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: 03-10-2014
Ordering Physician: Dr. Edward Viner

Risk of Developing Pancreatic Cancer Based on:

- CPMC Pancreatic Cancer Variants
  - rs3790844
  - rs401681
  - rs4885093

- Family History
- Smoking
- Body Mass Index

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 three genetic variants, but does not represent your complete genetic risk for pancreatic 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

Pancreatic 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 3 genetic variants, family history, smoking, and body mass index.

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 10,000 African Americans between 40 and 49 years old have pancreatic cancer.

<table>
<thead>
<tr>
<th>Chart Color</th>
<th>Relative Risk Due To:</th>
<th>Minimum Risk</th>
<th>Maximum Risk</th>
<th>Your Risk</th>
<th>Interpretation</th>
</tr>
</thead>
</table>
|             | Genetic Variants      | 0.51         | 1.69         | 1.44      | Based on your combination of genetic variants, you are 44% more likely (or 1.44 times as likely) to develop pancreatic cancer than an average individual. 
*Having this combination of genetic variants increases your risk of pancreatic cancer.* |
|             | Family History        | 1.00         | 1.80         | 1.80      | Based on your family history, you are 80% more likely (or 1.80 times as likely) to develop pancreatic cancer compared to someone who does not have a first degree relative with pancreatic cancer. 
*Having a parent, sibling, or child with pancreatic cancer contributes to your risk of pancreatic cancer.* |
|             | Smoking Status        | 1.00         | 1.70         | 1.00      | Because you are not a smoker, you are at a lower risk to develop pancreatic cancer compared to current and former smokers. |
|             | Body Mass Index       | 1.00         | 1.50         | 1.00      | Based on your BMI you are at a lower risk of developing pancreatic cancer compared to individuals who have a BMI of 25 or higher (overweight or obese). |
Pancreatic Cancer (Multi-variant Version #1)

The table and picture below show how many individuals will fall into each of the genetic risk categories for pancreatic cancer based on 3 genetic variants.

<table>
<thead>
<tr>
<th>Genetic Risk</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced Risk</td>
<td>12 in 100 people</td>
</tr>
<tr>
<td>Average Risk</td>
<td>80 in 100 people</td>
</tr>
<tr>
<td>Elevated Risk</td>
<td>8 in 100 people</td>
</tr>
</tbody>
</table>
**Pancreatic Cancer**

**Multi-variant Genetic Risk**

The CPMC tested 3 sites of genetic variation in 3 genes associated with pancreatic cancer. Your result for each genetic variant tested is shown below in yellow.

<table>
<thead>
<tr>
<th>Variants Tested</th>
<th>Reference Value</th>
<th>Your Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs3790844</td>
<td>AA</td>
<td>AA</td>
</tr>
<tr>
<td>rs401681</td>
<td>CC</td>
<td>CT</td>
</tr>
<tr>
<td>rs4885093</td>
<td>AA</td>
<td>GG</td>
</tr>
</tbody>
</table>
Based on your combination of genetic variants, you are 44% more likely (or 1.44 times as likely) to develop pancreatic cancer than an average individual.

Having this combination of genetic variants increases your risk of pancreatic cancer.

The CPMC tested 3 sites of genetic variation in 3 genes associated with pancreatic 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 pancreatic cancer.

These results are based on multiple studies.
Pancreatic Cancer
Risk Due To Family History
You reported that a first degree relative (parent, sibling or child) has pancreatic cancer.

<table>
<thead>
<tr>
<th>Chart Color</th>
<th>Minimum Risk</th>
<th>Maximum Risk</th>
<th>Your Risk</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.00</td>
<td>1.80</td>
<td>1.80</td>
<td>Based on your family history, you are 80% more likely (or 1.80 times as likely) to develop pancreatic cancer compared to someone who does not have a first degree relative with pancreatic cancer. Having a parent, sibling, or child with pancreatic cancer contributes to your risk of pancreatic cancer.</td>
</tr>
</tbody>
</table>

Risk is compared based on family history.

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

A relative risk greater than 1.00 indicates an increased risk.

These results are based on multiple studies.
Pancreatic Cancer
Risk Due To Smoking Status
You reported that you do not smoke.

<table>
<thead>
<tr>
<th>Chart Color</th>
<th>Minimum Risk</th>
<th>Maximum Risk</th>
<th>Your Risk</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.00</td>
<td>1.70</td>
<td>1.00</td>
<td>Because you are not a smoker, you are at a lower risk to develop pancreatic cancer compared to current and former smokers.</td>
</tr>
</tbody>
</table>

Risk is compared based on smoking habits.
People who are current smokers or former smokers are compared to people who have never smoked to determine relative risk.
A relative risk of greater than 1.00 indicates an increased risk.

These results are based on multiple studies.
### Pancreatic Cancer

#### Risk Due To Body Mass Index

According to the height and weight you reported, you are not overweight or obese (BMI <25.00).

<table>
<thead>
<tr>
<th>Chart Color</th>
<th>Minimum Risk</th>
<th>Maximum Risk</th>
<th>Your Risk</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.00</td>
<td>1.50</td>
<td>1.00</td>
<td>Based on your BMI you are at a lower risk of developing pancreatic cancer compared to individuals who have a BMI of 25 or higher (overweight or obese).</td>
</tr>
</tbody>
</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.
Pancreatic 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 3 sites of genetic variation in 3 genes associated with pancreatic cancer. Background information about each genetic variant tested is shown below.

<table>
<thead>
<tr>
<th>Genetic Variants</th>
<th>Variant Type</th>
<th>Gene</th>
<th>Chromosomal Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs3790844</td>
<td>A=non-protective, G=protective</td>
<td>NR5A2</td>
<td>1p32.1</td>
</tr>
<tr>
<td>rs401681</td>
<td>C=non-risk, T=risk</td>
<td>CLPTM1L</td>
<td>5p15.33</td>
</tr>
<tr>
<td>rs4885093</td>
<td>A=non-risk, G=risk</td>
<td>KLF5/KLF12</td>
<td>13q22.1</td>
</tr>
</tbody>
</table>
Pancreatic 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 64% of the risk for pancreatic cancer.

It is estimated that 36% of the risk for pancreatic 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 pancreatic cancer. We are only able to tell you about your family history risk, 3 genetic risk factors, and 2 non-genetic risk factors for pancreatic cancer.
This risk of having pancreatic 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 10,000 African Americans between 40 and 49 years old have pancreatic cancer.
Limitations

Pancreatic Cancer

- These results alone do NOT diagnose pancreatic cancer. Pancreatic cancer must be diagnosed by your health care provider.
- This result does NOT mean that you have or will absolutely develop pancreatic cancer.
- This result does NOT mean that you will not develop pancreatic cancer in the future.
- This result ONLY assesses your risk for developing pancreatic cancer due to the factors presented in this report and does not mean that other genetic variants or risk factors for pancreatic 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 pancreatic 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.
- 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.
- 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

Pancreatic 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 Pancreatic Cancer Research Risk Algorithm Version 1 (March 11, 2014)]


Clinical Report for Pancreatic 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: 03-10-2014
Ordering Physician: Dr. Edward Viner

<table>
<thead>
<tr>
<th>Gene/Region</th>
<th>Variant Tested</th>
<th>Reference Genotype</th>
<th>Your Result</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>NR5A2</td>
<td>rs3790844</td>
<td>AA</td>
<td>AA</td>
<td>Without considering other genetic variants, individuals with this result are at a higher risk to develop pancreatic cancer compared to someone with one or two copies of the protective variant. These risk estimates are based on studies involving multiple populations that include individuals with African-American, Asian, and European ancestry.*</td>
</tr>
<tr>
<td>CLPTM1L</td>
<td>rs401681</td>
<td>CC</td>
<td>CT</td>
<td>Without considering other genetic variants, individuals with this result are 20% more likely (or 1.20 times as likely) to develop pancreatic cancer as someone with no copies of this variant. These risk estimates are based on studies involving multiple populations that include individuals with African-American, Asian, and European ancestry.*</td>
</tr>
<tr>
<td>KLF5/KLF12</td>
<td>rs4885093</td>
<td>AA</td>
<td>GG</td>
<td>Without considering other genetic variants, individuals with this result are 50% more likely (or 1.50 times as likely) to develop pancreatic cancer as someone with no copies of this variant. These risk estimates are based on a study in an Asian population*</td>
</tr>
</tbody>
</table>

Other Risks
Other genetic variants and other risk factors including co-morbidities, lifestyle and family history may contribute to the risk of pancreatic 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 Caucasian populations are provided.

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