Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

TUMOR BIOLOGY AND HUMAN GENETICS

Differential expression of DNA repair machinery genes in normal bronchial tissue and non-small cell lung cancer (NSCLC)

G. Selvaggi , S. Saviozzi , P. Ceppi , M. Volante , M. Iacono , S. Novello...

Show More

Abstract

22017

Background: Genes involved in DNA repair and/or replication have been recently investigated as predictive markers of response to chemotherapy in NSCLC. However, few data on the expression of these genes in NSCLC tumor samples versus corresponding normal lung are currently available. Aim of this study was to evaluate differential mRNA levels of 22 DNA repair genes belonging to 5 different DNA

COMPANION ARTICLES

No companion articles

ARTICLE CITATION

DOI: 10.1200/jco.2008.26.15_suppl.22017
Journal of Clinical Oncology 26, no. 15_suppl (May 20, 2008) 22017-22017.

Published online May 20, 2008.

WE RECOMMEND

repair pathways: direct (DR), base excision (BER), nucleotide excision (NER), double strand break (DSBR) and post-replicative (PRR) repair. In addition, 6 genes involved in DNA replication (REP) and 2 telomere maintenance (TM) genes were also investigated. **Methods:** Total RNA was extracted from fresh snap-frozen tumors and corresponding normal tissues from 50 consecutive chemo-naive resected NSCLC patients. Transcript levels were quantified by Real-Time PCR (TaqMan), fold changes were calculated with the 2-ΔΔCt method and statistical significance assessed by Wilcoxon's test. POLR2A and 18SrRNA were used as reference genes and normal specimens as calibrators. **Results:** A significant overexpression in 13 out of 22 (60%) DNA repair and in 7 out of 8 (88%) REP and TM genes was detected (all p<0.0001). Three out of 22 (14%) DNA repair genes were instead significantly down-expressed. Interestingly, among DNA repair pathway, DSB genes were those with the highest overexpression rate, and high transcript levels were significantly associated with tumor grade and male gender. BRCA1, BRCA2, XRCC3, XRCC5, uracil-DNA glycosilase, thymidylate synthase and topoisomerase DNA IIIß (TOPIIIß) genes were correlated with poor prognosis at univariate, while at multivariate analysis only TOPIIIß (p=0.02) and tumor grade (p=0.04) were retained as independent prognostic markers adjusting for major clinico-pathological parameters. **Conclusion:** This pivotal study shows that the overexpression of DNA repair genes in lung tumors are correlated with a more aggressive phenotype. Moreover, DNA repair genes (TOPIIIß especially) should be further investigated as candidate prognostic markers in NSCLC.

Author Disclosure

Employment or Leadership	Consultant or Advisory Role	Stock Ownership	Honoraria	Other

Employment or Leadership	Consultant or Advisory Role	Stock Ownership	Honoraria	Other
			AstraZeneca Oncology, Eli Lilly, Janssen Cilag, Millennium, sanofi-aventis	

American Society of Clinical Oncology

and 5-2′-deoxy cytidine-nitrogen Impurity on the Influence of p16 Expression in Lung Cancer A549 Cells

HUA Cong-shu et al., Journal of Sichuan University (Medical Science Edition), 2018

Radiogenomic Analysis Demonstrates Associations between 18F-Fluoro-2-Deoxyglucose PET, Prognosis, and Epithelial-Mesenchymal Transition in Non–Small Cell Lung Cancer

Shota Yamamoto et al., Radiology, 2016