Results

Over all types of cancers, the PIK3CA gene had 6 cancer-mutation combinations that occurred in more than 20% of the samples given a cancer type[1]. Of these, 2 had a significant proteomic cis effect[2], and 3 had a significant transcriptomic cis effects[3]. There were no significant phosphoproteomic cis effects[4].

To analyze trans effects, we restricted our analysis to proteins that shared the Akt signaling pathway. For the proteomic trans effects, 4 out of the 6 cancer-mutations had significant trans effects[5]. There were 99 significant trans effects ($p < 0.05$) between these combinations. Because of the limited number of these trans effects, only one gene appeared in multiple combinations—CDK2. We repeated this analysis looking at the top 25% most significant trans effects ($p < 0.241$). The most common trans effects were in HSP90AB1, which occurred in 5/5 cancer-mutation combinations, and MAPK3, JAK2, PIK3R1, THBS3, and STK11, which occurred in 4/5 cancer-mutation combinations[6].

We repeated the trans effect analysis with the transcriptomic effects and phosphoproteomic data. Of the 5 cancer-mutation combinations, 3 showed significant transcriptomic trans effects[7]. A total of 56 significant trans effects were divided among these. Only 3 genes—PPP2R2D, PIK3R6, and CHUK—appeared in multiple combinations. Similarly, there were only 2 combinations with significant phosphoproteomic trans effects[8], with a total of 38 effects divided between them. Only 2 genes appeared in multiple combinations. As with the proteomic data, we re-ran our analysis with the top 25% most significant effects. For the transcriptomic data ($p < 0.263$), the 4 most common trans effects occurred in 4/5 combinations[9]. For the phosphoproteomic data, taking the top 25% most significant trans effects resulted in $p < 0.991$, indicating that there was no significant overlap in phosphosites.

Discussion

Mutations in PIK3CA did not show many common effects across different cancers and mutations. The only consistency occurred with the cis effects, where almost all of the Amplification mutations showed a significant cis effect in proteomic and transcriptomic expression, while all of the Missense mutations showed almost indistinguishable expression from the wildtype tumors. Mutating PIK3CA had no distinguishable effect on its phosphoproteomic expression. As for trans effects,

[1] BRCA missense, COAD deletion, HNSCC amplification, LSCC amplification, OV amplification, UCEC missense
[2] HNSCC amplification, LSCC amplification
[3] HNSCC amplification, LSCC amplification, OV amplification
[5] BRCA missense, COAD deletion, HNSCC amplification, LSCC amplification
[7] GBM deletion, LSCC deletion, UCEC truncation
[8] LSCC deletion, OV deletion

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

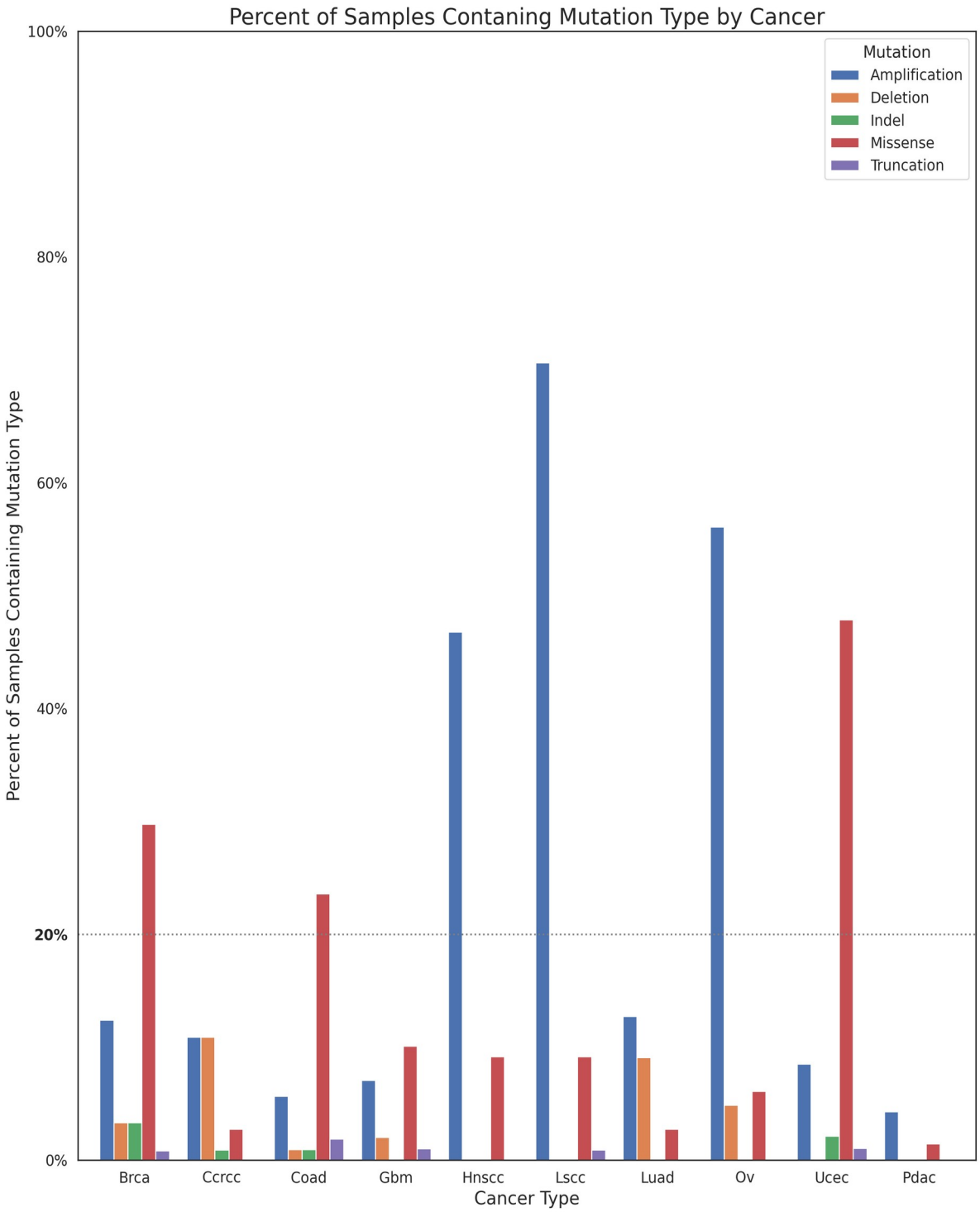

Figure 2: Significant proteomic cis effects ($p < 0.05$)

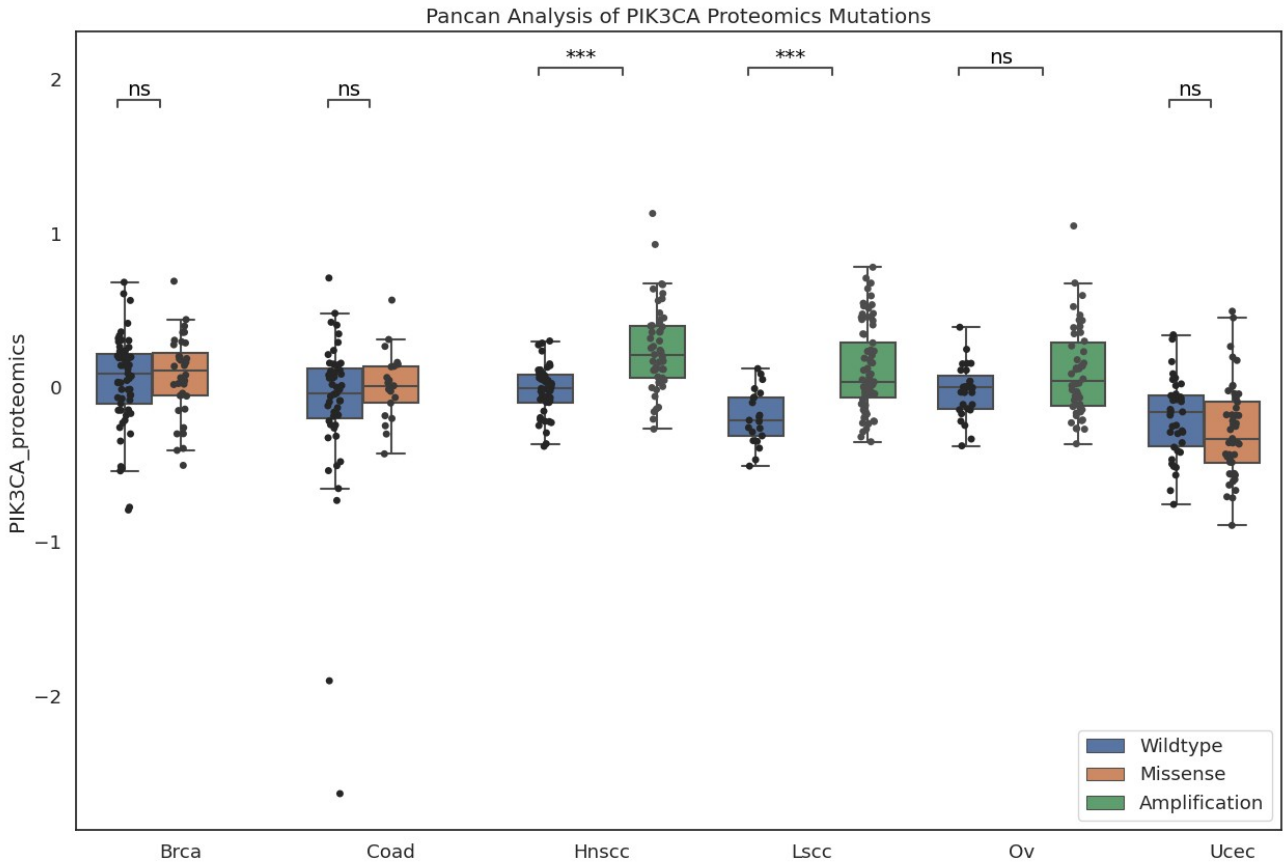

Figure 3: Significant transcriptomic cis effects ($p < 0.05$)

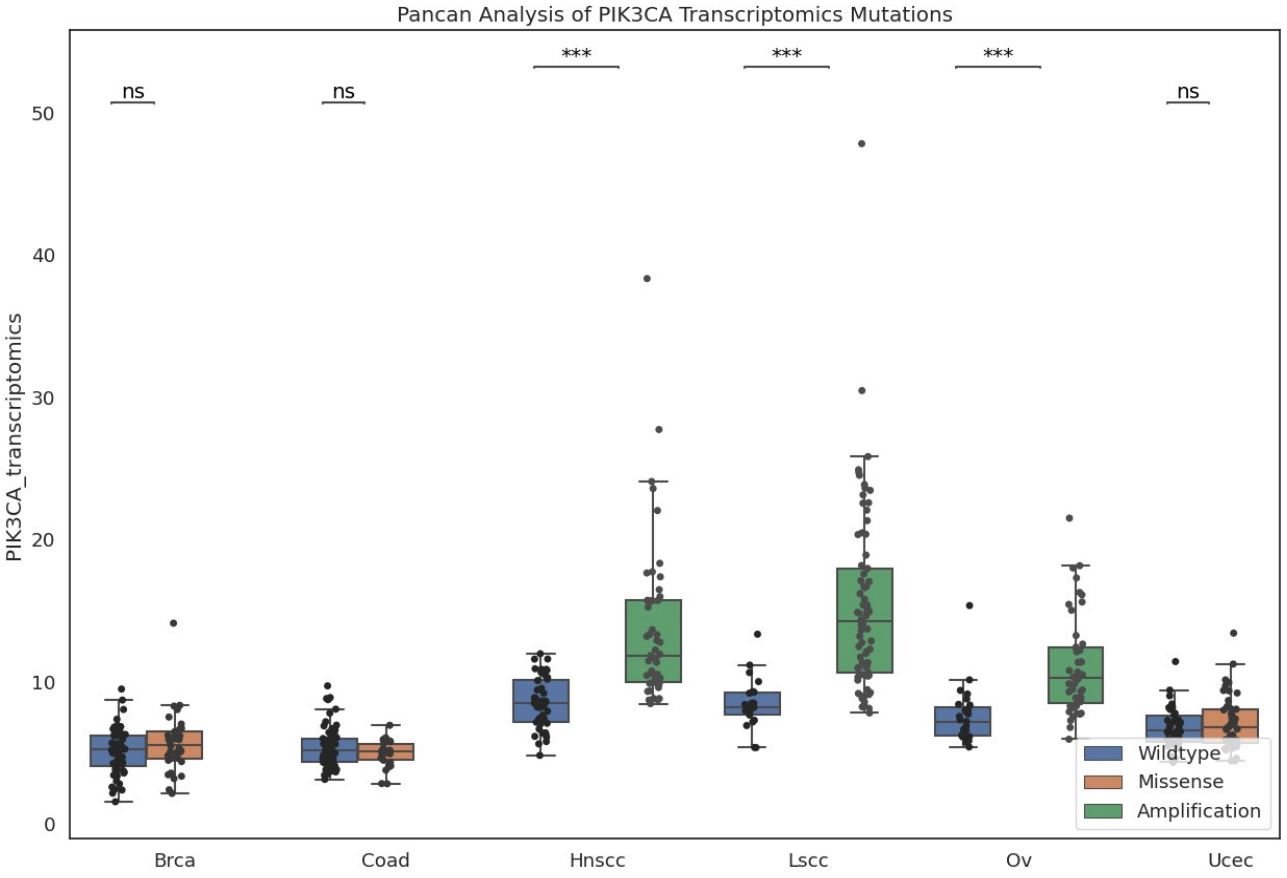

Figure 4: Phosphoproteomic cis effects at each site. There were no significant phosphoproteomic trans effects ($p < 0.05$)