Evaluation of a TP53 biomarker for lung cancer risk in nasal brushings and peripheral blood

Abstract Accepted:
AACR Annual Meeting
April 5-10, 2024
San Diego, CA

Control/Tracking Number: 24-A-3266-AACR
Activity: Abstract Submission
Current Date/Time: 11/20/2023 12:04:31 PM

Author Block: Erin L. Crawford[1], Daniel J. Craig[1], Patrick T. Gorman[1], Mohamed Omballi[1], Rami Ahmad[1], Eric L. Grogan[2], Stephen A. Deppen[2], **James C. Willey**[1]

[1]University of Toledo, Toledo, OH, [2]Vanderbilt University Medical Center, Nashville, TN

Abstract:

Background and Purpose: Early detection of lung cancer through annual screening with low-dose computed tomography (LDCT) scans enables potentially curative surgical or stereotactic body radiation therapy (SBRT) treatment and thereby significantly reduces mortality. However, LDCT screening among those currently eligible based primarily on age and smoking criteria yields a large number of false-positive findings and many lung cancers occur among individuals who currently are ineligible. A biomarker that identifies lung cancer risk independent from that caused by age and cigarette smoking might increase specificity and increase the number of people eligible for LDCT screening. Recently we demonstrated that a biomarker measuring TP53 somatic mutations in bronchial brush biopsy specimens from grossly normal airway epithelium was significantly associated with cancer status independent of age and smoking status. Additionally, the TP53 biomarker was synergistic with traditional risk score models (e.g. PLCOM2012 risk score). The goal of this pilot study was to test the TP53 biomarker in nasal brush biopsy specimens, a potential surrogate tissue obtained using less invasive collection methods. **Methods:** Nasal brushings from 10 lung cancer and 11 control subjects were collected at the University of Toledo and Vanderbilt University Medical Center under approved institutional protocols. Genomic DNA (gDNA) was extracted with the Qiagen AllPrep DNA/RNA kit using a modified protocol. Amplifiable copies of gDNA were measured using quantitative PCR. For each test a sample comprising 25,000amplifiable copies of gDNA was combined with 50,000 copies of a TP53 internal standard and a complexity control, then PCR amplified, purified and barcoded. Samples were pooled to create two NGS libraries, each with approximately equal numbers of cases and controls, and sequenced on an Illumina MiSeq (Two V3 flow cells, 2 x 250 paired-end). Bioinformatic analysis was conducted using Qiagen CLC Workbench. Variants were called using the Basic Variant Detection Tool. Poisson Exact Test was utilized to determine the significance of endogenous variants relative to internal standard variants at the same base position and a Bonferroni correction was applied to minimize false discovery. Comparison of variant numbers between cases and controls was conducted using an f-test followed by a paired t-test. **Results and Conclusions:** Consistent with previous results in airway epithelium, in this pilot study the TP53 mutation biomarker measured in nasal brushing was associated with lung cancer ($p=0.0085$). Measurement of the TP53 biomarker in nasal brush specimens in a larger case-control study currently is underway along with a pilot study in gDNA from peripheral blood.