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.
The CPMC is a research study investigating the utility of personalized genomic information on health and health behavior. Since most common health conditions are caused by an interaction between more than one genetic factor and non-genetic risk factors such as lifestyle, the genetic risk variant in this report does not represent your complete genetic risk for kidney 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.
Risk factors may be related to each other and risk estimates cannot be combined. This graph provides a summary of the relative risks for a genetic variant, family history, smoking status and BMI.

You reported you are Caucasian, between 60 and 69 years old; an estimated 3 in 1,000 Caucasians in your age group have kidney cancer.

### Interpretation

<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>1.90</td>
<td>1.00</td>
<td>1.90</td>
<td>You have 2 copies of the risk variant. Based on this result, you are 90% more likely (or 1.9 times as likely) to develop kidney cancer as someone with no copies of this variant. &lt;br&gt;<strong>Having this risk variant contributes to your risk of kidney cancer.</strong></td>
<td></td>
</tr>
<tr>
<td>Family History</td>
<td>2.21</td>
<td>1.00</td>
<td>2.21</td>
<td>Based on your family history, you are 2.21 times more likely to develop kidney cancer compared to someone who does not have any first degree relatives with kidney cancer. &lt;br&gt;<strong>Having at least one parent, sibling, or child with kidney cancer contributes to your risk of developing kidney cancer.</strong></td>
<td></td>
</tr>
<tr>
<td>Smoking Status</td>
<td>1.53</td>
<td>1.00</td>
<td>1.53</td>
<td>Because you are a current or former smoker, you are 53% times more likely (or 1.53 times as likely) to develop kidney cancer compared to never smokers. &lt;br&gt;<strong>Being a current or former smoker contributes to your risk of kidney cancer.</strong></td>
<td></td>
</tr>
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</tr>
</tbody>
</table>
| Body Mass Index | 1.36 | 1.00 | 1.89 | Based on your BMI you are 36% more likely (or 1.36 times as likely) to develop kidney cancer compared to individuals who have a BMI of less than 25 (not overweight).

*Being overweight (BMI of 25 or greater) contributes to your risk of kidney cancer.*
**Kidney Cancer**

**Risk Due To Genetic Variant #1 (rs7105934)**

*Your Result: 2 copies of the risk variant were detected (GG)*

Non-Risk Variant = A  Risk Variant = G

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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 were compared to people with no copies of the risk variant to determine relative risk.

A relative risk greater than 1.00 indicates an increased risk.

These results are based on multiple studies.
Based on your family history, you are 2.21 times more likely to develop kidney cancer compared to someone who does not have any first degree relatives with kidney cancer.

Having at least one parent, sibling, or child with kidney cancer contributes to your risk of developing kidney cancer.

Risk is compared based on family history.

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

A relative risk greater than 1.00 indicates an increased risk.

These results are based on multiple studies.
Because you are a current or former smoker, you are 53% times more likely (or 1.53 times as likely) to develop kidney cancer compared to never smokers.

*Being a current or former smoker contributes to your risk of kidney cancer.*

Risk is compared based on smoking habits.

Men who are current or former smokers were compared to men who have never smoked to determine relative risk.

A relative risk of greater than 1.00 indicates an increased risk.

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These results are based on multiple studies.
Kidney Cancer
Risk Due To Body Mass Index

According to the height and weight you reported, you may be overweight (BMI = 25.0-29.9).

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</table>

Risk is compared based on Body Mass Index (BMI). BMI is used to determine if someone is overweight or obese.

People who are overweight (BMI 25-29.9) or obese (BMI ≥ 30) are compared to people who are not overweight (BMI < 25) to determine relative risk.

A relative risk greater than 1.00 indicates an increased risk.

These results are based on multiple studies.
**Kidney Cancer - Variant #1 (rs7105934)**

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

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

<table>
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<th>How Common Is This Variant?</th>
<th></th>
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<td>Non-Risk Variant = A</td>
<td>Risk Variant = G</td>
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- **AA** - 12 in 100 people have 2 copies of the non-risk variant
- **AG** - 21 in 100 people have 1 copy of the non-risk variant and 1 copy of the risk variant
- **GG** - 67 in 100 people have 2 copies of the risk variant

This data is based on studies in worldwide populations.

| Gene: Intergenic | Chromosome: 11q13.31 |
Kidney 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 body mass index) account for about 92% of the risk for kidney cancer.

It is estimated that 8% of the risk for kidney 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 kidney cancer. We are only able to tell you about your family history risk, 1 genetic risk factor, and 2 non-genetic risk factors at this time.
The risk of kidney cancer increases with age and differs across populations.

You reported you are Caucasian, between 60 and 69 years old; an estimated 3 in 1,000 Caucasians in your age group have kidney cancer.
Limitations

Kidney Cancer

- These results alone do NOT diagnose kidney cancer. Kidney cancer must be diagnosed by your health care provider.
- This result does NOT mean that you have or will absolutely develop kidney cancer.
- This result does NOT mean that you will not develop kidney cancer in the future.
- This result ONLY assesses your risk for developing kidney cancer due to the factors presented in this report and does not mean that other genetic variants or risk factors for kidney 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 kidney cancer than any individual or multiple genetic variant(s).
- 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

Kidney Cancer

This condition and genetic variant 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 Kidney Cancer Risk Algorithm Version 1 (October 15, 2015)]


Clinical Report for Kidney Cancer Genetic Variant 1 (rs7105934)

Name: STEVE CPMC
Race/Ethnicity: White (Caucasian)
Sample Type: Saliva
Gender: Male
Date of Birth: Date Collected: 11-30-2016
Coriell ID: DEMOSTEVE
Lab Accessioning Number: DEMOSTEVE
Date Received: Date of Report: 11-30-2016
10-06-2015

Name of Gene/Region: Intergenic
Chromosomal Location: 11q13.31

Variants tested | Result | Reference Genotype
--- | --- | ---
rs7105934 | GG | AA

Interpretation
Individuals with this result are 90% more likely (or 1.90 times as likely) to develop kidney cancer as someone with no copies of this variant.
These risk estimates are based on studies in European 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 kidney cancer. For additional information on other risk factors please see the accompanying CPMC research report.


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 kidney cancer. This test is not diagnostic for kidney cancer and cannot rule out the risk of developing kidney 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