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- 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: | STEVE CPMC | Gender: | Male |
| Date of Birth: | | Date Collected: | 11-30-2016 |
| Coriell ID: | DEMOSTEVE | Date Received: | 11-30-2016 |
| Lab Accessioning Number: | DEMOSTEVE | Date of Report: | 07-29-2009 |
| Ordering Physician: | Dr. Edward Viner | | |

Risk of Developing Melanoma Based on:

- CPMC Melanoma Variant 1 (rs910873)
- Family History

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 one genetic variant, but does not represent your complete genetic risk for melanoma. These results were generated as part of this research study in a CLIA-approved laboratory.

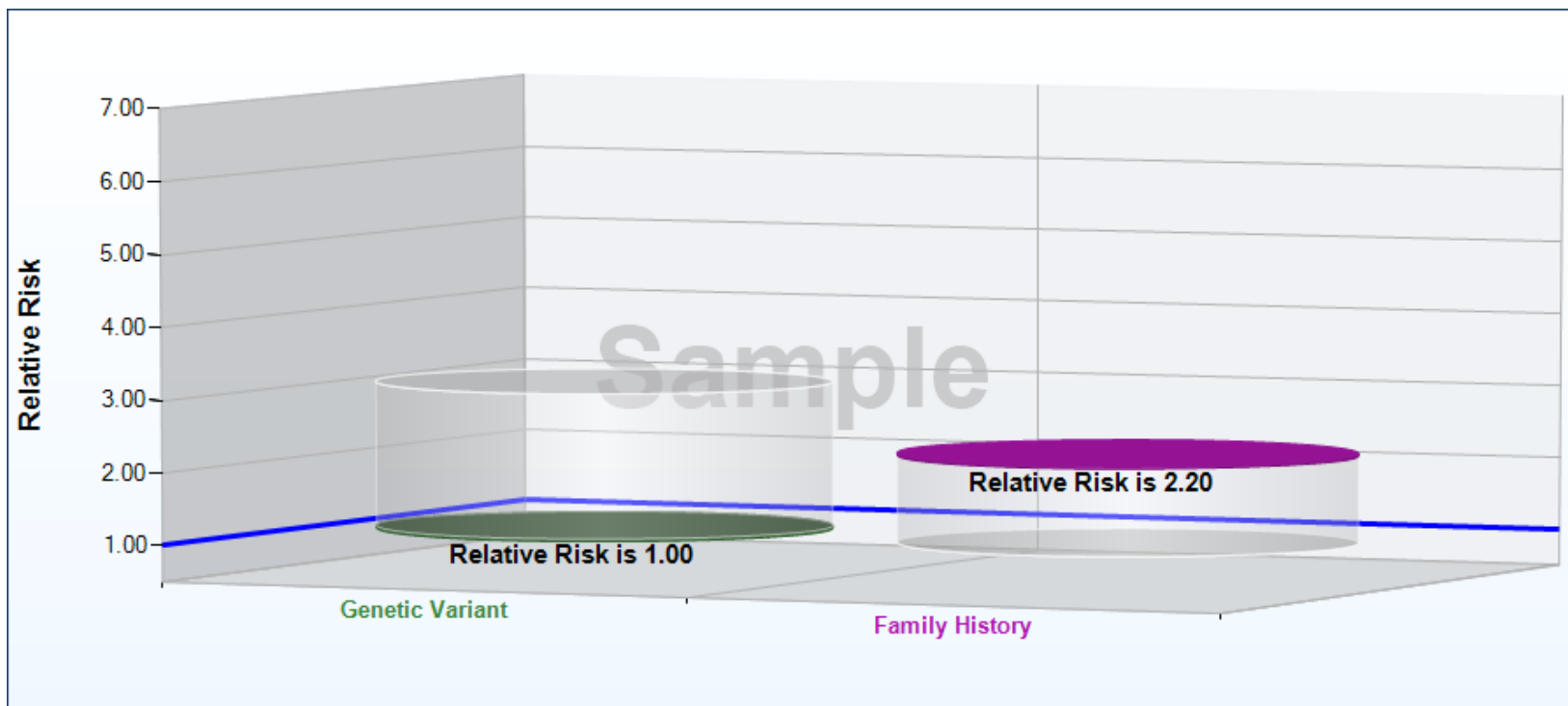
More information about the study, how to interpret CPMC results, and how we calculate risk is available on our website <http://cpmc.coriell.org> or by contacting our genetic counselor. Participants may schedule an appointment with our board-certified genetic counselor through the web portal by clicking 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

Melanoma

Risk factors may be related to each other and risk estimates cannot be combined.
 This graph provides a summary of the relative risks for one genetic variant and family history.



You reported you are a Caucasian man, between 60 and 69 years old; an estimated 6 in 1,000 Caucasian men in your age group have melanoma.

| Chart Color | Relative Risk Due To: | Your Risk | Minimum Risk | Maximum Risk | Interpretation |
|-------------|-----------------------|-----------|--------------|--------------|---|
| | Genetic Variant | 1.00 | 1.00 | 3.00 | You have 2 copies of the non-risk variant. Based this result, you are at lower risk to develop melanoma compared to someone with one or two copies of this variant. |
| | Family History | 2.20 | 1.00 | 2.20 | Based on your family history, you are 2.20 times more likely to develop melanoma than someone who does not have a first degree relative with (parent, sibling, or child) melanoma. <i>Having a first degree relative with melanoma contributes to your risk of melanoma.</i> |

Melanoma

Risk Due To Genetic Variant #1 (rs910873)

Your Result: 2 copies of the non-risk variant were detected (CC).

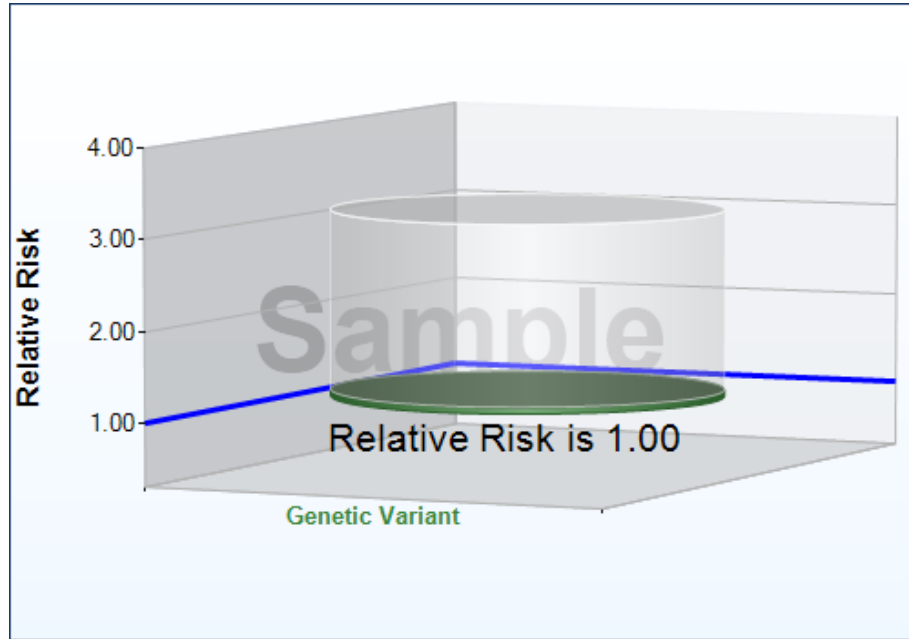
Non-Risk Variant = C Risk Variant = T

| Chart Color | Your Risk | Minimum Risk | Maximum Risk | Interpretation |
|-------------|-----------|--------------|--------------|---|
| | 1.00 | 1.00 | 3.00 | You have 2 copies of the non-risk variant. Based this result, you are at lower risk to develop melanoma compared to someone with one or two copies of this variant. |

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 1.00 indicates an increased risk.



These results are based on a single study.

Melanoma

Risk Due To Family History

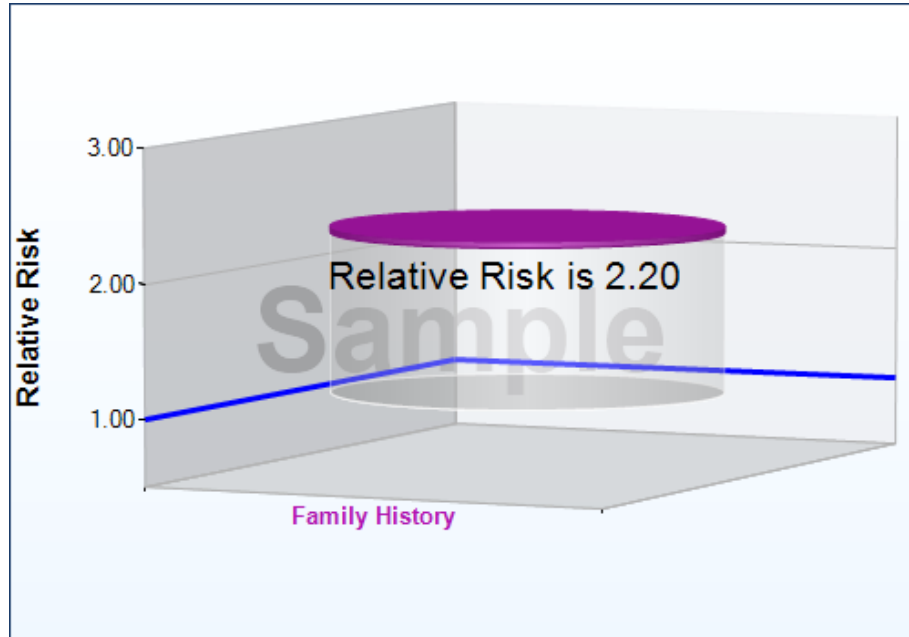
You reported that at least one first degree relative (parent, sibling or child) has melanoma.

| Chart Color | Your Risk | Minimum Risk | Maximum Risk | Interpretation |
|-------------|-----------|--------------|--------------|--|
| | 2.20 | 1.00 | 2.20 | <p>Based on your family history, you are 2.20 times more likely to develop melanoma than someone who does not have a first degree relative with (parent, sibling, or child) melanoma.</p> <p><i>Having a first degree relative with melanoma contributes to your risk of melanoma.</i></p> |

Risk is compared based on family history.

People with a first degree relative (parent, sibling, or child) with melanoma are compared to people with no first degree relatives with melanoma to determine relative risk of developing melanoma.

A relative risk greater than 1.00 indicates an increased risk.



These results are based on a single study.

Melanoma - Variant #1 (rs910873)

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 melanoma.

How Common Is This Variant?

Non-Risk Variant = C Risk Variant = T

CC - 89 in 100 people have 2 copies of the non-risk variant

CT - 10 in 100 people have 1 copy of the non-risk variant and 1 copy of the risk variant

TT - 1 in 100 people have 2 copies of the risk variant

This frequency is based on data from European populations.



Gene: **PIGU**

Chromosome: **20q11.22**

Causes

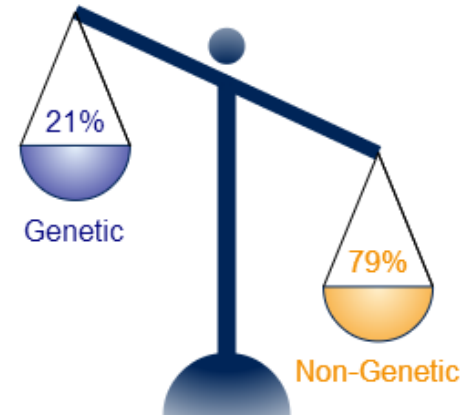
Genetic vs. Non-Genetic Risk Factors

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

It is estimated that **non-genetic** factors (like sun exposure) account for about **79%** of the risk of melanoma.

It is estimated that **21%** of the risk for melanoma is based on **genetic** risk factors. This estimate accounts for both known and unknown gene variants.

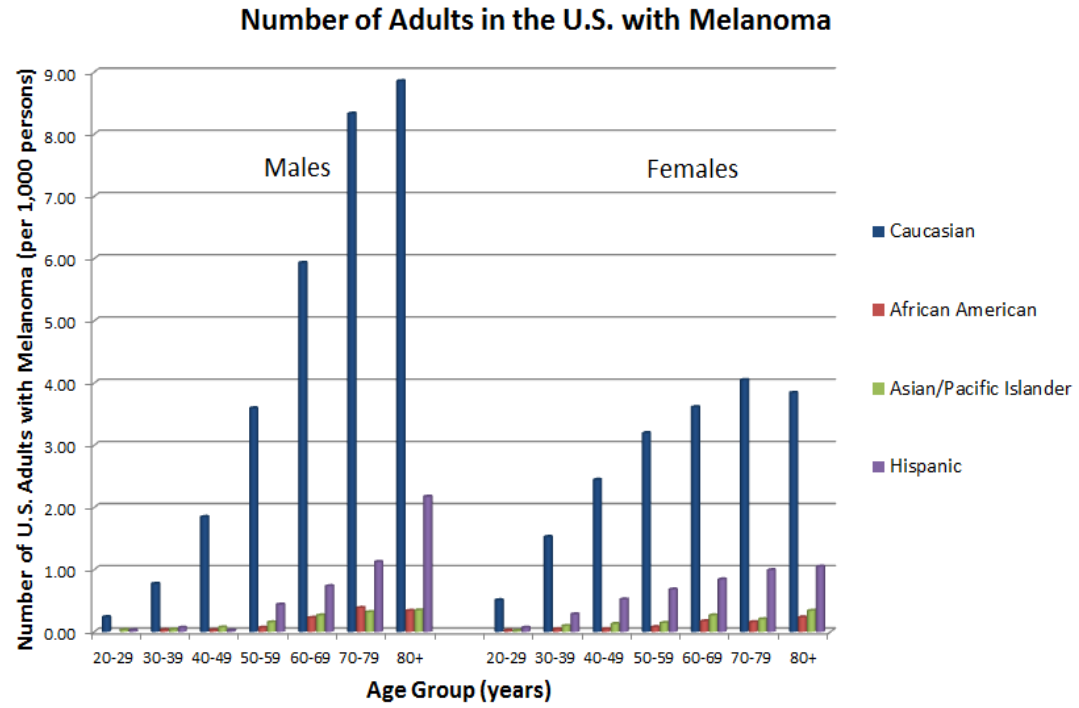
There are many different genetic and non-genetic risk factors that contribute to the risk of melanoma. We are only able to tell you about your family history risk and 1 genetic risk variant at this time.



How Common

Age, ancestry, and gender contribute to your risk of melanoma.

You reported you are a Caucasian man, between 60 and 69 years old; an estimated 6 in 1,000 Caucasian men in your age group have melanoma.



Limitations

Melanoma

- This result alone does NOT diagnose melanoma. Melanoma must be diagnosed by your health care provider.
- This result does NOT mean that you have or will absolutely develop melanoma.
- This result does NOT mean that you will not develop melanoma in the future.
- This result ONLY assesses your risk for developing melanoma due to the factors presented in this report and does not mean that other genetic variants or risk factors for melanoma are present or absent.
- Personal risk factors, such as age, family history or lifestyle, may have a greater impact on your risk to develop melanoma 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

Melanoma

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 Melanoma Risk Algorithm Version 1 (July 29, 2009)]

1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. *Genet Med.* 13(2):131-139.
2. Horner, MJ et al. (eds). SEER Cancer Statistics Review, 1975-2005, National Cancer Institute. Bethesda, MD, Surveillance Epidemiology and End Results based on November 2008 SEER data submission, posted to the SEER web site, 2009.
3. Czene, K et al. (2002). Environmental and Heritable Causes of Cancer Among 9.6 Million Individuals in the Swedish Family-Cancer Database. *International Journal of Cancer.* 99:260-266.
4. Brown, KM et al. (2008). Common sequence variants on 20q11.22 confer melanoma susceptibility. *Nature Genetics.* 40(7):838-840.
5. Cho, E et al. (2005). Risk Factors and Individual Probabilities of Melanoma for Whites. *Journal of Clinical Oncology.* 23 (12):2669-2675.
6. McVean G.A. et al (2012). An integrated map of genetic variation from 1,092 human genomes. *Nature.* 491; 56-65.

Sample Results



Coriell Institute for Medical Research

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Clinical Report for Melanoma Genetic Variant 1 (rs910873)

| | | | |
|---------------------------------|-------------------|------------------------|------------|
| Name: | STEVE CPMC | Sample Type: | Saliva |
| Race/Ethnicity: | White (Caucasian) | Gender: | Male |
| Date of Birth: | | Date Collected: | 11-30-2016 |
| Coriell ID: | DEMOSTEVE | Date Received: | 11-30-2016 |
| Lab Accessioning Number: | DEMOSTEVE | Date of Report: | 07-29-2009 |
| Ordering Physician: | Dr. Edward Viner | | |

| Name of Gene/Region: PIGU | | Chromosomal Location: 20q11.22 |
|---------------------------|---|--------------------------------|
| Variants tested | Result | Reference Genotype |
| rs910873 | CC | CC |
| Interpretation | Individuals with this result are at a lower risk to develop melanoma compared to someone with one or two copies of the risk variant. These risk estimates are based on studies in a European population. 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 melanoma. For additional information on other risk factors please see the accompanying CPMC research report. | |

Risk interpretation based on Coriell's Melanoma Risk Algorithm Version 2 (July 10, 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 melanoma. This test is not diagnostic for melanoma and cannot rule out the risk of developing melanoma 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 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

1. Brown, KM et al. (2008). Common sequence variants on 20q11.22 confer melanoma susceptibility. Nature Genetics. 40(7):838-840.