Evaluation of reverse phase protein array (RPPA)-based pathway-activation profiling in 84 non-small cell lung cancer (NSCLC) cell lines as platform for cancer proteomics and biomarker discovery.

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Abstract

The reverse phase protein array (RPPA) approach was employed for a quantitative analysis of 71 cancer-relevant proteins and phosphoproteins in 84 non-small cell lung cancer (NSCLC) cell lines and by monitoring the activation state of selected receptor tyrosine kinases, PI3K/AKT and MEK/ERK1/2 signaling, cell cycle control, apoptosis, and DNA damage. Additional information on NSCLC cell lines such as that of transcriptomic data, genomic aberrations, and drug sensitivity was analyzed in the context of proteomic data using supervised and non-supervised approaches for data analysis. First, the unsupervised analysis of proteomic data indicated that proteins clustering closely together reflect well-known signaling modules, e.g. PI3K/AKT- and RAS/RAF/ERK-signaling, cell cycle regulation, and apoptosis. However, mutations of EGFR,

ERBB2, RAF, RAS, TP53, and PI3K were found dispersed across different signaling pathway clusters. Merely cell lines with an amplification of EGFR and/or ERBB2 clustered closely together on the proteomic, but not on the transcriptomic level. Secondly, supervised data analysis revealed that sensitivity towards anti-EGFR drugs generally correlated better with high level EGFR phosphorylation than with EGFR abundance itself. High level phosphorylation of RB and high abundance of AURKA were identified as candidates that can potentially predict sensitivity towards the aurora kinase inhibitor VX680. Examples shown demonstrate that the RPPA approach presents a useful platform for targeted proteomics with high potential for biomarker discovery. This article is part of a Special Issue entitled: Biomarkers: A Proteomic Challenge.

Beteiligte Forschungseinheiten

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