Saliva mRNA expression profiling for early stage non-small cell lung cancer (NSCLC) screening

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Background: Strategies to identify high risk individuals who may develop lung cancer are sorely needed. Radiographic screening has several drawbacks including cost, high false positive rate, and exclusion of never-smokers who account for up to 13% of new diagnoses. Sputum collection can be difficult in up to half of former smokers. Alternatively, saliva is readily available and easy to collect. We have previously shown high sensitivity and specificity in distinguishing newly diagnosed oral squamous cell carcinoma from matched controls (Li et al. Clin Cancer Res 2004). Others have shown a correlation of salivary and serum levels of soluble Her2/neu in women with breast cancer compared to benign tumor and healthy controls (Streckfus et al. Clin Cancer Res 2000). These studies led us to embark on a pilot study to validate mRNA expression on a gene exon array platform and to explore gene exon signatures discriminating between early-stage NSCLC and healthy controls.

Methods: Saliva is currently being collected from healthy subjects ages 40-79, (current and former smokers ≥20 pack-year) and never-smokers <100 cigarettes/lifetime and histologically-confirmed, untreated stage I-II NSCLC patients along with a medical history questionnaire. Exclusion criteria included: active pulmonary infection within 6 months, steroid inhaler use ≥6 months, or history of other invasive cancer within past 5 years. A one-time saliva specimen is being obtained between 9-10 am to avoid diurnal variation, mixed with a RNA stabilization agent, and stored at -70°C. RNA is then extracted, amplified, and hybridized to the Affymetrix Human Exon 1.0 arrays (which contain 1.4 million probe sets). Array data is analyzed after appropriate normalization.

Results: As proof-of-principal of the value of the exon array discovery platform, saliva mRNA expression was performed on 18 healthy subjects [14 males (3 never-smokers), 11 females (8 never-smokers)]. All of whom were able to provide adequate sample for analysis. Our data demonstrate that we have successfully amplified salivary RNA, hybridized to the exon array and have developed the statistical and informatics tools to harness the diagnostic information. Using these developed tools and the healthy cohort of subjects, we have identified and validated gender-specific salivary exon signatures.

Conclusions: Preliminary results with saliva mRNA exon-level expression profiling suggest that quality samples are easily obtainable and the technique is feasible. Updated results with NSCLC specimens will be presented. Supported by International Association for the Study of Lung Cancer Fellowship Award (GJW) and R01-DE15970-03 (DTW).

SCLC: Combined Modality Therapy

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Phase II study of Irinotecan (I) and carboplatin (C) with early concurrent radiotherapy (CR/RT) in limited-stage small cell lung cancer (LS-SCLC) patients (pts)

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