

## Respiragene™ Research Update - Feb 2010

### Respiragene™ Test Utility Confirmed in Six-Year Prospective Study

The ability of the Respiragene test to identify smokers at greatest risk of developing lung cancer has been further validated by results of a large-scale prospective study of smokers in Auckland, New Zealand.

Interim findings as of December 2009 of an on-going prospective study of 1,212 individuals demonstrate similar key results for risk identification as those derived from the initial studies which underpinned development of the Respiragene test: i.e. the participants who developed lung cancer during the study had significantly higher Respiragene scores than the control group with normal lung function at the outset of the study.

Asymptomatic smokers or former smokers with high Respiragene scores - individuals therefore at relatively high risk of developing lung cancer - may benefit from targeted prevention measures including such interventions as smoking cessation counseling and related therapies, prioritization for early lung cancer detection screening and emerging chemoprevention strategies<sup>1 2</sup>.

Initial results from the prospective study, were presented at the “Frontiers in Cancer Prevention Conference, organized by the American Association of Cancer Research in December 2009, and are being submitted for publication.

### Methodology

A group of 1,212 high risk individuals (smokers/former smokers, aged over 40, smoking for more than 20 years) were recruited and followed for a mean of six years in two centers in New Zealand. Participants in this study (“Prospective Study”) included 484 smokers with normal lung function who had also participated in an earlier study, characterized by a cross-sectional methodological approach (“Cross-Sectional Study”)³. The Prospective Study also included 728 participants with confirmed diagnosis of COPD at the outset of the study. Participants who developed lung cancer over the period were identified and tracked. All survey participants underwent spirometry, completed an American Thoracic Society Respiratory Questionnaire and were genotyped. For each participant, genotype data and three non-genetic factors (age, presence of COPD and family history of lung cancer) were combined, according to the pre-defined Respiragene algorithm, to derive their Respiragene score.

The Respiragene scores from this study were then compared with the scores from the initial Cross-Sectional study of 930 smokers, which included 446 lung cancer cases, in addition to the control group of 484 smokers with normal lung function.

## Key Results

### 1. Respiragene Score: Prospective and Cross-Sectional Studies

Table 1 Results Summary

	Number of Participants	Respiragene Score (mean)	Respiragene Score 4+ (%)
<b>Normal Lung Function*</b>	484	2.3	38%
<b>With Lung Cancer</b>			
- <b>Prospective</b>	52	7.2	81%
- <b>Cross-Sectional</b>	446	7.1	80%

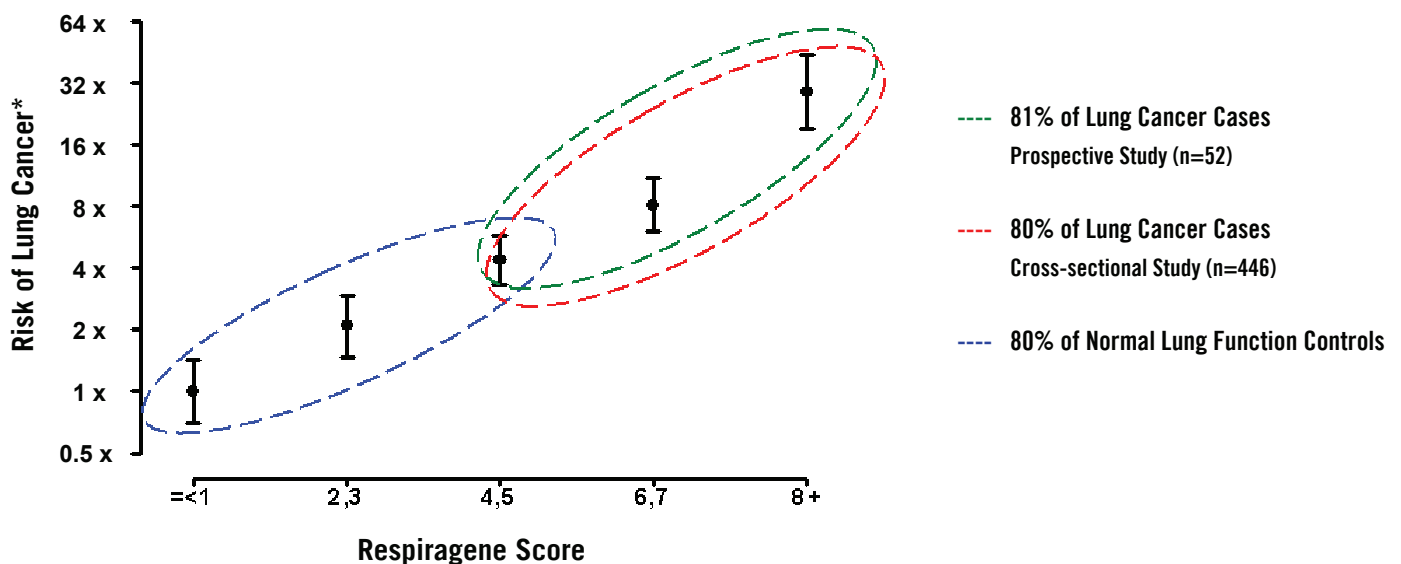
\* smokers and former smokers assessed with normal lung function at the outset of the studies, comprising a control group

### 2. High Respiragene Score an Indicator of High Risk of Lung Cancer.

52 participants developed lung cancer during the follow-up period of the Prospective Study. The initial Cross-Sectional Study included 446 lung cancer cases. In both studies, the lung cancer participants were comparable to the non-cancer survey participants on all the variables tracked (i.e. age, gender, smoking history, family history), except for their Respiragene score.

In both studies, the mean Respiragene Score was significantly higher for the group with lung cancer than for the normal lung function control group (Respiragene Score of 7.2 /7.1 for the groups with lung cancer compared with 2.3 for the control group). Of the lung cancer cases identified in both studies, around 80% had Respiragene scores of 4 or over, putting them in the “High risk” or “Very high risk” categories. This can be compared with 38% for the control group of smokers assessed with normal lung function.

Figure 1 Respiragene Scores for Lung Cancer Cases Vs. Control Group



\* Compared with a reference group of smokers with normal lung function

## References

1. Young RP, Hopkins RJ, Smith M, et al. Smoking cessation: the potential role of risk assessment tools as motivational triggers. *PMJ* 2010; 86:26-33
2. Sanderson SC, Wardle J. Will genetic testing for complex diseases increase motivation to quit smoking? Anticipated reactions in a survey of smokers. *Health Education and Behaviour* 2005; 32: 640-653
3. A gene-based risk score for lung cancer susceptibility in smokers and ex-smokers R P Young, R J Hopkins, B A Hay et al *Postgrad Med J* 2009;85:515-524

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