


[illegible]

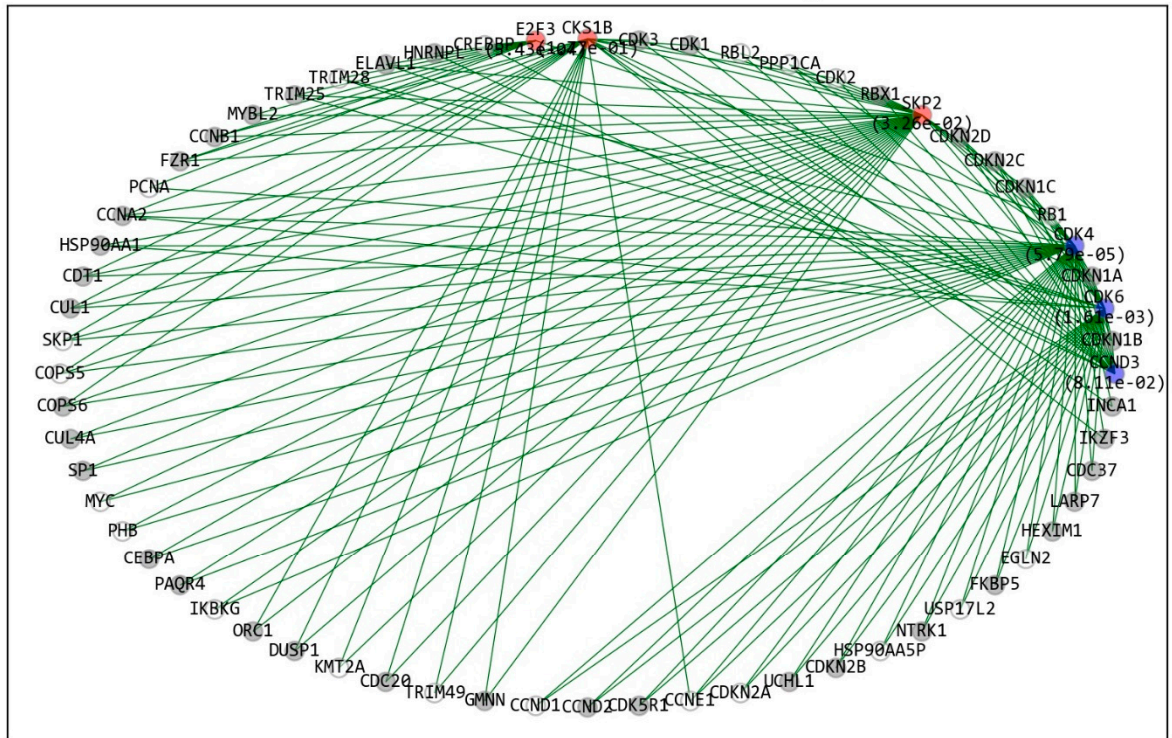
GIN2 for KEAP1 on PPI in CRISPR screening



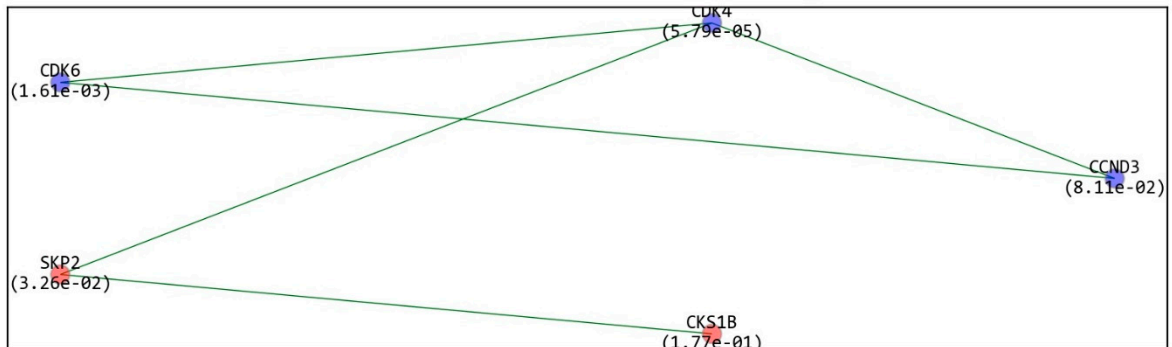
GIN1 for KEAP1 on PPI in CRISPR screening



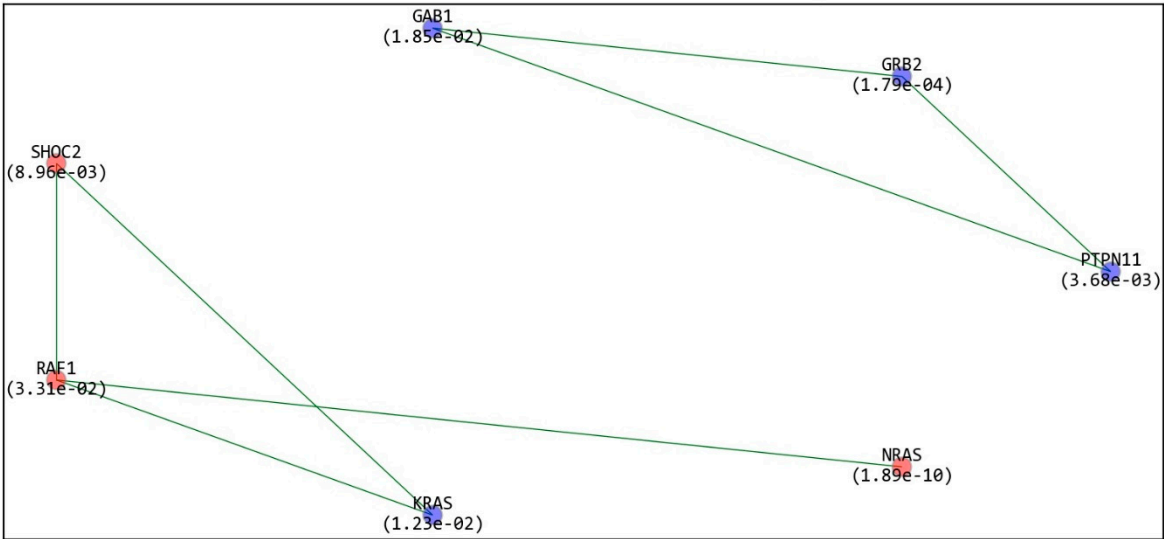
GIN2 for RB1 on PPI in CRISPR screening



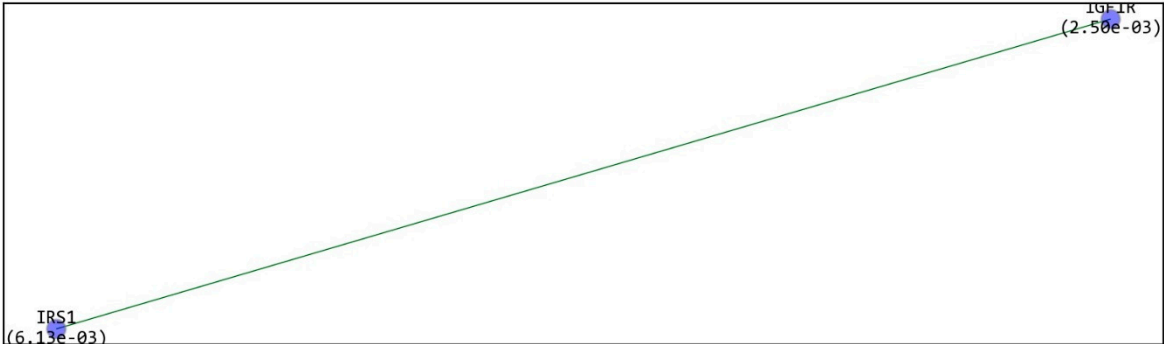
GIN1 for RB1 on PPI in CRISPR screening



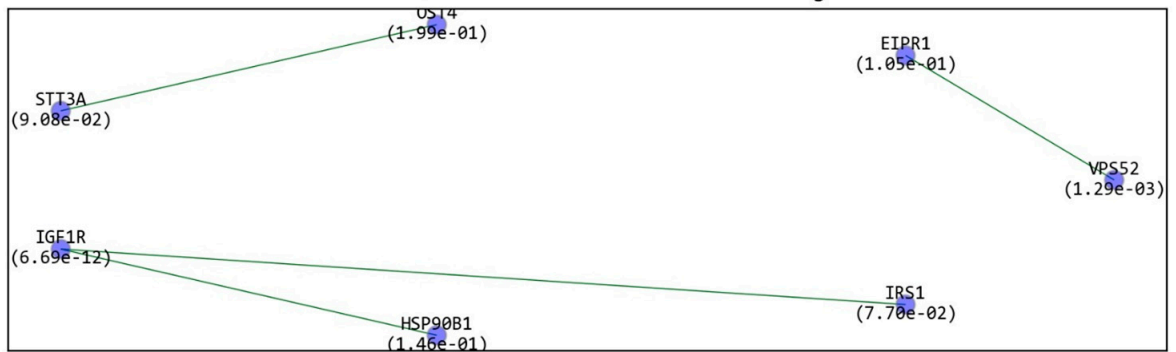
GIN1 for NRAS on PPI in CRISPR screening



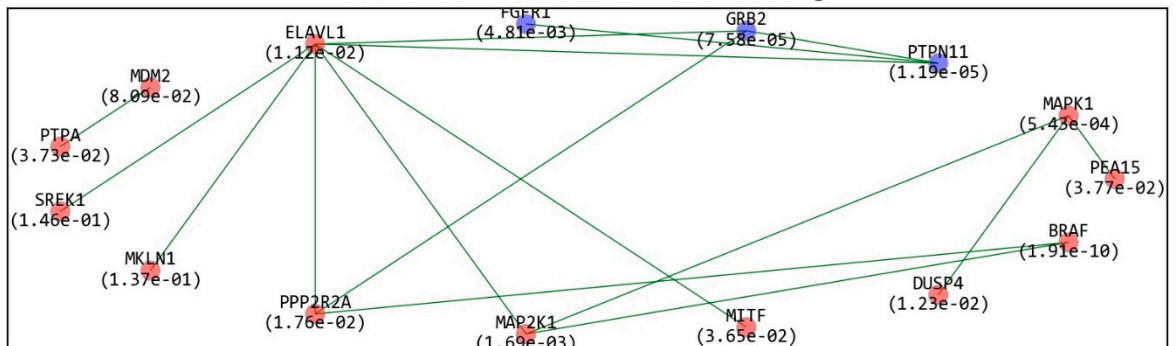
GIN1 for CTCF on PPI in CRISPR screening



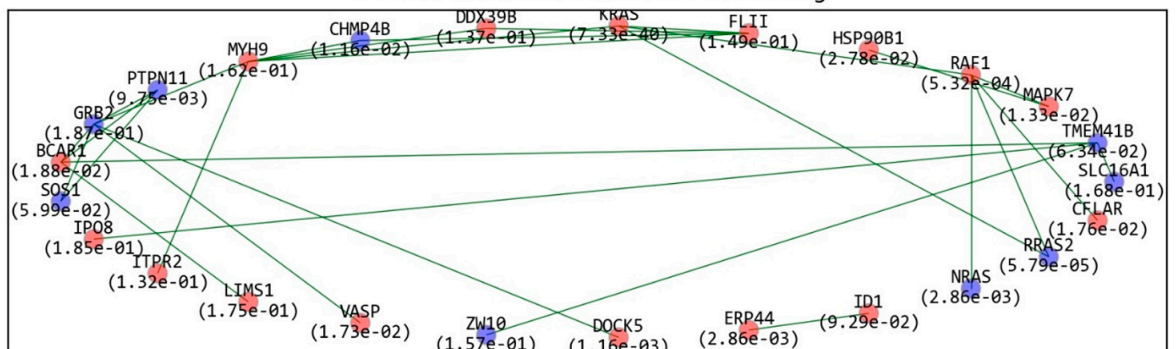
GIN1 for PTEN on PPI in CRISPR screening



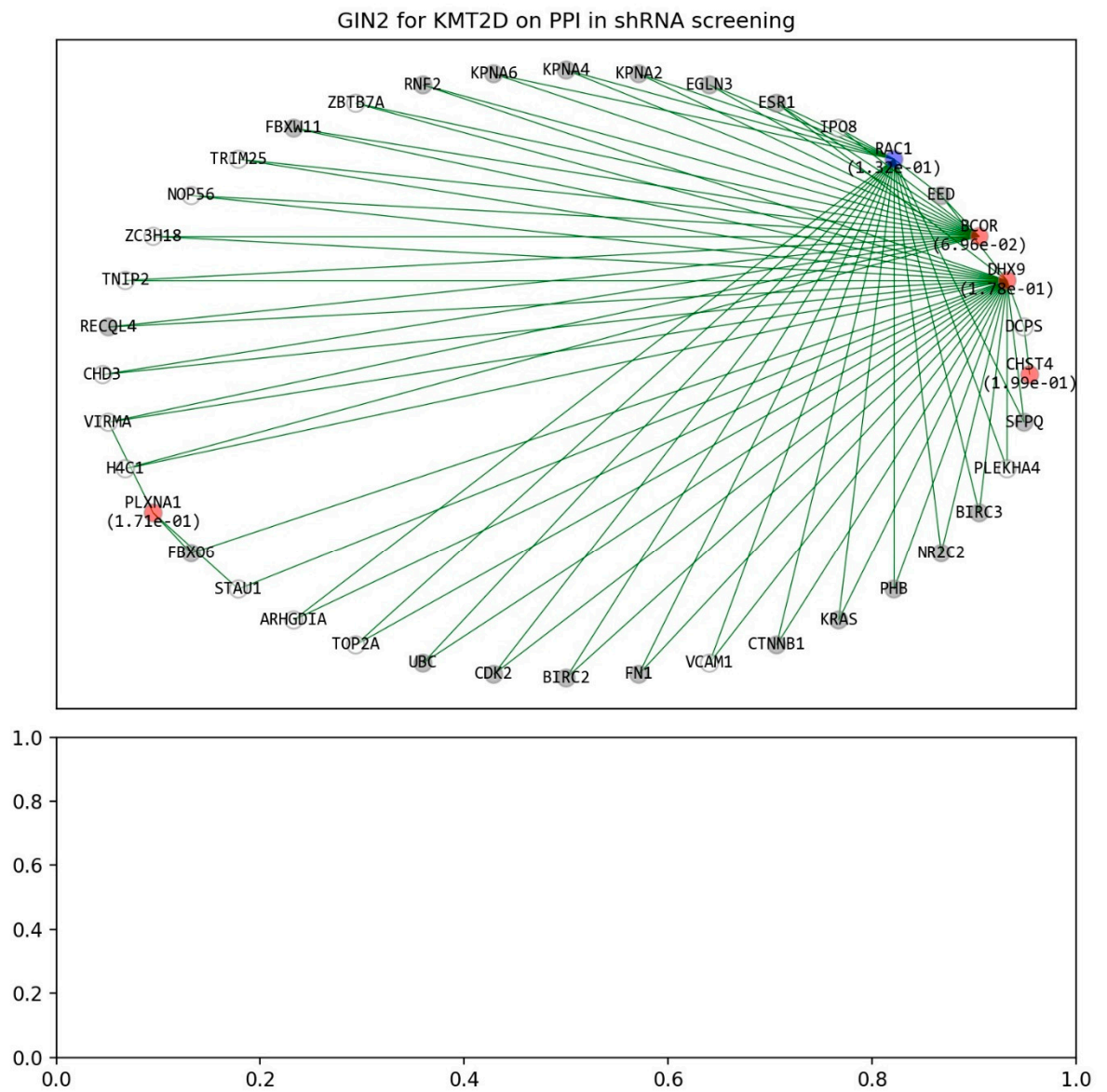
GIN1 for BRAF on PPI in CRISPR screening



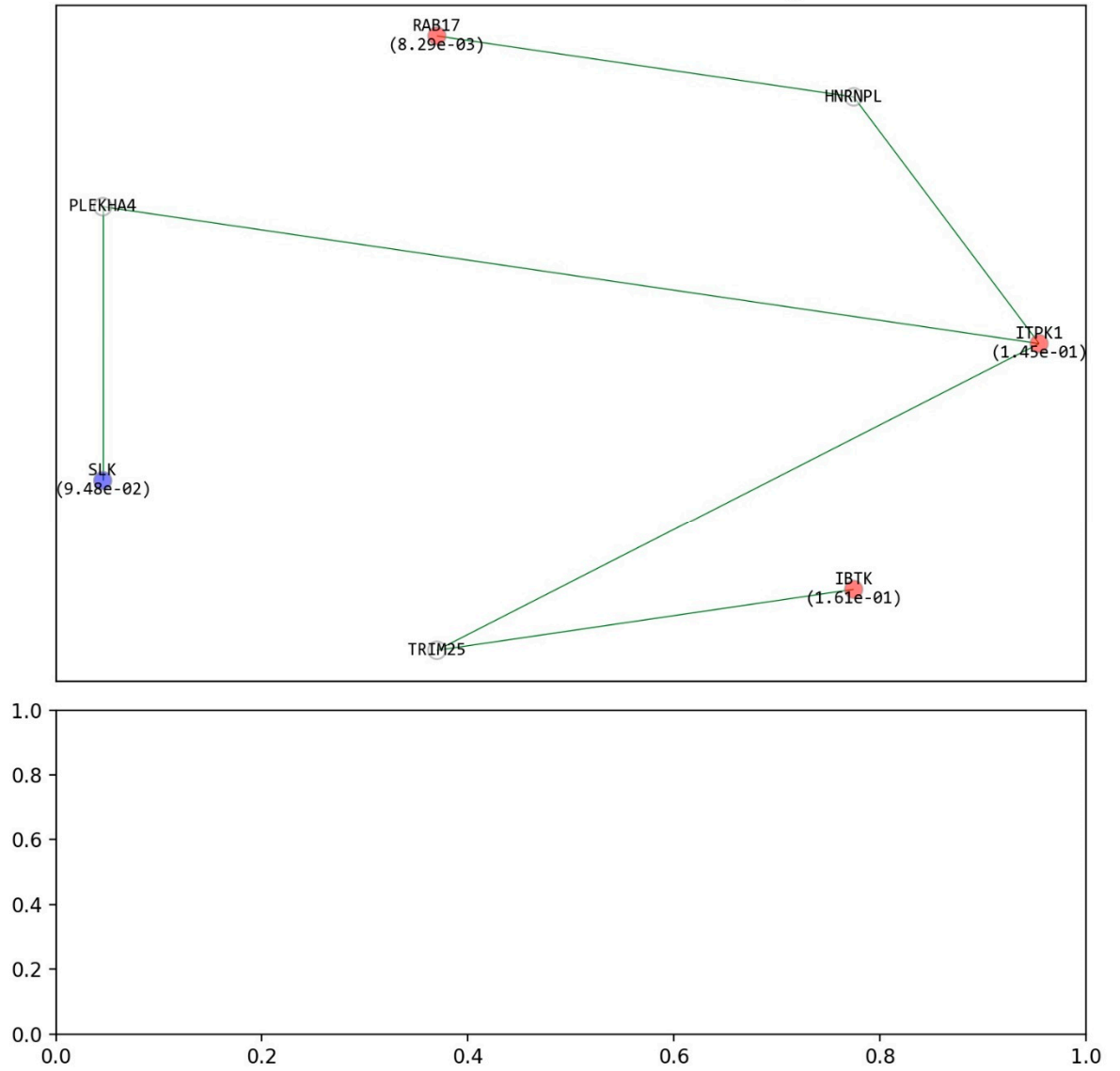
GIN1 for KRAS on PPI in CRISPR screening



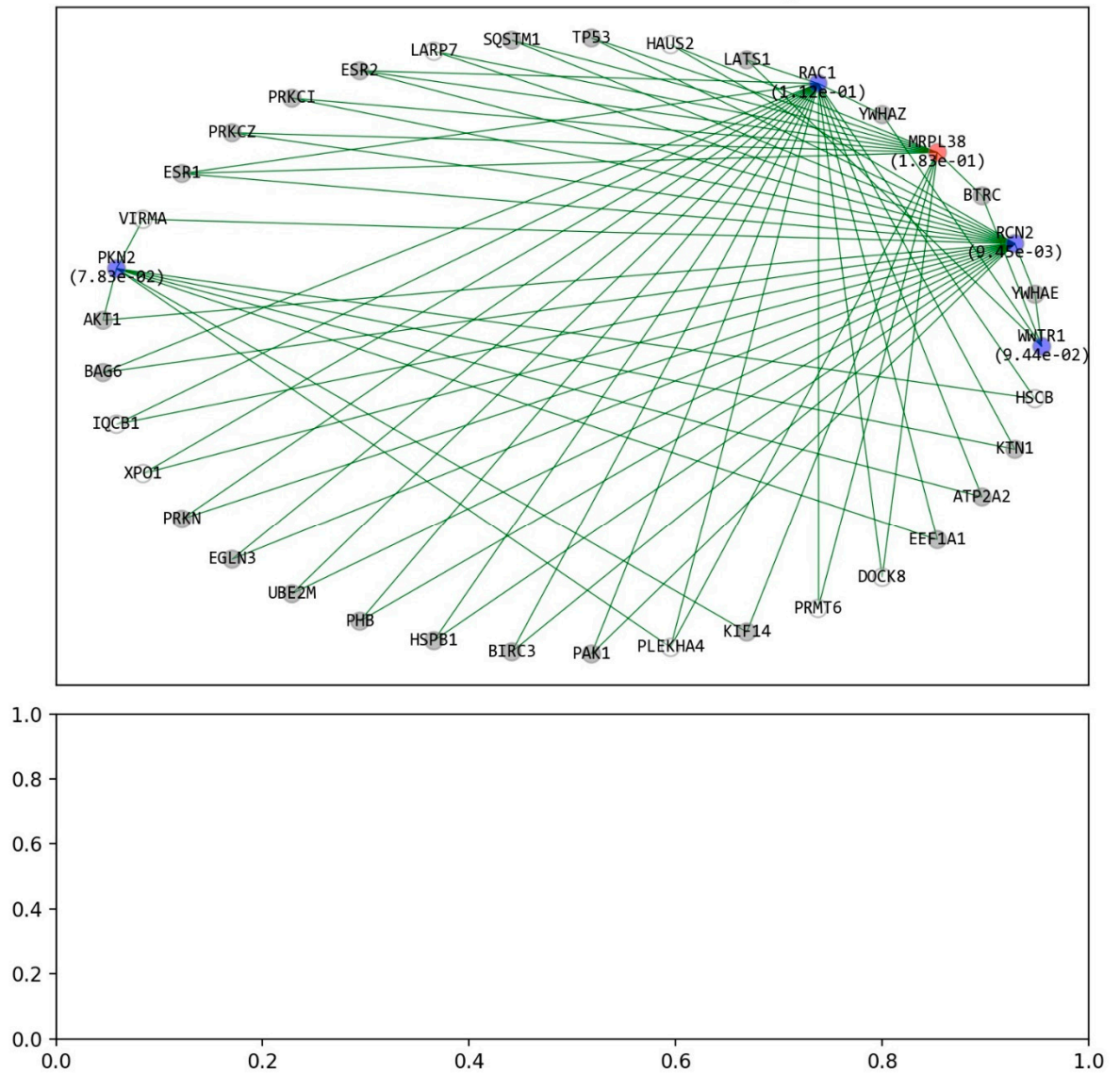
2. SPNs based on PPI networks from shRNA screening



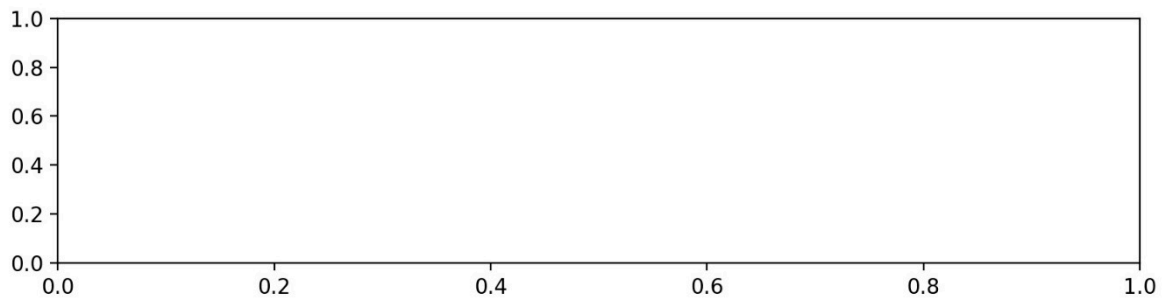
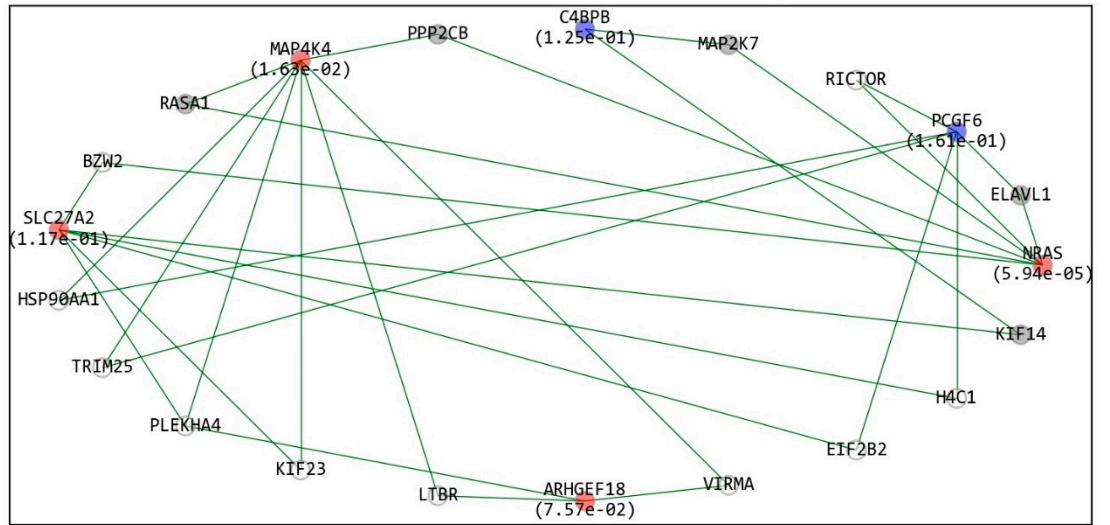
GIN2 for KMT2B on PPI in shRNA screening



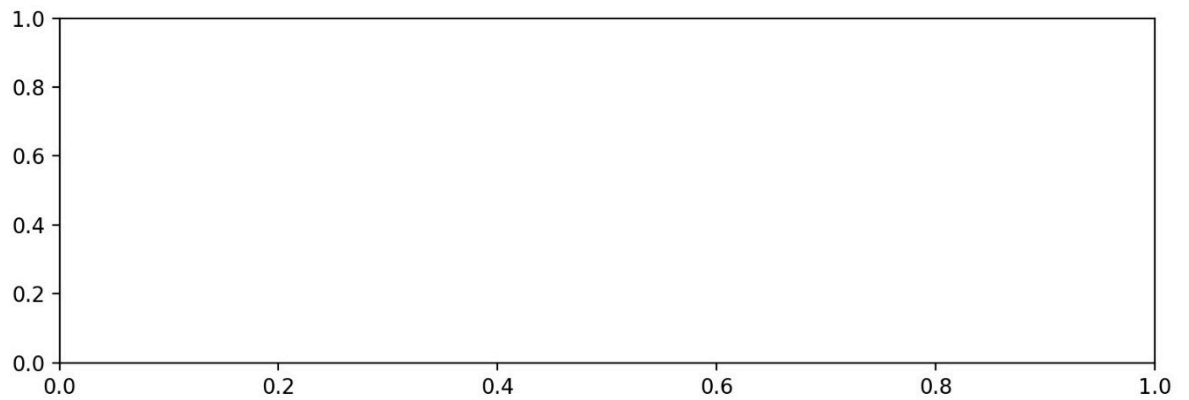
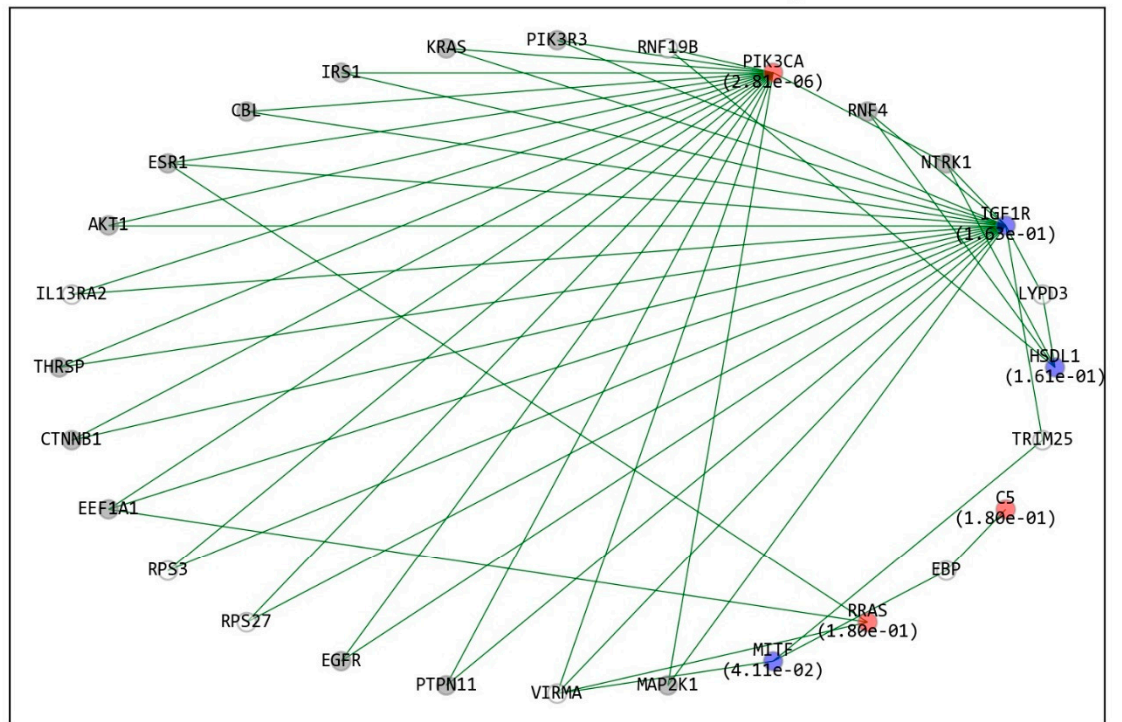
GIN2 for MYH9 on PPI in shRNA screening



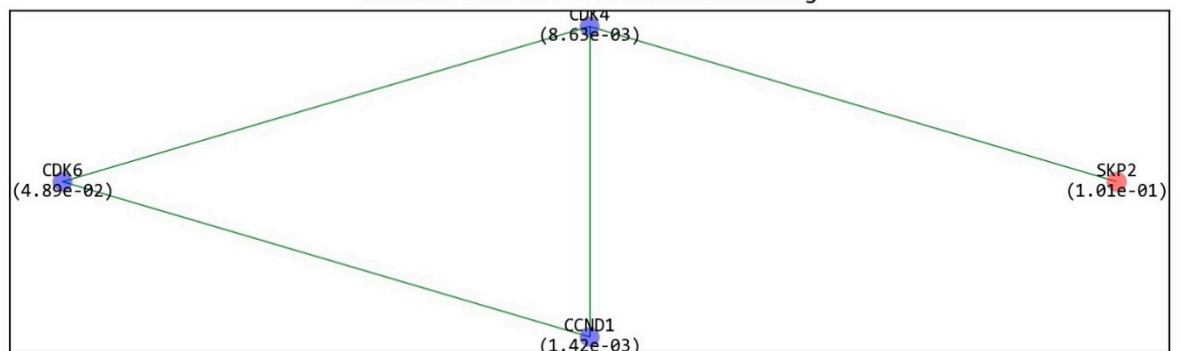
GIN2 for NRAS on PPI in shRNA screening



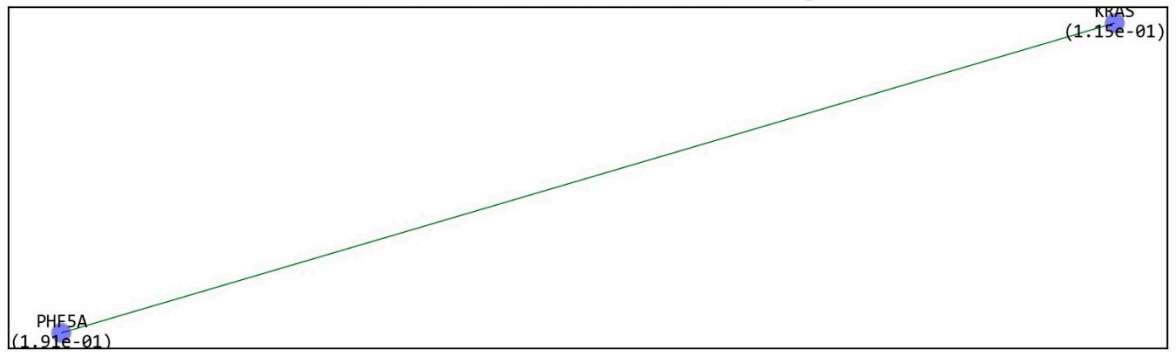
GIN2 for PIK3CA on PPI in shRNA screening



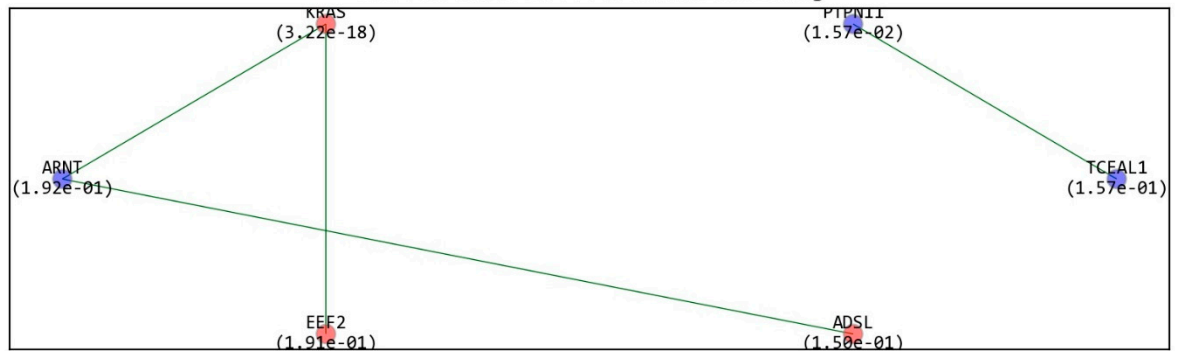
GIN1 for RB1 on PPI in shRNA screening



GIN1 for VHL on PPI in shRNA screening



GIN1 for KRAS on PPI in shRNA screening



GIN1 for BRAF on PPI in shRNA screening

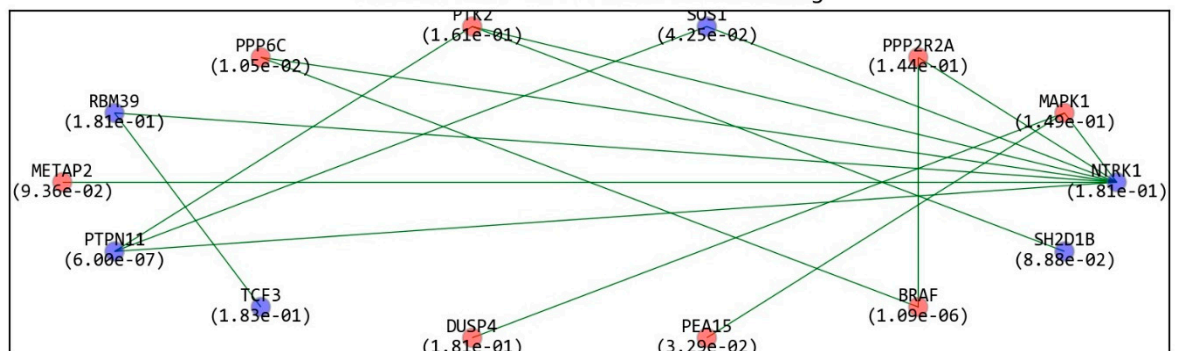


Figure S7. The sensitive GIs among the original GIs with exclusion procedure (SGWE) and without the exclusion procedure (SGOE) were compared to synthetic lethal interactions in MISL and synlethDB. The recall and precision measures are used.

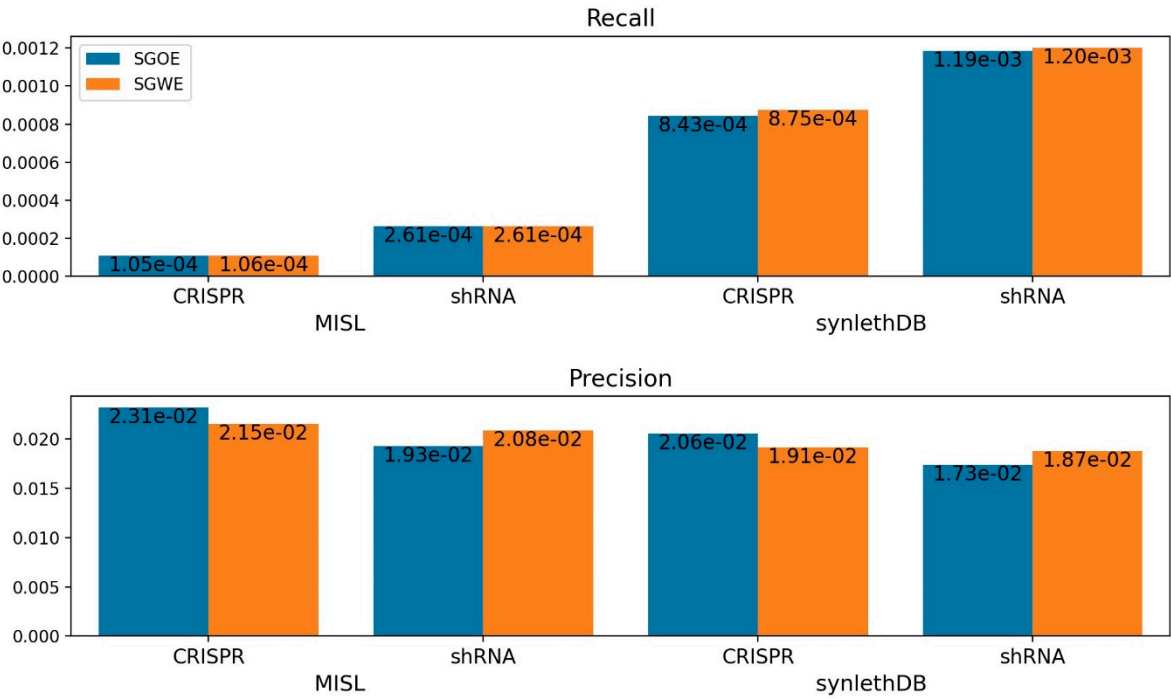


Figure S8. The recall of the sensitive GIs with no RP, RP2, and RP1. The sensitive GIs refined based on KEGG/PPI networks were evaluated with the SLIs in synlethDB and MISL. INIT: the initial sensitive GIs after mapping on the molecular networks (no RP was applied). RP2: the sensitive GIs after applying RP2 to the initial GIs. RP1: the sensitive GIs after applying RP1 to the initial GIs. RP: refining process. GI: genetic interaction.

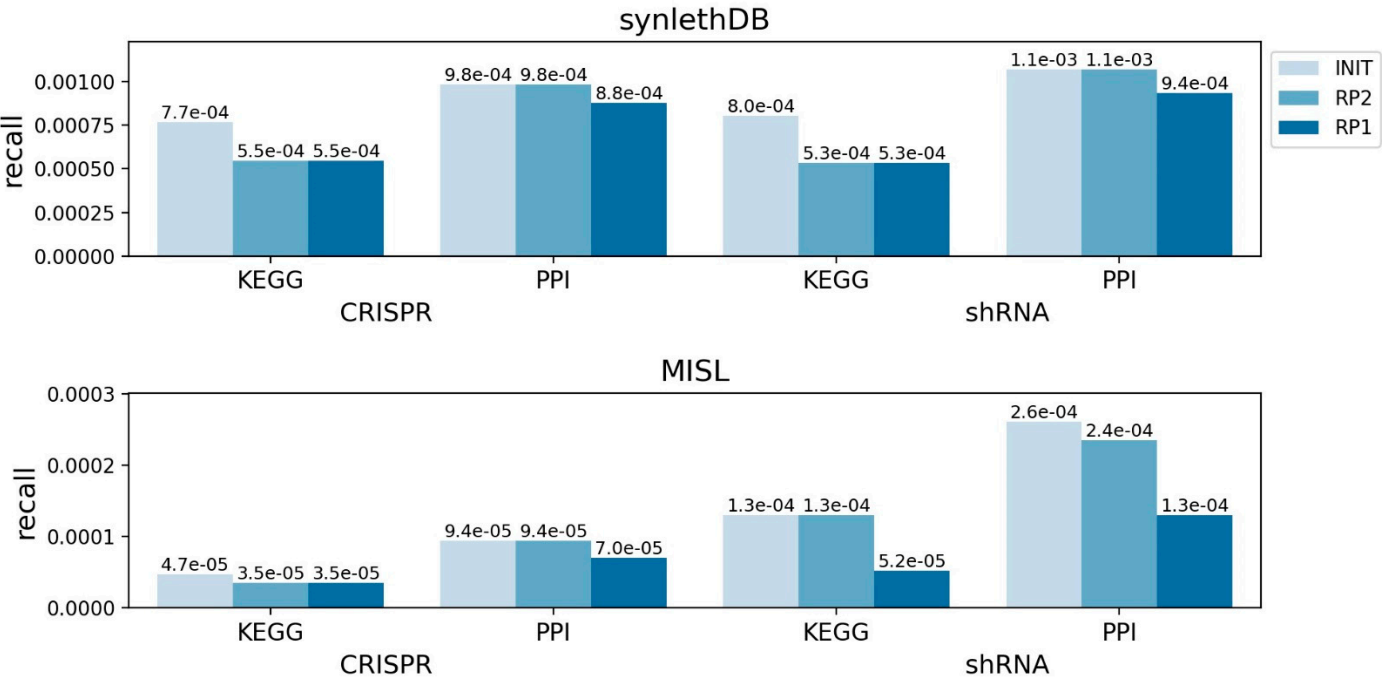
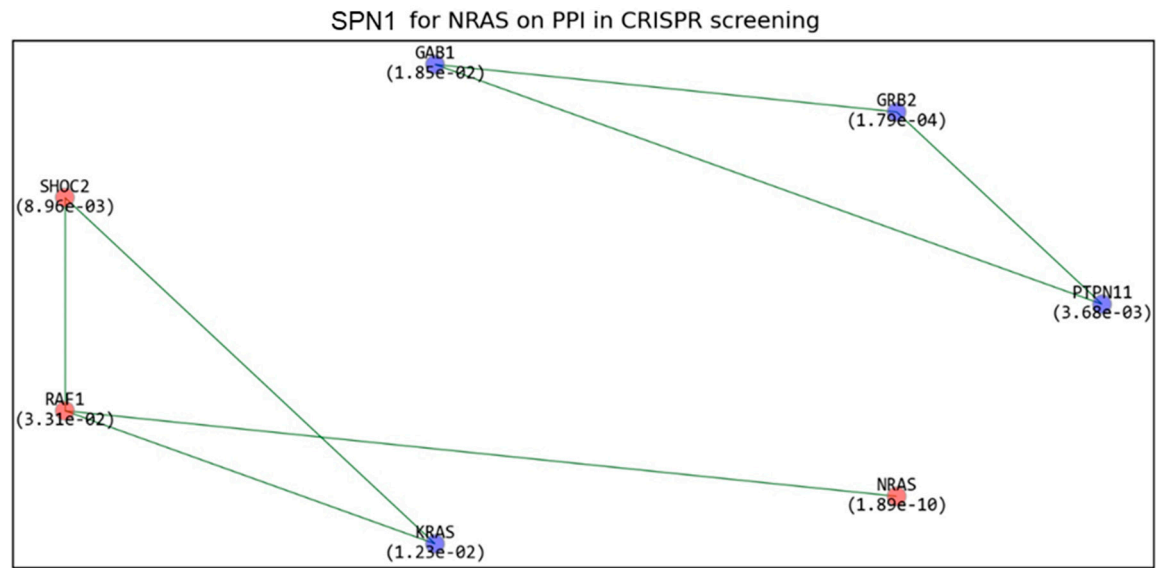


Figure S9. (a) the SPN1 on PPI for the mutated NRAS from CRISPR screening (b) the SPN1 on KEGG for the mutated NRAS from CRISPR screening.

(a)



(b)

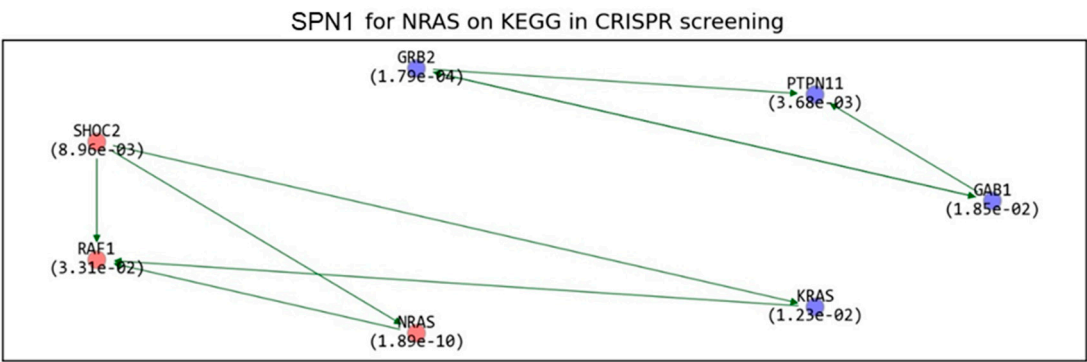


Figure S10. The number of cell lines for each cancer type in CRISPR and shRNA screening. The first bar represents the number of cell lines of the all considered cancer.

