Results

The TP53 gene had 12 cancer-mutation combinations that occurred in more than 20% of the samples given a cancer type[1]. Of these, 8 had a significant proteomic cis effect[2], and 4 had a significant transcriptomic cis effects[3]. There were 8 phosphoproteomic sites with significant cis effects[4].

To analyze trans effects, we restricted our analysis to proteins that shared one of 5 pathways with TP53[5]. For the proteomic trans effects, only 5 out of the 12 cancer-mutations had significant trans effects. However, there were 118 significant trans effects between these combinations[6]. The most common trans effects were with MAP2K, which appeared in 5/5 mutation combinations, and PFAS, which appeared in 4/5 mutation combinations.

We repeated the trans effect analysis with the transcriptomic effects and phosphoproteomic data. Of the 12 cancer-mutation combinations, 9 showed significant transcriptomic trans effects. A total of 265 significant trans effects were divided among these[7]. The most common trans effects were PAFAH1B1 , which appeared in 5/9 combinations, and MAP2K4, which appeared in 4/9 combinations. 4 combinations showed significant phosphoproteomic trans effects, with a total of 103 significant effects[8]. These effects were fairly unique, with only 5 effects appearing in even two cancer-mutation combinations[9].

Discussion

The tumor samples that had a mutated TP53 gene showed effects that were common across several cancers and mutations. Many combinations showed highly significant proteomic and transcriptomic cis-effects ($p < 0.01$ and $p < 0.001$). Interestingly, the phosphorylation site S315 showed similarly highly significant phosphoproteomic cis effects, although this was not shared by TP53's other phosphorylation sites. The samples also had many significant proteomic and transcriptomic trans effects, many of which were shared among most cancer-mutation combinations. This indicates that mutating TP53 produces wide-ranging proteomic and transcriptomic effects across the genome.

The phosphoproteomic data did not show such clear results. Mutating TP53 seemed to have clear cis effects on many of its own phosphosites. However, despite many genes having more than one phosphosite, there were far fewer significant phosphoproteomic trans effects than proteomic or transcriptomic. Of these, there were hardly any common trans effects between the cancer-mutation combinations. This may indicate that a mutated TP53 does not exert as clear of an influence on other genes' phosphoproteomics as it does their proteomics and transcriptomics. However, our approach with phosphoproteomic data was fairly naive, considering each phosphosite independently. Perhaps a more sophisticated analysis of phosphoproteomic data would yield more significant results.

[1] BRCA deletion, COAD deletion, HNSCC missense, HNSCC truncation, LSCC deletion, LSCC missense, LUAD deletion, LUAD missense, OV deletion, OV missense, PDAC deletion, PDAC missense
[2] COAD deletion, HNSCC missense, LSCC missense, LUAD deletion, LUAD missense, OV missense, PDAC deletion, PDAC missense
[3] BRCA deletion, COAD deletion, HNSCC truncation, LUAD deletion
[4] All at site TP53.S315; PDAC deletion, PDAC missense, COAD deletion, HNSCC missense, LSCC missense, LUAD deletion, LUAD missense, OV missense
[5] MAPK signaling pathway, DNA damage response, Wnt signaling pathway and pluripotency, TP53 network, and G1 to S cell cycle control.
[6] BRCA deletion, COAD deletion, HNSCC truncation, HNSCC missense, LSCC deletion, LSCC missense, LUAD deletion, LUAD missense, OV deletion, OV missense, PDAC deletion, PDAC missense
[7] BRCA deletion, COAD deletion, LSCC deletion, LUAD deletion, PDAC deletion,
[8] COAD deletion, LSCC deletion, PDAC deletion, PDAC missense
[9] PPP3CB.S478, WEE1.S150, WEE1.S165T173, MAPK11.S271, BRCA.S114

Figure 1: Mutations that occurred in more than 20% of each cancer sample group

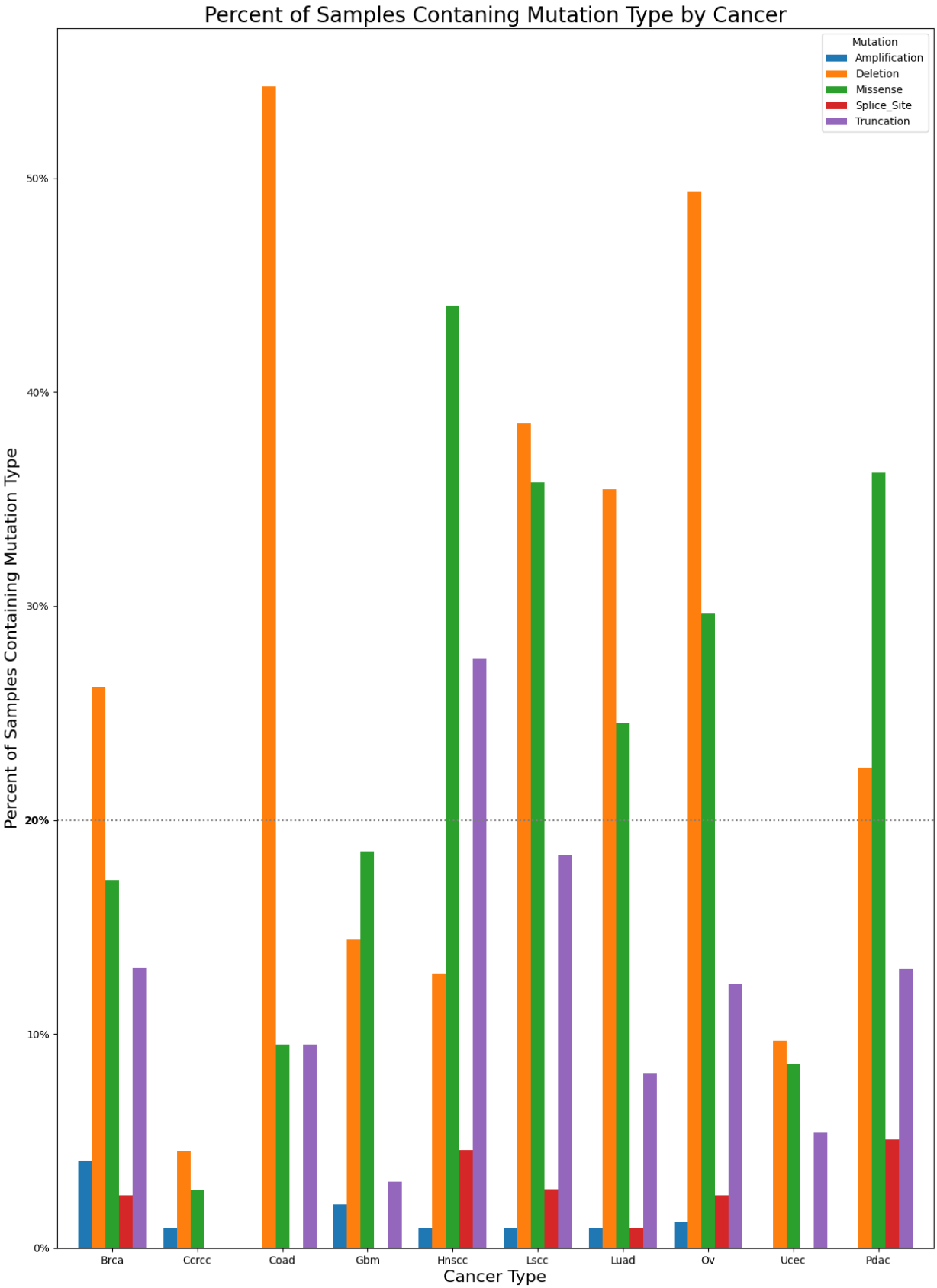

Figure 2: Significant proteomic cis effects (p < 0.05)

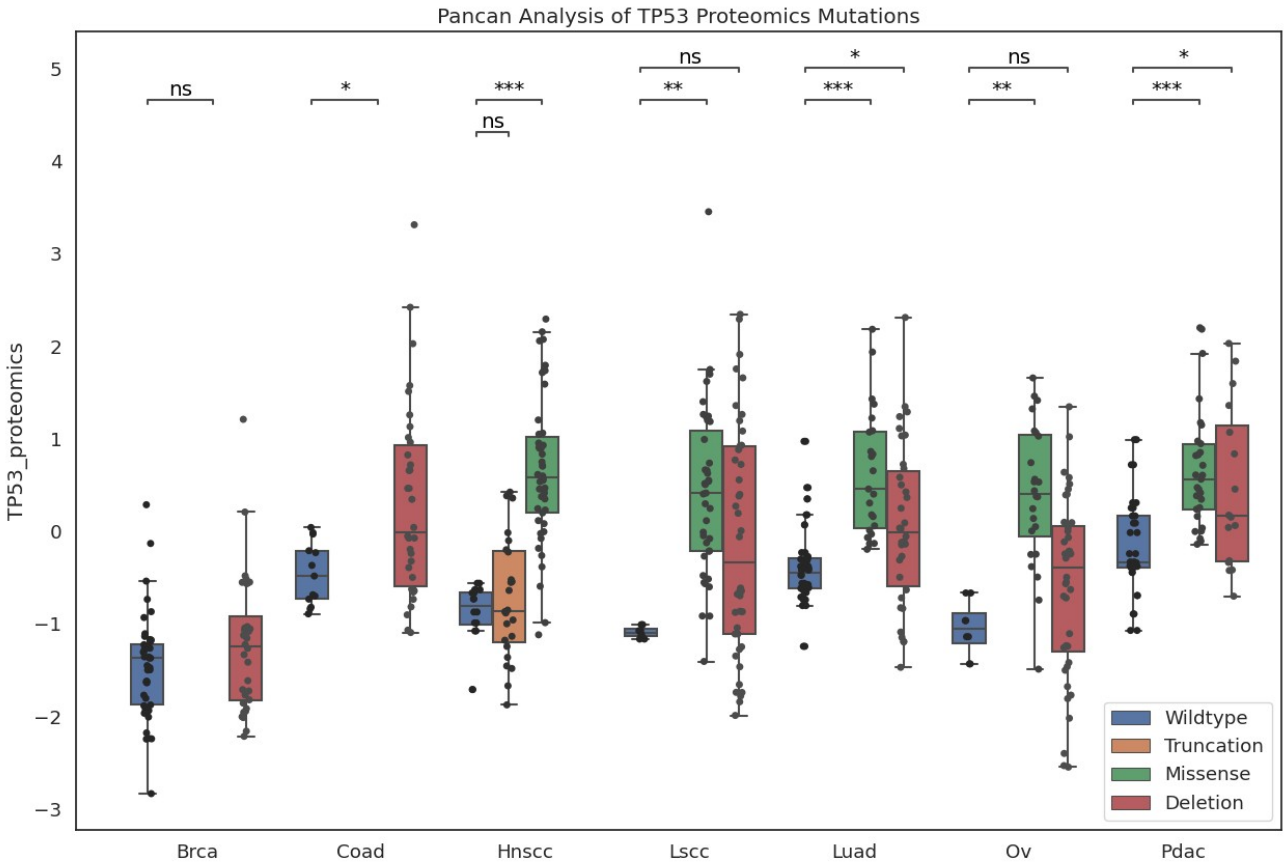

Figure 3: Significant transcriptomic cis effects (p < 0.05)

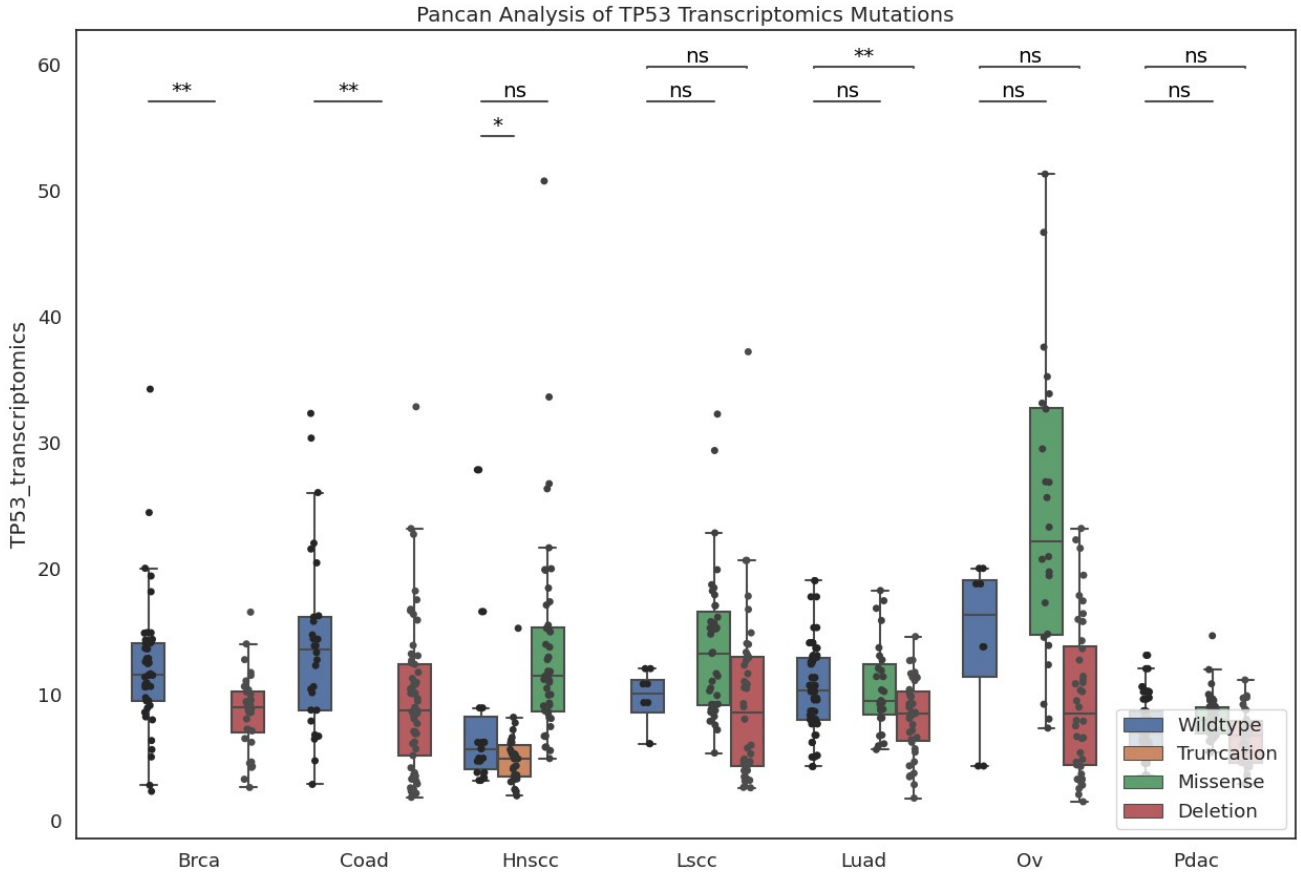

Figure 4: Significant phosphoproteomic cis effects at site TP53.S315 ($p < 0.05$). Two other sites were measured (S314 and S392), but there were no significant effects in either.

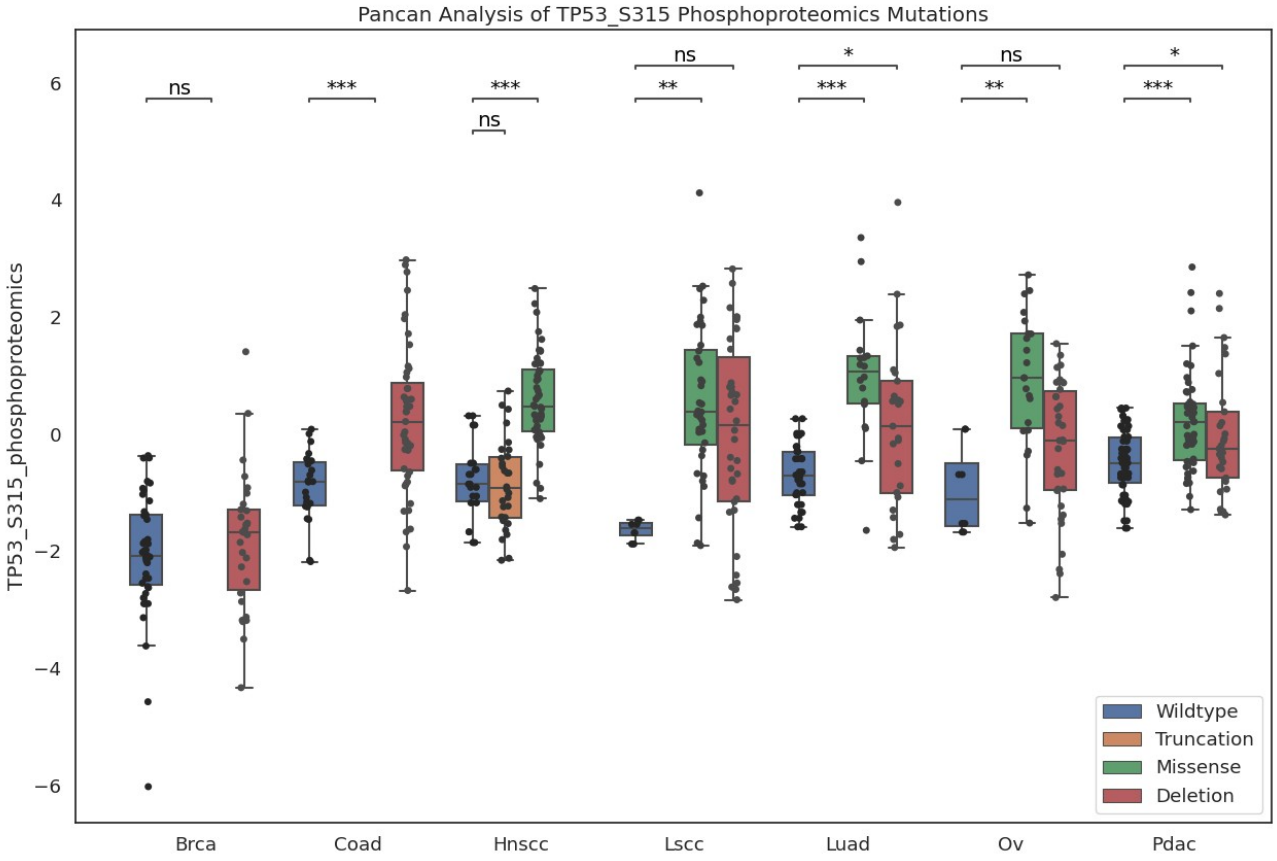

Figure 6: Most common genes with significant proteomic trans effects ($p < 0.05$) across different cancer-mutation combinations

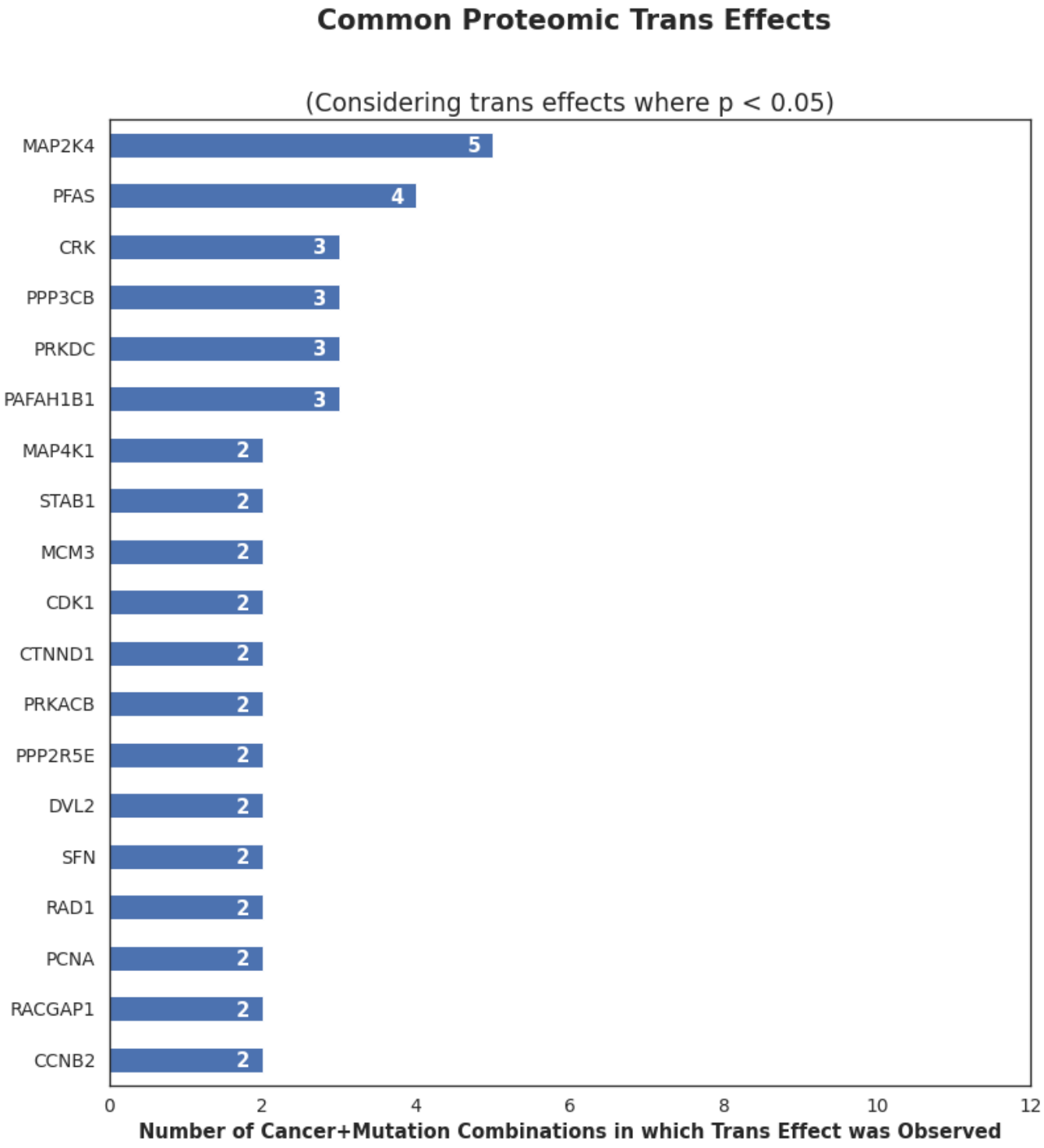

Figure 7: Most common genes with significant transcriptomic trans effects ($p < 0.05$) across different cancer-mutation combinations