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.
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: 09-05-2013
Ordering Physician: Dr. Edward Viner

Risk of Developing Bladder Cancer Based on:

- CPMC Bladder Cancer Variant 1 (rs9642880)
- Family History
- Smoking
- Childbearing History
- Age at First Menstrual Period

The CPMC is a research study investigating the utility of personalized genomic information on health and health behavior. At this time, the CPMC is reporting one genetic variant per health condition. Since most common health conditions are caused by an interaction between more than one genetic factor and non-genetic factors such as lifestyle, the genetic variant risk in this report does not represent your complete genetic risk for bladder 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 counselors. Participants may schedule an appointment with one of our board-certified genetic counselors through the web portal by clicking on "request an appointment". Our genetic counselors 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.
You reported you are an African American woman, between 30 and 39 years old; less than 1 in 10,000 African American women in your age group have bladder cancer.

<table>
<thead>
<tr>
<th>Chart Color</th>
<th>Relative Risk Due To:</th>
<th>Your Risk</th>
<th>Minimum Risk</th>
<th>Maximum Risk</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic Variant</td>
<td>1.50</td>
<td>1.00</td>
<td>1.50</td>
<td>You have 2 copies of the risk variant. Based on this result, you are 50% more likely (or 1.5 times as likely) to develop bladder cancer as someone with no copies of this variant.</td>
<td></td>
</tr>
<tr>
<td>Family History</td>
<td>1.00</td>
<td>1.00</td>
<td>2.00</td>
<td>Based on your family history, you are at a lower risk to develop bladder cancer compared to someone who has a parent with bladder cancer.</td>
<td></td>
</tr>
<tr>
<td>Age at First Menstrual Period</td>
<td>1.00</td>
<td>0.57</td>
<td>1.00</td>
<td>Because you reported that you were 14 years of age or younger when you had your first menstrual period, you are at a higher risk of bladder cancer compared to women who were 15 years of age or older when they had their first menstrual period.</td>
<td></td>
</tr>
<tr>
<td>Childbearing History</td>
<td>1.00</td>
<td>0.76</td>
<td>1.00</td>
<td>Because you reported that you have never given birth to a child, you are at a greater risk of bladder cancer compared to women who have given birth to at least one child.</td>
<td></td>
</tr>
<tr>
<td>Smoking Status</td>
<td>1.00</td>
<td>1.00</td>
<td>4.70</td>
<td>Because you are not a smoker, you are at a lower risk to develop bladder cancer compared to current and former smokers.</td>
<td></td>
</tr>
</tbody>
</table>
Bladder Cancer
Risk Due To Genetic Variant #1 (rs9642880)
Your Result: 2 copies of the risk variant were detected (TT)
Non-Risk Variant = G  Risk Variant = T

<table>
<thead>
<tr>
<th>Chart Color</th>
<th>Your Risk</th>
<th>Minimum Risk</th>
<th>Maximum Risk</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.50</td>
<td>1.00</td>
<td>1.50</td>
<td></td>
<td>You have 2 copies of the risk variant. Based on this result, you are 50% more likely (or 1.5 times as likely) to develop bladder cancer as someone with no copies of this variant.</td>
</tr>
</tbody>
</table>

Having this risk variant contributes to your risk of bladder cancer.

Genetic Variant Risk is based on the number of copies of this genetic risk variant.

People with one or two copies of the risk variant are compared to people with no copies of the risk variant to determine relative risk.

A relative risk greater than 1.0 indicates an increased risk.

These risk estimates are based on a study conducted in a Caucasian population.
Bladder Cancer
Risk Due To Family History
You reported that neither of your parents have bladder cancer.

<table>
<thead>
<tr>
<th>Chart Color</th>
<th>Your Risk</th>
<th>Minimum Risk</th>
<th>Maximum Risk</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.00</td>
<td>1.00</td>
<td>2.00</td>
<td></td>
<td>Based on your family history, you are at a lower risk to develop bladder cancer compared to someone who has a parent with bladder cancer.</td>
</tr>
</tbody>
</table>

Risk is compared based on family history.

People with a parent with bladder cancer were compared to people without a parent with bladder cancer to determine relative risk of developing bladder cancer.

A relative risk greater than 1.0 indicates an increased risk.

These risk estimates are based on a study conducted in a Caucasian population.
Bladder Cancer
Risk Due To Age at First Menstrual Period
You reported that you were 14 years old or younger when you had your first menstrual period.

<table>
<thead>
<tr>
<th>Chart Color</th>
<th>Your Risk</th>
<th>Minimum Risk</th>
<th>Maximum Risk</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.00</td>
<td>0.57</td>
<td>1.00</td>
<td></td>
<td>Because you reported that you were 14 years of age or younger when you had your first menstrual period, you are at a higher risk of bladder cancer compared to women who were 15 years of age or older when they had their first menstrual period.</td>
</tr>
</tbody>
</table>

Risk is compared based on the age you were when you had your first menstrual period.

To determine relative risk, women who were 15 years of age or older when they had their first menstrual period were compared to women who were 14 years old or younger when they had their first menstrual period.

A relative risk less than 1.0 indicates a reduction of risk.

These results are based on a study conducted on multiple populations of differing racial and ethnic backgrounds.
### Bladder Cancer
**Risk Due To Childbearing History**
You reported that you do not have children.

<table>
<thead>
<tr>
<th>Chart Color</th>
<th>Your Risk</th>
<th>Minimum Risk</th>
<th>Maximum Risk</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.00</td>
<td>0.76</td>
<td>1.00</td>
<td>Because you reported that you have never given birth to a child, you are at a greater risk of bladder cancer compared to women who have given birth to at least one child.</td>
</tr>
</tbody>
</table>

Risk is based on whether you have given birth to a child.

Women who have given birth to at least one child are compared to women who have never given birth to a child to determine relative risk.

A relative risk less than 1.0 indicates a reduction of risk.

These results are based on a study conducted on multiple populations of differing racial and ethnic backgrounds.
Because you are not a smoker, you are at a lower risk to develop bladder cancer compared to current and former smokers.

Risk is compared based on smoking habits. Women who are current smokers or former smokers are compared to women who have never smoked to determine relative risk. A relative risk of greater than 1.0 indicates an increased risk.

These risk estimates are based on a study conducted on multiple populations of differing racial and ethnic backgrounds.
Bladder Cancer - Variant #1 (rs9642880)

We all have 2 copies of every gene, one from each of our parents. Each copy may have small changes called genetic variants. Some genetic variants are associated with an increased risk of disease. Some genetic variants are associated with a decreased risk of disease.

Having one or two copies of this variant increases your risk for bladder cancer.

How Common Is This Variant?

Non-Risk Variant = G  Risk Variant = T

<table>
<thead>
<tr>
<th>Variant</th>
<th>Frequency</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>GG</td>
<td>8%</td>
<td>8 in 100 people have 2 copies of the non-risk variant</td>
</tr>
<tr>
<td>GT</td>
<td>35%</td>
<td>35 in 100 people have 1 copy of the non-risk variant and 1 copy of the risk variant</td>
</tr>
<tr>
<td>TT</td>
<td>57%</td>
<td>57 in 100 people have 2 copies of the risk variant</td>
</tr>
</tbody>
</table>

This data is based on studies in African American populations.

Gene: MYC  Chromosome: 8q24.21
Causes

Genetic vs. Non-Genetic Risk Factors

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

It is estimated that non-genetic factors (like smoking) account for about 93% of the risk of bladder cancer.

It is estimated that 7% of the risk for bladder 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 bladder cancer. We are only able to tell you about your family history risk, 1 genetic and 3 non-genetic risk factors at this time.
How Common

The risk of having bladder cancer increases with age. Men have a slightly greater risk of developing bladder cancer than women. Caucasians have a greater risk of bladder cancer than individuals of other races.

You reported you are an African American woman, between 30 and 39 years old; less than 1 in 10,000 African American women in your age group have bladder cancer.

Age, race, and gender contribute to your risk of bladder cancer.
Limitations

Bladder Cancer

- This result alone does NOT diagnose bladder cancer. Bladder cancer must be diagnosed by your health care provider.
- This result does NOT mean that you have or will absolutely develop bladder cancer.
- This result does NOT mean that you will not develop bladder cancer in the future.
- This result ONLY assesses your risk for developing bladder cancer due to the factors presented in this report and does not mean that other genetic variants or risk factors for bladder cancer are present or absent.
- The relative risk information presented in this report represents the risk of developing bladder cancer for individuals who do not have a history of bladder cancer.
- Personal risk factors, such as age, family history or lifestyle, may have a greater impact on your risk to develop bladder cancer than any individual genetic variant.
- Risk estimates are based on current available 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.
- For some risk factors data may be provided by gender. Every effort will be made to provide you with risk information based on your reported gender. However, when risk data is not available for both genders, risk results for the available gender will be provided.
**Methods**

**Bladder 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.

Sample Results

Coriell Institute for Medical Research
Coriell Genotyping and Microarray Center
403 Haddon Avenue Camden, NJ 08103
Phone: 856-966-7377 Fax: 856-964-0254  www.coriell.org

Clinical Report for Bladder Cancer Genetic Variant 1 (rs9642880)

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: 09-05-2013
Ordering Physician: Dr. Edward Viner

Name of Gene/Region: MYC
Chromosomal Location: 8q24.21

<table>
<thead>
<tr>
<th>Variants tested</th>
<th>Result</th>
<th>Reference Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs9642880</td>
<td>TT</td>
<td>GG</td>
</tr>
</tbody>
</table>

Interpretation
Individuals with this result are 50% more likely (or 1.5 times as likely) to develop bladder cancer as someone with no copies of this variant.
These risk estimates are based on studies in Caucasian populations. When race/ethnicity specific risk estimates are not available, risk estimates based on Caucasian populations are provided.

Other Risks
Other genetic variants and other risk factors including co-morbidities, lifestyle and family history may contribute to the risk of bladder cancer. For additional information on other risk factors please see the accompanying CPMC research report.

Risk interpretation based on Coriell's Bladder Cancer Risk Algorithm Version 1 (September 10, 2013)

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 bladder cancer. This test is not diagnostic for bladder cancer and cannot rule out the risk of developing bladder cancer in the future. Risk estimates are based on current available literature (see reference). 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

References

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