Title:

Identification of prognostic candidates using comprehensive kinase activity assay in non-small cell lung cancer biopsy samples

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Introduction: EGFR mutations are strong predictive markers for EGFR-tyrosine kinase inhibitor (EGFR-TKI) therapy in patients with non-small-cell lung cancer (NSCLC). NSCLC patients with sensitizing EGFR mutations spend better prognoses, some patients exhibit worse prognosis. We hypothesized that various activities of kinases could be potential predictive biomarkers for EGFR-TKI treatment in NSCLC patients harboring the sensitizing EGFR mutations.

Methods: In 18 patients with stage IV NSCLC, EGFR mutations were detected using panel sequencing and comprehensive kinase activity assay was performed using the peptide array Pamstation12 for 100 tyrosine kinases. For the kinase activity assay, extracted protein from

biopsied tumor samples were used. Prognosis was observed prospectively after the administration of EGFR-TKIs. Finally, the kinase profiles were analyzed in combination with the prognoses of the patients.

Results: The kinase activity analysis identified specific kinase features consisting of 102 peptides and 35 kinases in NSCLC patients with sensitizing EGFR mutations. Network analysis and pathway analysis revealed several kinases and pathways commonly activated. Highly activation of several kinases was also elucidated in patients with poor prognosis.

Conclusion: Comprehensive kinase activity profiles may provide predictive biomarkers for screening patients with advanced NSCLC harboring sensitizing EGFR mutations.