News Release

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Session B61: Managing Lung Cancer Screening and Its Downstream Findings
Monday, May 18, 2015, 9:30 a.m. – 4:15 p.m.
Location: Colorado Convention Center

Adding Genetic Information Changes Risk Profile of Smokers and Results in Greater Adherence to CT Lung Screening

Researchers have found that adding genetic information to a former or current smoker's clinical risk profile results in a reclassification of their risk for lung cancer in about one in four patients. Preliminary findings from their lung cancer screening feasibility study also suggests that those whose genetic and clinical risk placed them in the highest risk category were more likely to adhere to follow-up computed tomography (CT) scans during screening.

The results of this study, conducted at El Camino Hospital in Mountain View, CA, follows on the heels of the National Lung Screening Trial which enrolled more than 53,000 current or former heavy smokers between the ages of 55 and 74. Those in the CT screening arm of this trial had a 20 percent lower risk of dying from lung cancer if they underwent an annual CT scan of their lungs compared to annual chest x-rays.

Implementation of a successful CT screening program requires that eligible participants be screened in a timely manner. While past studies have demonstrated that participation in lung cancer screening is improved in the context of risk assessment, this is the first study to report on the effects of gene-based risk assessment and screening adherence.

"Outside clinical trials, adherence to screening is typically 50 to 60 percent," said lead investigator Robert Young, MD, PhD, associate professor of medicine and molecular genetics, at the University of Auckland, New Zealand, who will present the results at ATS 2015, May 15 to 20 in Denver. "What our study shows is that risk assessment using personal genetic information is not only of great interest to screening participants, it appears to improve their compliance with screening."

In the community-based study (called REACT), all 157 screening participants agreed to and underwent gene-based risk testing for lung cancer. Young and his colleagues then assigned each participant to one of three risk categories—very high, high and moderate—by combining genetic data with the participant's age, family history of lung cancer and whether they reported having chronic obstructive pulmonary disease, or COPD.

The genetic component represents the net effect of 20 single nucleotide polymorphisms (SNPs) that have been implicated in the development of lung cancer by Dr. Young and other research groups. When present, these SNPs confer either an increased risk of lung cancer (12 susceptibility-related SNPs) or a reduced risk (8 protective-related SNPs). With this personal genetic information, the researchers reclassified 28 percent of the participants: 22 percent were re-assigned to a higher risk category and 6 percent to a lower one.

Overall adherence to the CT screening follow-up protocol was 63 percent. As expected, adherence was greatest in the very high risk category: 71 percent. Those in the high and moderate risk categories both had 52 percent adherence. The difference was significant (71% vs 52%, OR=2.3, $P<0.05$).

"Not only does adding personalized genetic data contribute to a better assessment of lung cancer risk, it appears to improve screening adherence," Dr. Young said.

This study was jointly funded by Synergenz Bioscience Ltd and the El Camino Hospital Trust.

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** Please note that numbers in this release may differ slightly from those in the abstract. Many of these investigations are ongoing; the release represents the most up-to-date data available at press time.*

Abstract 63646

Low-Dose Computer Tomography (CT) Lung Cancer Screening in the Community: A Prospective Cohort Study (REACT) Incorporating a Gene-Based Lung Cancer Risk Test
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Abstract Body

Rationale: Following the results of the National Lung Screening Trial (NLST), CT screening for lung cancer is widely recommended in the US. Recent studies show that targeting of very high risk smokers, using validated multivariate risk models for lung cancer, improves cancer detection rates and lives saved from screening. Moreover, adherence to screening outside clinical trials is typically 50-60% and shown to be highly dependent on an individual's risk perception.

Aim: In a community based study of CT screening for lung cancer in volunteer smokers, the utility of a gene-based risk test in assessing risk and affecting adherence to a positive CT scan was examined. The primary aim of this study was to assess the utility of adding personalized genetic data (based on the presence or absence of risk single nucleotide polymorphism (SNP) genotypes) to a clinical risk score and determine how many people were reclassified according to their gene-based risk. The secondary aim was to assess how this gene-based risk assignment affected follow-up according to the screening protocol.

Methods: Following local media-based advertising, 157 current or former smokers (>50 yrs old with ≥20 pack year history) volunteered for CT screening (using the IELCAP protocol) and were followed up for a mean of 2.4 years. In addition to CT screening, participants were assigned their baseline risk category (moderate, high or very high risk) according to a published gene-based risk algorithm, combining clinical risk variables with risk SNP genotypes, to derive a composite lung cancer risk score.

Results: All 157 screening participants accepted gene-based risk assessment involving a mouth swab for DNA and a simple clinical questionnaire. Results were given following their baseline CT scan in 154 (98%) of participants. SNP genotype results contributed to overall lung cancer risk in 88% of participants (compared to age=68%, FHx=29% and self-reported COPD=15%). SNP genotype was the sole basis of risk assignment in 18% of participants. Adding SNP scores to the clinical risk score re-assigned screening participants into different risk categories in 28% (44/157). Importantly, timely adherence to the CT screening protocol was greater in those with very high risk compared to other risk categories (71% vs 52%, OR=2.3, P<0.05). There was no evidence of demotivating effects in the moderate (lowest) risk group (see Table 1).

Conclusion: Personalised SNP data makes an important contribution to overall assignment of lung cancer risk and significantly improves screening adherence. Gene-based risk stratification helps improve lung cancer screening.

Table 1. Adherence to CT Screening Follow up According to the Lung Cancer Risk Category in REACT Participants (Moderate, High, Very High).

Adherence	**Lung Cancer Risk Score Category**			
	Moderate	High	Very High	Total
Timely Adherence N=46 (%)	8/12 (38%)	8/27 (30%)	30/59[2](51%)	46/107 (43%)
Overall Adherence N=67 (%)	11/12 (52%)	14/27 (52%)	42/59[1](71%)	67/107 (63%)
No Adherence N=40 (%)	10/21 (48%)	13/27 (48%)	17/59 (29%)	40/107 (37%)
Total with + CT Scan /Total Screened N=154 (%)	21/43 (49%)	27/41 (66%)	59/70 (84%)	107/154 (69%)

All REACT Participants N=157 (%)	43 (27%)	42 (27%)	72(46%)	157 (100%)

1. Overall adherence (Timely and Late Adherence) in "Very High" risk compared to "High and "Moderate risk groups: Odds Ratio = 2.3 (95% CI =1.02-5.05, P=0.047).

2. Timely Adherence compared to Late and No Adherence in "Very High" risk compared to "High" and "Moderate" risk groups: Odds ratio = 2.1 (95% CI = 0.94-4.55, P=0.08 and P=