Deep plasma proteome profiling to discover drug treatment related novel biomarkers in non-small cell lung cancer

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Abstract Content:

Background: Immune checkpoint inhibitors (ICIs) have revolutionized the treatment of various cancers. A better understanding of ICI induced dynamics and response / resistance mechanisms may contribute to the optimization of treatment strategies. In early-stage non-small cell lung cancer (NSCLC) cohort with neoadjuvant chemoimmunotherapy, we utilized the plasma proteomics platform to deepen the understanding of disease biology and explore potential response and resistance biomarkers.

Methods: Plasma samples were collected from longitudinal timepoints of neoadjuvant chemoimmunotherapy. An unbiased MS-based plasma proteomics platform were used to process the plasma samples. Taking advantage of the protein corona formed on the surface of nanoparticles, low-abundance protein related to immunomodulation and signal transduction were enriched and identified. A comprehensive statistical analysis framework was adapted to reveal mechanism and explore predictive and prognostic biomarkers. Immunotherapy induced changes of blood protein were estimated by linear mixed model. Molecular insights was studied by mediation analysis. In association analysis with clinical outcomes, classic logistic regression was applied for binary clinical outcomes, while cox proportional hazard model for survival outcomes.

Results: 180 longitudinal plasma samples from 92 individuals were profiled, and 2303 proteins were quantified in peripheral blood. Consistency between quantitative proteomics and established techniques were demonstrated by known biomarker CA125, CRP and gender related proteins. 541 upregulated proteins and downregulated 504 proteins after neoadjuvant chemoimmunotherapy were identified. Pathway enrichment analysis revealed that neoadjuvant chemoimmunotherapy promoted immune activation.

Conclusion: Deep plasma proteome profiling enable deeper understanding of the dynamics and mechanisms induced by ICI treatment.