

Report Contents

- 1. Coriell Personalized Medicine Collaborative Research Study Report. This report includes all data included in the clinical report as well as supplemental interpretations and educational material. This research report is based on Questionnaires Finalized on 08/01/2010**
- 2. Clinical Report. This report was generated and approved by Coriell's CLIA certified genotyping laboratory.**



Sample Results

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CPMC Research Study Report

Name:	NATALIE DEMO	Gender:	Female
Date of Birth:		Date Collected:	11-30-2016
Coriell ID:	DEMONAT	Date Received:	11-30-2016
Lab Accessioning Number:	DEMONAT	Date of Report:	09-08-2015
Ordering Physician:	Dr. Edward Viner		

Risk of Developing Lung Cancer Based on:

- **CPMC Lung Cancer Variants**
 - rs938682
 - rs2736100
- **Family History**
- **Smoking**

The CPMC is a research study investigating the utility of personalized genomic information on health and health behavior. Most common health conditions are caused by an interaction between multiple genetic variants and non-genetic risk factors such as lifestyle and environment. The genetic variant risk in this report is based on two genetic variants, but does not represent your complete genetic risk for developing lung cancer. These results were generated as part of this research study in a CLIA-approved laboratory.

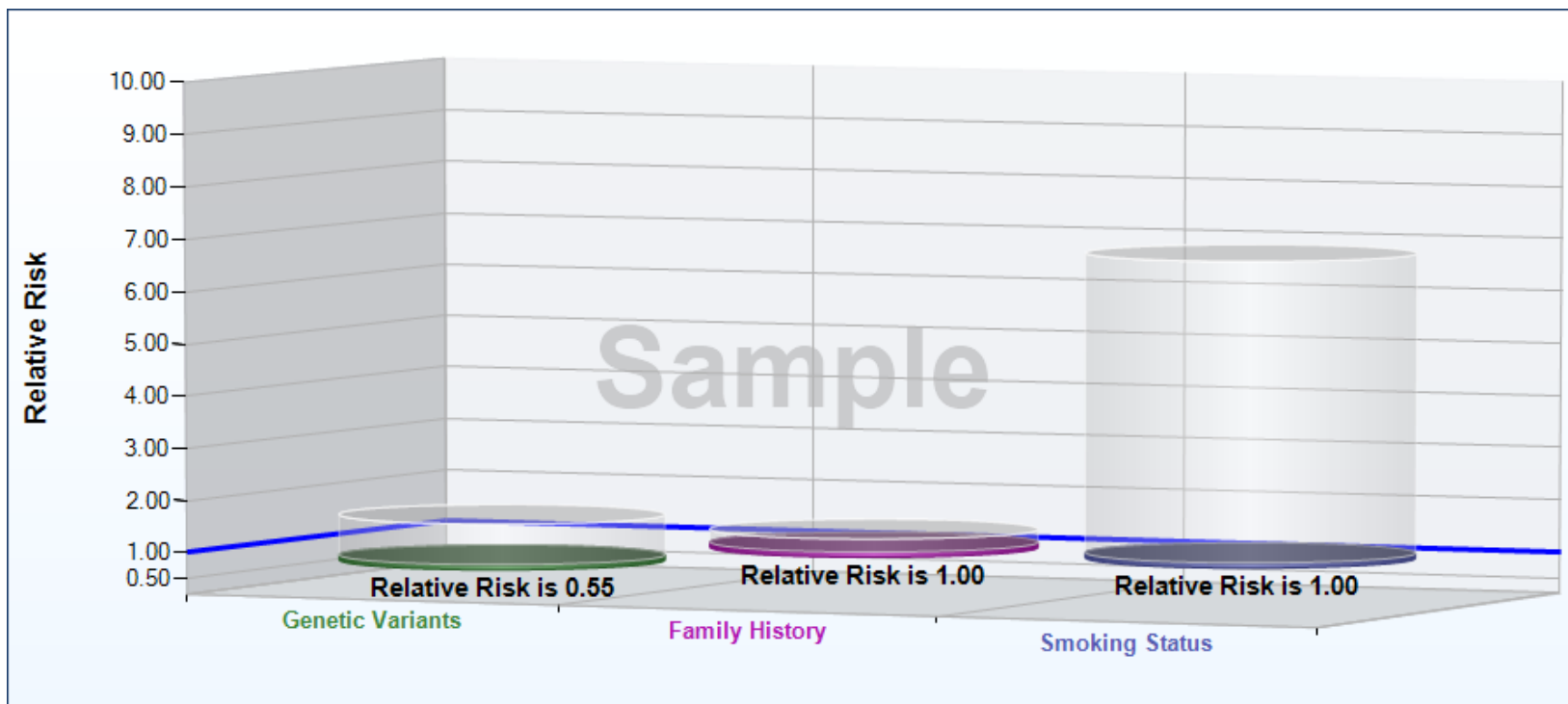
More information about the study, how to interpret CPMC results, and how we calculate risk is available on our website <http://cpmc.coriell.org> or by contacting our genetic counselor. Participants may schedule an appointment with our board-certified genetic counselor through the web portal by clicking on "request an appointment". Our genetic counselor also can be reached by email at cpmcgc@coriell.org or by phone at 888-580-8028.

This research report includes all data included in the clinical report as well as supplemental interpretations and educational material. Please see the report that follows for the official clinical report.

Genetic Variant Result, Details and Population Data

Lung Cancer

Risk factors may be related to each other and risk estimates cannot be combined.
 This graph provides a summary of the relative risk for 2 genetic variants, family history, and smoking.



You reported you are African American, 40 years old or younger; data for African Americans in your age group is not available, however, an estimated less than 1 in 1,000 African Americans between 40 and 49 years old have lung cancer.

Chart Color	Relative Risk Due To:	Minimum Risk	Maximum Risk	Your Risk	Interpretation
	Genetic Variants	0.55	1.33	0.55	Based on your combination of genetic variants, you are 45% less likely (or 0.55 times as less likely) to develop lung cancer than an average individual. <i>Having this combination of genetic variants lowers your risk of developing lung cancer.</i>
	Family History	1.00	1.25	1.00	Based on your family history, you are at a lower risk to develop lung cancer compared to someone with a first degree relative (parent, sibling, or child) with lung cancer.
	Smoking Status	1.00	6.71	1.00	Because you are not a smoker, you are at a lower risk to develop lung cancer compared to ever smokers.

How Common

Lung Cancer (Multi-variant Version #1)

The table and picture below show how many individuals will fall into each of the genetic risk categories for lung cancer based on 2 genetic variants.

Reduced Risk	9 in 100 people
Average Risk	76 in 100 people
Elevated Risk	15 in 100 people



Your Genetic Results

Lung Cancer

Multi-variant Genetic Risk

The CPMC tested 2 sites of genetic variation in 2 genes associated with lung cancer.
Your result for each genetic variant tested is shown below in yellow.

Variants Tested	Reference Value	Your Result
rs2736100	AA	AA
rs938682	GG	GG

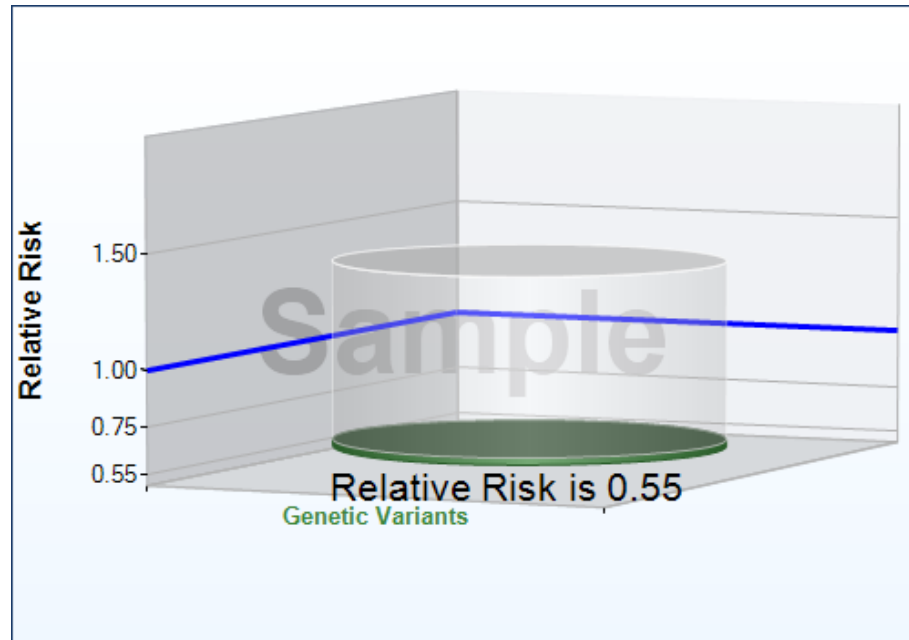
Lung Cancer Multi-variant Genetic Risk

Chart Color	Genetic Risk Score	Risk Category	Interpretation
	0.55	Decreased	<p>Based on your combination of genetic variants, you are 45% less likely (or 0.55 times as less likely) to develop lung cancer than an average individual.</p> <p><i>Having this combination of genetic variants lowers your risk of developing lung cancer.</i></p>

The CPMC tested 2 sites of genetic variation in 2 genes associated with lung cancer.

Your risk due to the genetic variants tested was estimated and compared to the genetic risk of an average individual.

Other genetic variants, not currently included in this CPMC test, may also influence your risk to develop lung cancer.



These results are based on multiple studies.

Lung Cancer Risk Due To Family History

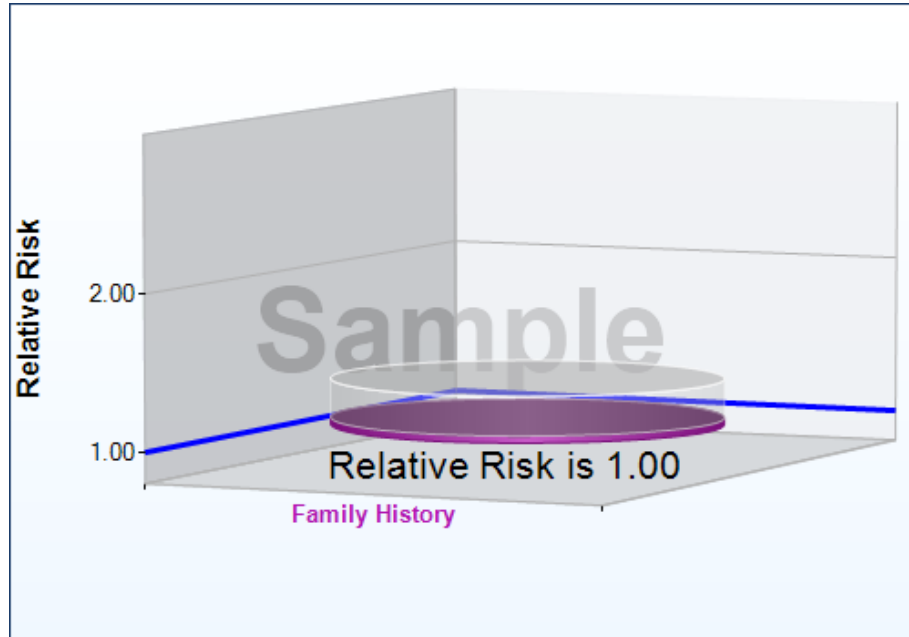
You reported that none of your first degree relatives (parents, siblings or children) have had lung cancer.

Chart Color	Minimum Risk	Maximum Risk	Your Risk	Interpretation
	1.00	1.25	1.00	Based on your family history, you are at a lower risk to develop lung cancer compared to someone with a first degree relative (parent, sibling, or child) with lung cancer.

Risk is compared based on family history.

People with a first degree relative with lung cancer were compared to people with no family history of lung cancer to determine relative risk of developing lung cancer.

A relative risk greater than 1.00 indicates an increased risk.



These results are based on multiple studies.

Lung Cancer

Risk Due To Smoking Status

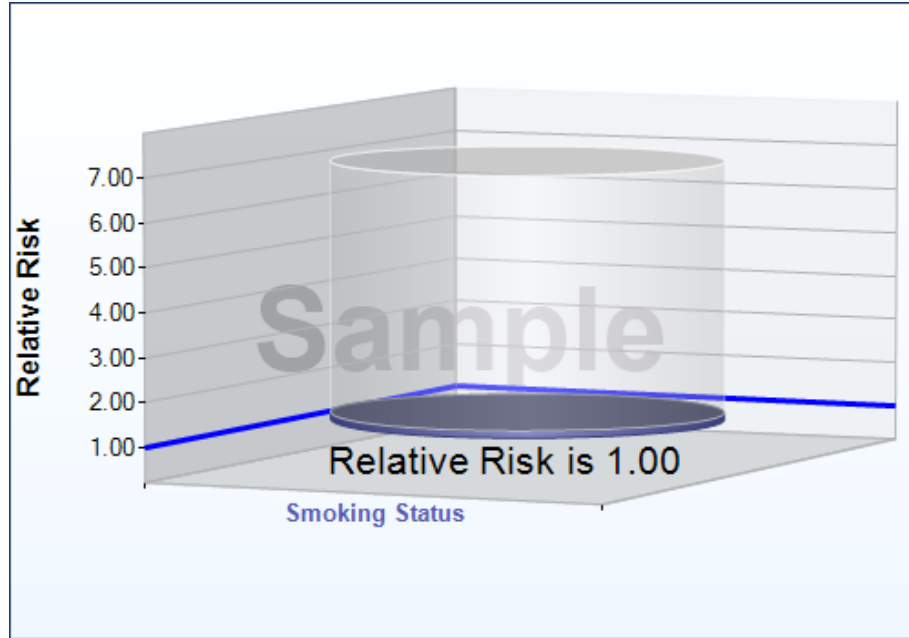
You reported that you do not smoke.

Chart Color	Minimum Risk	Maximum Risk	Your Risk	Interpretation
	1.00	6.71	1.00	Because you are not a smoker, you are at a lower risk to develop lung cancer compared to ever smokers.

Risk is compared based on smoking habits.

Women who are current and former smokers were compared to women who have never smoked to determine relative risk.

A relative risk greater than 1.00 indicates an increased risk.



These results are based on multiple studies.

Lung Cancer (Multi-variant Version #1)

We all have 2 copies of every gene, one inherited from each of our parents.

Each copy may have small changes called genetic variants.

Some genetic variants are associated with an increased risk of developing a disease.

Some genetic variants are associated with a decreased risk of developing a disease.

The CPMC tested 2 sites of genetic variation in 2 genes associated with lung cancer.

Background information about each genetic variant tested is shown below.

Genetic Variants	Variant Type	Gene	Chromosomal Location
rs2736100	A = non-risk C = risk	<i>TERT</i>	5p15
rs938682	G = non-risk A = risk	<i>CHRNA3</i>	15q25

Causes

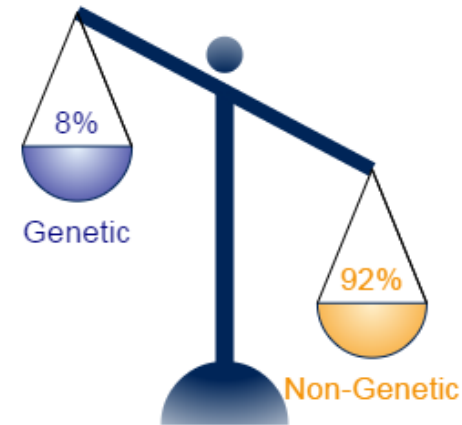
Genetic vs. Non-Genetic Risk Factors

Lung cancer can be caused by both genetic factors and non-genetic (or environmental) risk factors.

It is estimated that **non-genetic** factors (like smoking and diet) account for about **92%** of the risk for developing lung cancer.

It is estimated that **8%** of the risk for developing lung cancer is based on **genetic** risk factors. This estimate accounts for both known and unknown gene variants.

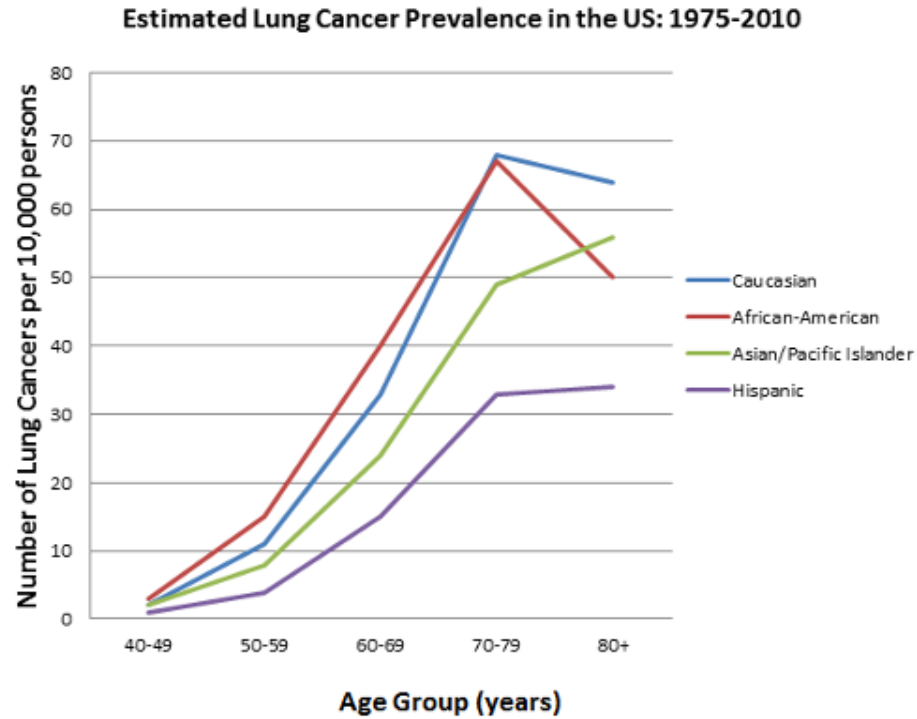
There are many different genetic and non-genetic risk factors that contribute to the risk of lung cancer. We are only able to tell you about your family history risk, 2 genetic risk factors, and 1 non-genetic risk factor for lung cancer.



Prevalence

The risk of lung cancer increases with age and differs across populations.

You reported you are African American, 40 years old or younger; data for African Americans in your age group is not available, however, an estimated less than 1 in 1,000 African Americans between 40 and 49 years old have lung cancer.



Limitations

Lung Cancer

- These results alone do NOT diagnose lung cancer. Lung cancer must be diagnosed by your health care provider.
- This result does NOT mean that you have or will absolutely develop lung cancer.
- This result does NOT mean that you will not develop lung cancer in the future.
- This result ONLY assesses your risk for developing lung cancer due to the factors presented in this report and does not mean that other genetic variants or risk factors for lung cancer are present or absent.
- Personal risk factors, such as age, family history or lifestyle, may have a greater impact on your risk to develop lung cancer than any individual or multiple genetic variant(s).
- Our method of estimating genetic risk due to multiple genetic variants requires complete data. If data are missing for any individual genetic variant included in our analysis, we will not be able to provide you a genetic risk estimate.
- Risk estimates are based on current available scientific literature.
- Although rare, it is possible that you may receive an incorrect result; 100% accuracy of reported results cannot be guaranteed.
- Occasionally there may be a specific variant on a gene chip that is not able to be read or interpreted. In this case you will not receive a result for that variant. It is expected that you will receive results for about 95% of variants approved by the ICOB.
- Relative risks used to estimate risk of disease for CPMC participants are based on groups of people with the same risk or protective factor as the individual CPMC participant. In some cases, the relative risk is estimated based upon an odds ratio and known or assumed disease prevalence.
- Separate risk estimates for each risk or protective factor have been given. Risk or protective factors may be related to each other and risk estimates cannot be combined.
- Risk information for non-genetic factors is based on information you provided in your medical, family, lifestyle questionnaire. If you did not provide answers or if you answered “do not know”, risk estimates for some factors may not be available.
- Risk information for non-genetic factors is based on information you provided in your medical, family, lifestyle questionnaire and may not be reflective of your current risk if any of these factors have changed. You will be given the opportunity to update your medical, family and lifestyle questionnaire responses periodically.
- Every effort will be made to provide you with risk information based on your reported race/ethnicity. However, data may not be available for all races/ethnicities for all risk factors. Please see your individual results to determine which race/ethnicity the data given is based on.

Methods

Lung Cancer

This condition and genetic variant(s) were approved by the Informed Cohort Oversight Board (ICOB)

Test Methodology

Saliva samples were collected using Oragene DNA Collection Kits (DNA Genotek) and DNA was extracted manually according to the manufacturer's instructions. Purified DNA was quantified using UV absorbance at 260 nm. Five hundred nanograms of the resulting DNA from each sample were used as template in the Affymetrix Genome-Wide Human SNP Nsp/Sty 6.0 GeneChip assay. Data analysis was performed using Affymetrix Genotyping Console software.

See [CPMC Technical Paper](#) for genetic variant selection and reporting methodology.

[Risk interpretation based on Coriell's Lung Cancer Research Risk Algorithm Version 1 (July 22, 2014)]

1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. *Genet Med.* 13(2):131-139.
2. Goddard, G.H. et al (2010). Risk categorization for complex disorders according to genotype relative risk and precision in parameter estimates. *Genet Epidemiol.* 34(6):624-32.
3. Crouch, D.J. et al (2012). REGENT: a risk assessment and classification algorithm for genetic and environmental factors. *Eur J Hum Genet.* 21(1):109-11.
4. McVean G.A. et al (2012). An integrated map of genetic variation from 1,092 human genomes. *Nature.* 491; 56-65.
5. Lee, P.N. et al (2012). Systematic review with meta-analysis of the epidemiological evidence in the 1900s relating smoking to lung cancer. *BMC Cancer.* 12; 385.
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8. Nie W., Zang Y., Chen J., et al. (2014). TERT rs2736100 polymorphism contributes to lung cancer risk: A meta-analysis including 49,869 cases and 73,464 controls. *Tumor Biol.* [EPub Ahead of Print]. DOI: 10.1007/s13277-014-1734-2.
9. Howlander N, Noone AM, Krapcho M, Garshell J, Miller D, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2011, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2011/, based on November 2013 SEER data submission, posted to the SEER web site, April 2014.

Sample Results



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Clinical Report for Lung Cancer (Multi-variant)

Name:	NATALIE DEMO	Sample Type:	Saliva
Race/Ethnicity:	Black or African-American	Gender:	Female
Date of Birth:		Date Collected:	11-30-2016
Coriell ID:	DEMONAT	Date Received:	11-30-2016
Lab Accessioning Number:	DEMONAT	Date of Report:	09-08-2015
Ordering Physician:	Dr. Edward Viner		

Gene/Region	Variant Tested	Reference Genotype	Your Result	Interpretation
TERT	rs2736100	AA	AA	Without considering other genetic variants, individuals with this result are at a lower risk to develop lung cancer compared to someone with one or two copies of this genetic risk variant. These risk estimates are based on studies involving multiple populations that include individuals with Asian and European ancestry.*
CHRNA3	rs938682	GG	GG	Without considering other genetic variants, individuals with this result are at a lower risk to develop lung cancer compared to someone with one or two copies of this genetic risk variant. These risk estimates are based on studies involving multiple populations that include individuals with Asian and European ancestry.*
Other Risks		Other genetic variants and other risk factors including co-morbidities, lifestyle and family history may contribute to the risk of lung cancer. For additional information on other risk factors please see the accompanying CPMC research report.		

*When race/ethnicity specific risk estimates are not available, risk estimates based on European populations are provided.

Risk interpretation based on Coriell's Lung Cancer Clinical Risk Algorithm Version 1 (July 22, 2014)

Test Limitations

DNA-based testing is highly accurate, however there are many sources of potential error including: mis-identification of samples, rare technical errors, trace contamination of PCR reactions, and rare genetic variants that interfere with analysis. There may be other variants, not included in this test, that influence the risk to develop lung cancer. This test is not diagnostic for lung cancer and cannot rule out the risk of developing lung cancer in the future. Risk estimates are based on current available literature (see references). This test or one or more of its components was developed and its performance characteristics determined by the Coriell Institute for Medical Research. It has not been approved by the Food and Drug Administration (FDA). The FDA has determined that such approval is not necessary. The Coriell Institute is regulated under the Clinical Laboratory Improvement Amendments (CLIA) of 1988 as qualified to perform high-complexity testing.

Test Methodology

Saliva samples were collected using Oragene DNA Collection Kits (DNA Genotek) and DNA was extracted manually according to the manufacturer's instructions or automatically using a DNAAdvance Kit (Agencourt). Purified DNA was quantified using UV absorbance at 260 nm. Five hundred nanograms of the resulting DNA from each sample were used as template in the Affymetrix Genome-Wide Human SNP Nsp/Sty 6.0 GeneChip assay. Data analysis was performed using Affymetrix Genotyping Console software.

Electronically signed by

Marie Hoover, PhD, Laboratory Director

This clinical report only includes data generated in the CLIA approved genotyping laboratory, for additional information please see the CPMC research report.

References

1. Broderick P., Wang Y., Vijayakrishnan J., et al. (2009). Deciphering the impact of common genetic variation on lung cancer risk: A genome-wide association study. *Cancer Res.* 69(16):6633-6641.
2. Nie W., Zang Y., Chen J., et al. (2014). TERT rs2736100 polymorphism contributes to lung cancer risk: A meta-analysis including 49,869 cases and 73,464 controls. *Tumor Biol.* [Epub Ahead of Print]. DOI: 10.1007/s13277-014-1734-2.

