A 10-DNA Repair Gene Signature Predicts Benefits from Adjuvant Chemotherapy (ACT) In Patients with Non-Small Cell Lung Cancer (NSCLC)

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Several clinical trials showed ACT benefit in NSCLC patients, but the effect was modest with serious adverse effects. Identifying patients who may benefit from ACT will improve clinical decisions and outcome. Mutagenesis is a hallmark of malignancy, and many cancer treatments function by introducing more DNA damage for cell killing. Therefore, DNA damage repair is very important in both tumorigenesis and cancer treatment. A prognostic signature with 10 DNA repair genes for overall survival (OS) was developed by using gene expression data from the clinical trial JBR10 (ACT:n=71; placebo:n=62). We first selected 37 DNA repair genes (out of 254 genes) significantly associated with OS in univariate analysis ($p<0.05$), then we performed stepwise selection with cross-validation, and used likelihood ratio test to achieve the optimal COX regression model. The expression signature (CHAF1B, SMARCA2, CSNK1E, EXO1, TEP1, NTHL1, DCLRE1B, POLE, RIF1, MMS19) predicts 2-year disease free survival with AUC= 0.8. In addition to its prognostic value, it predicted ACT effect. The patients with lower risk score showed significantly better OS after ACT (Hazard ratio-HR: 0.1; 95%CI: 0.02-0.5). The OS predictive model was further validated by Director's Challenge Lung Study (n=440, HR: 0.5; 95%CI: 0.4-0.7).

Key words: Gene signature, Non-small Cell Lung Cancer, Adjuvant Therapy, Model Selection, Validation, Prognostics