UTHealth
The University of Texas Health Science Center at Houston
School of Biomedical Informatics

CPH Seminar in Precision Medicine

"Integrating Proteomics with Drug Screen Provides Novel Information Content"

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Cancer cell lines serve as models for mechanistic investigation and drug development. While genomic features have been characterized for thousands of cell lines, their protein levels and function, which are poorly predicted by genomic and transcriptomic analysis, remain unclear. Here we describe proteomic profiling of 706 cell lines using reverse-phase protein arrays (RPPAs) that has been linked to concordant DNA, RNA, and miRNA omics and drug screening data. The integrative analysis revealed 10 protein-based clusters and identified commonality and differences between proteomic pattern and multi –omics measurements. The protein rewiring driven by significantly mutated subnetworks in cell lines recapitulates the pattern in patient samples from The Cancer Genome Atlas, thus lays the ground to link protein and particular protein phosphorylation levels to drug sensitivity in the preclinical setting. We explored predictive biomarkers of 481 therapeutic compounds from the Cancer Therapeutic Response Portal (CTRP v2) and 140 compounds from Genomics of Drug Sensitivity in Cancer (GDSC). The identified protein biomarkers provided complementary information and more robust predictive power compared to the corresponding mRNA markers. We validated the previous reported relationship between drug response and genetic features and identified unexpected associations between phosphorylated EGFR with a BTK inhibitor, ibrutinib and novel roles of EMT in drug sensitivity and resistance. Our data demonstrate the opportunity to leverage proteomic measurements from cell lines to enhance prediction of drug sensitivity in cancer patients. To facilitate broad access to these data, we developed a user-friendly data portal, the MD Anderson Cell Lines Project, for data analysis and download, which will be hosted within the Cancer Proteome Atlas (TCPAportal.org).

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