
Phosphoproteome Integration Reveals Patient-Specific Networks in Prostate Cancer.

Journal: Cell

Publication Year: 2016

Authors: Justin M Drake, Evan O Paull, Nicholas A Graham, John K Lee, Bryan A Smith, Bjoern Titz, Tanya Stoyanova, Claire M Faltermeier, Vladislav Uzunangelov, Daniel E Carlin, Daniel Teo Fleming, Christopher K Wong, Yulia Newton, Sud Sudha, Ajay A Vashisht, Jiaoti Huang, James A Wohlschlegel, Thomas G Graeber, Owen N Witte, Joshua M Stuart

PubMed link: 27499020

Funding Grants: Center of Excellence for Stem Cell Genomics - Stanford

Public Summary:

We used clinical tissue from lethal metastatic castration-resistant prostate cancer (CRPC) patients obtained at rapid autopsy to evaluate diverse genomic, transcriptomic, and phosphoproteomic datasets for pathway analysis. Using Tied Diffusion through Interacting Events (TieDIE), we integrated differentially expressed master transcriptional regulators, functionally mutated genes, and differentially activated kinases in CRPC tissues to synthesize a robust signaling network consisting of druggable kinase pathways. Using MSigDB hallmark gene sets, six major signaling pathways with phosphorylation of several key residues were significantly enriched in CRPC tumors after incorporation of phosphoproteomic data. Individual autopsy profiles developed using these hallmarks revealed clinically relevant pathway information potentially suitable for patient stratification and targeted therapies in late stage prostate cancer. Here, we describe phosphorylation-based cancer hallmarks using integrated personalized signatures (pCHIPS) that shed light on the diversity of activated signaling pathways in metastatic CRPC while providing an integrative, pathway-based reference for drug prioritization in individual patients.

Scientific Abstract:

We used clinical tissue from lethal metastatic castration-resistant prostate cancer (CRPC) patients obtained at rapid autopsy to evaluate diverse genomic, transcriptomic, and phosphoproteomic datasets for pathway analysis. Using Tied Diffusion through Interacting Events (TieDIE), we integrated differentially expressed master transcriptional regulators, functionally mutated genes, and differentially activated kinases in CRPC tissues to synthesize a robust signaling network consisting of druggable kinase pathways. Using MSigDB hallmark gene sets, six major signaling pathways with phosphorylation of several key residues were significantly enriched in CRPC tumors after incorporation of phosphoproteomic data. Individual autopsy profiles developed using these hallmarks revealed clinically relevant pathway information potentially suitable for patient stratification and targeted therapies in late stage prostate cancer. Here, we describe phosphorylation-based cancer hallmarks using integrated personalized signatures (pCHIPS) that shed light on the diversity of activated signaling pathways in metastatic CRPC while providing an integrative, pathway-based reference for drug prioritization in individual patients.

Source URL: <https://www.cirm.ca.gov/about-cirm/publications/phosphoproteome-integration-reveals-patient-specific-networks-prostate>