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Identification of proteogenomic landscape of whole genome doubling reveals putative therapeutic targets in each cancer type

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Whole-genome doubling (WGD) is a frequently occurring event in cancer, giving rise to genetically unstable tetraploid cells and promoting the development of tumors. While the distinctive genomic changes associated with WGD are well-recognized, the proteogenomic characteristics and kinase cascades responsible for WGD in cancer have remained largely uncharted. In this study, we uncovered the proteogenomic attributes linked to WGD by harnessing comprehensive datasets encompassing genomics, transcriptomics, proteomics, and phosphoproteomics sourced from the Clinical Proteomic Tumor Analysis Consortium (CPTAC). This dataset featured 1,060 patients across ten distinct cancer types, including lung adenocarcinoma (LUAD), lung squamous cell carcinoma (LSCC), glioblastoma (GBM), pancreatic ductal adenocarcinoma (PDAC), breast cancer (BRCA), high-grade serous carcinoma (HGSC), colon adenocarcinoma (COAD), uterine corpus endometrial carcinoma (UCEC), head and neck squamous cell carcinoma (HNSCC), and clear cell renal cell carcinoma (CCRCC). WGD frequencies exhibited variations among these cancer types, with HGSC displaying the highest frequency and PDAC the lowest. Furthermore, an analysis of mutational signatures unveiled unique WGD-related patterns in each cancer type. Although LUAD and LSCC exhibited moderate WGD events, the most pronounced disparities between WGD-positive and WGD-negative samples were observed through differential expression analyses. The investigation into activated transcription factors and kinases associated with WGD revealed the dual nature of WGD's role in cancer biology. Finally, building upon these findings, we endeavored to propose potential drug targets linked to WGD in cancer.