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:	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:**	08-08-2013
Ordering Physician:	Dr. Edward Viner		

Risk of Developing Testicular Cancer Based on:

- **CPMC Testicular Cancer Variant 1 (rs995030)**
- **Family History**
- **Ancestry**
- **Height**

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 testicular cancer. These results were generated as part of this research study in a CLIA-approved laboratory.

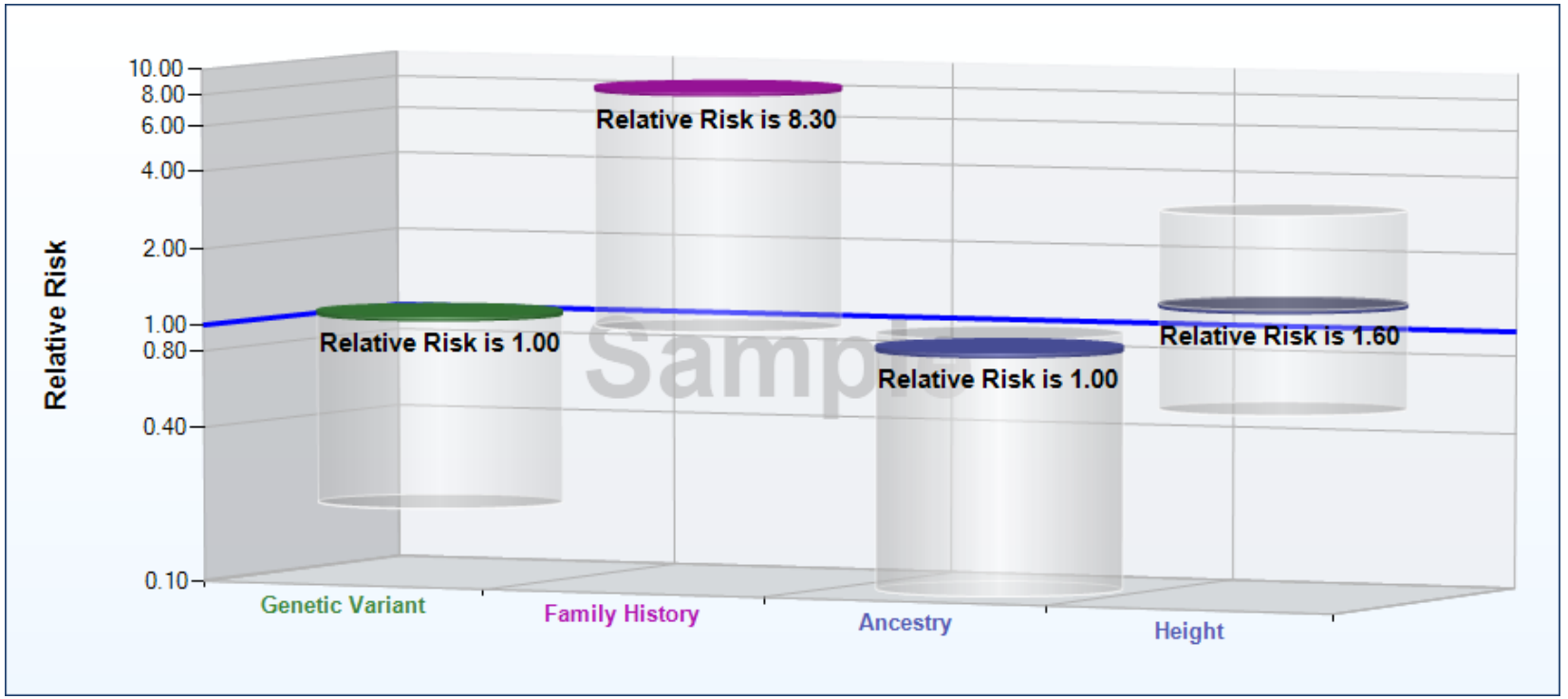
More information about the study, how to interpret CPMC results, and how we calculate risk is available on our website http://cpmc.coriell.org or by contacting our genetic counselors. Participants may schedule an appointment with one of our board-certified genetic counselors through the web portal by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

Genetic Variant Result, Details and Population Data

Testicular Cancer

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



You reported you are Caucasian, between 60 and 69 years old; 4 in 10,000 Caucasian men in your age group have testicular cancer.

Chart Color	Relative Risk Due To:	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	Genetic Variant	**1.00**	0.15	1.00	**You have 2 copies of the non-protective variant. Based on this result, you are at higher risk to develop testicular cancer compared to men with one or two copies of this protective genetic variant.**
	Family History	**8.30**	1.00	8.30	**Based on your family history, you are 8.3 times more likely to develop testicular cancer than men who does not have a father or brother with testicular cancer.** *Having a brother with testicular cancer contributes to your risk of testicular cancer.*
	Ancestry	**1.00**	0.15	1.00	**Because you are Caucasian, you are at a higher risk of testicular cancer compared to men of African or Asian Indian ancestry.**
	Height	**1.60**	0.80	3.40	**Based on your height, you are 60% more likely (or 1.6 times as likely) to develop testicular cancer as man who is either 5 feet 9 inches or 5 feet 10 inches tall.** *Your height contributes to your risk of testicular cancer.*

Testicular Cancer

Risk Due To Genetic Variant #1 (rs995030)

Your Result: 2 copies of the non-protective variant were detected (GG)

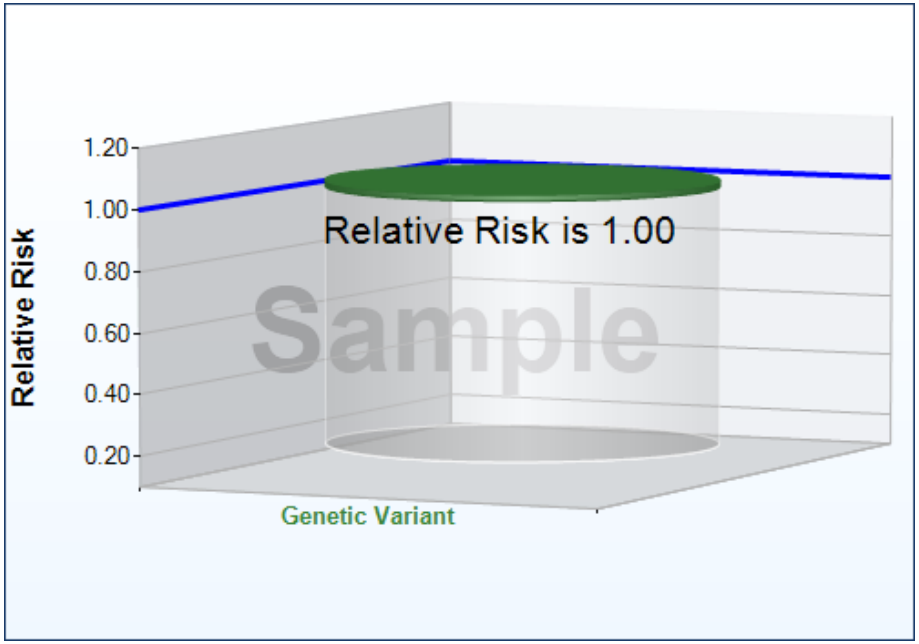
Non-Protective Variant = G Protective Variant = A

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	0.15	1.00	**You have 2 copies of the non-protective variant. Based on this result, you are at higher risk to develop testicular cancer compared to men with one or two copies of this protective genetic variant.**

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

Men with one or two copies of the protective variant are compared to men with no copies of the protective variant to determine relative risk.

A relative risk less than 1.0 indicates a *decreased* risk.



These risk estimates are based on a study conducted in a Caucasian population.

Testicular Cancer

Risk Due To Family History

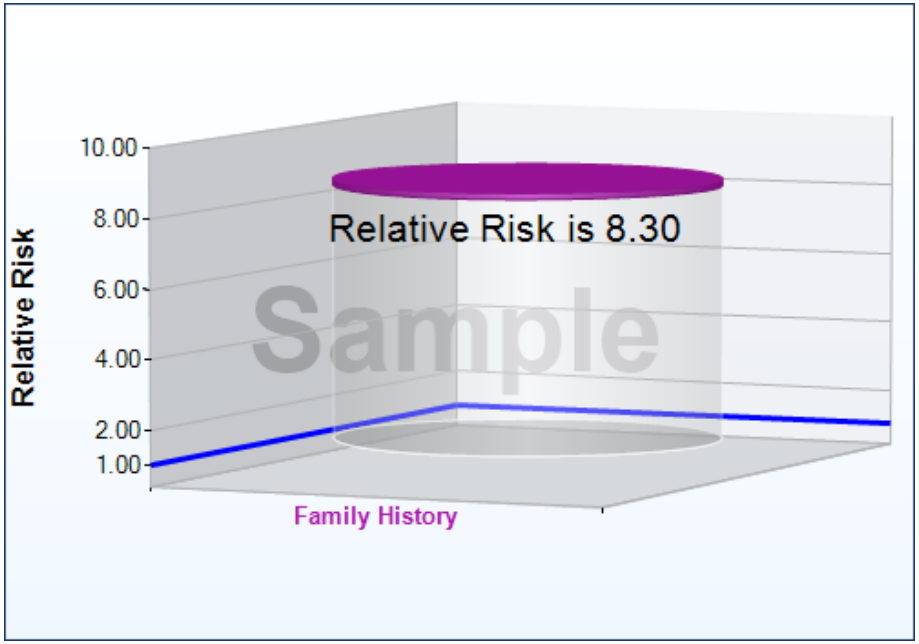
You reported that at least one brother has testicular cancer.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	8.30	1.00	8.30	**Based on your family history, you are 8.3 times more likely to develop testicular cancer than men who does not have a father or brother with testicular cancer.** *Having a brother with testicular cancer contributes to your risk of testicular cancer.*

Risk is compared based on family history.

Men with a father or brother with testicular cancer are compared to men with no father or brother(s) with testicular cancer to determine relative risk of developing testicular 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.

Testicular Cancer

Risk Due To Ancestry

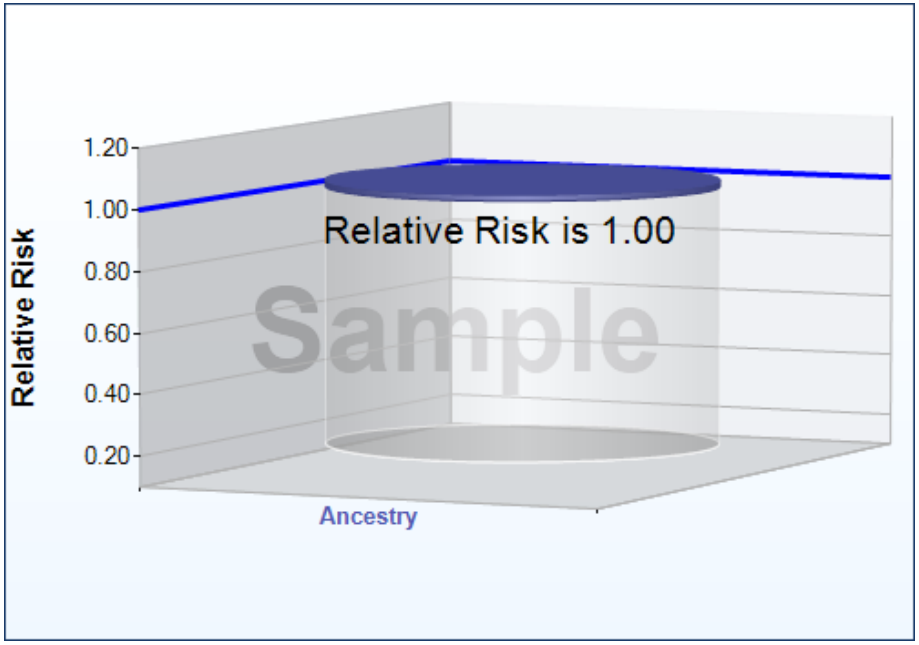
You reported that you are of Caucasian ancestry.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	0.15	1.00	**Because you are Caucasian, you are at a higher risk of testicular cancer compared to men of African or Asian Indian ancestry.**

Risk is compared based on your ancestry.

Men who are of Caucasian ancestry are compared to men of African or Asian Indian ancestry to determine relative risk.

A relative risk less than 1.0 indicates a *decreased* risk.



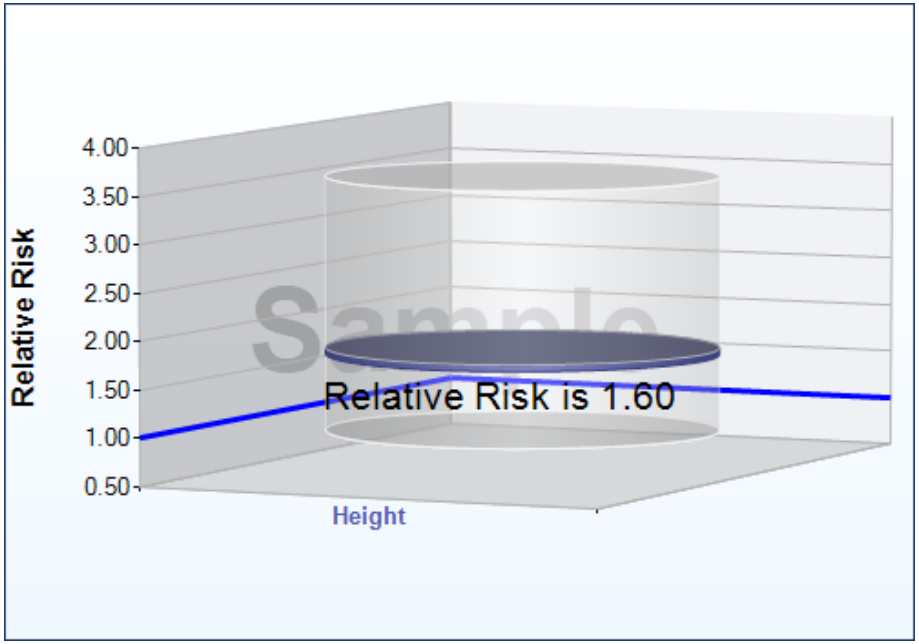
These results are based on a study conducted on multiple populations of different racial and ethnic backgrounds.

Testicular Cancer

Risk Due To Height

According to the height you reported, you are either 6 feet 1 inch or 6 feet 2 inches tall.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.60	0.80	3.40	**Based on your height, you are 60% more likely (or 1.6 times as likely) to develop testicular cancer as man who is either 5 feet 9 inches or 5 feet 10 inches tall.** *Your height contributes to your risk of testicular cancer.*



Risk is compared based on height. It is not known exactly how height influences the risk of testicular cancer. Height is known to be determined early in life by a combination of genetics, nutrition and environmental hormone exposure.

Men who are either 5 feet 9 inches or 5 feet 10 inches tall were compared to men who are taller or shorter to determine relative risk.

A relative risk less than 1.0 indicates a *decreased* 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.

Testicular Cancer
Other Risk Factors

In addition to height, ancestry and genetic variants, there are other risk factors for testicular cancer that are not captured by our questionnaires.

The following risk factor may also increase your risk of testicular cancer:

- **Cryptorchidism**- a congenital condition where a testicle has not descended into the scrotum. Typically only one testicle is affected, but in some cases both testicles are affected. This condition typically corrects itself within the first few months of life, but if not, surgery can be performed to correct it.

  Males who had cryptorchidism are 4.3 times as likely to develop testicular cancer compared to males who did not have cryptorchidism.

Testicular Cancer - Variant #1 (rs995030)

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.

This genetic variant is **protective**. Having one or two copies of this variant **lowers** your risk for testicular cancer.

How Common Is This Variant?

Non-Protective Variant = G **Protective Variant = A**

GG - 64 in 100 people have 2 copies of the non-protective variant

GA - 32 in 100 people have 1 copy of the non-protective variant and 1 copy of the protective variant

AA - 4 in 100 people have 2 copies of the protective variant

This data is based on studies in Caucasian populations.

Gene: KITLG **Chromosome: 12q21.32**

Causes

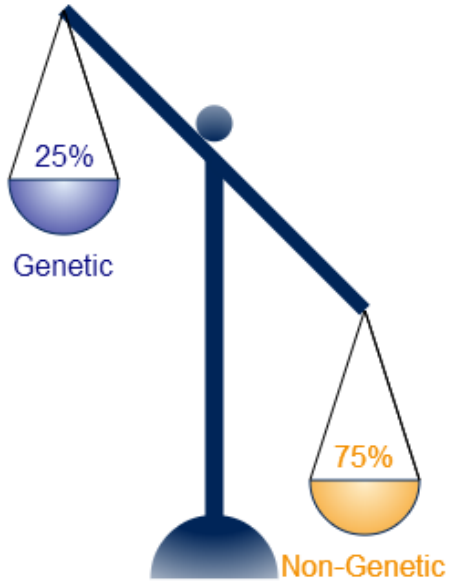
Genetic vs. Non-Genetic Risk Factors

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

It is estimated that **non-genetic** factors (like ancestry and height) account for about **75%** of the risk of testicular cancer.

It is estimated that **25%** of the risk for testicular 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 testicular cancer. We are only able to tell you about your family history risk, 1 genetic and 2 non-genetic risk factors at this time.

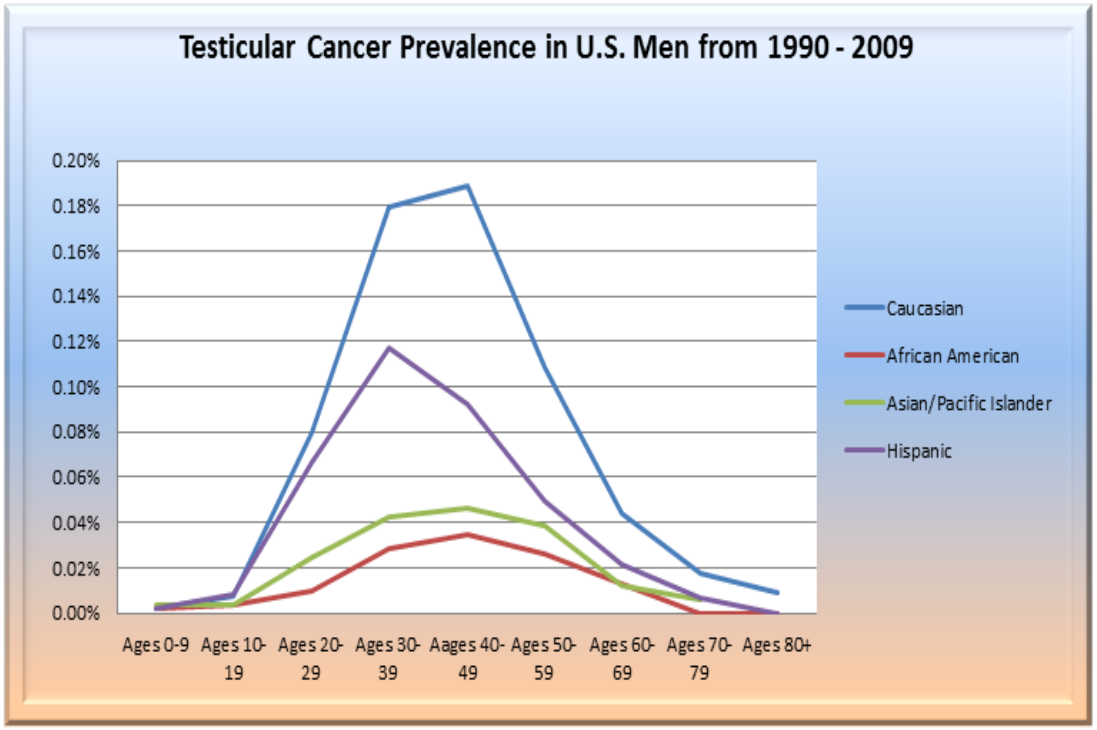


How Common

Testicular cancer is more common among Caucasians.

You reported you are Caucasian, between 60 and 69 years old; 4 in 10,000 Caucasian men in your age group have testicular cancer.

Age and race contribute to the risk of testicular cancer.



Limitations

Testicular Cancer

- This result alone does NOT diagnose testicular cancer in men. Testicular cancer must be diagnosed by a health care provider.
- This result does NOT mean that a man will have or will absolutely develop testicular cancer.
- This result does NOT mean that a man will not develop testicular cancer in the future.
- This result ONLY assesses the risk for developing testicular cancer due to the factors presented in this report and does not mean that other genetic variants or risk factors for testicular cancer are present or absent.
- The relative risk information presented in this report represents the risk of developing testicular cancer for men who do not have a history of testicular cancer.
- Personal risk factors, such as age, family history or lifestyle, may have a greater impact on the risk to develop testicular 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 provided in the medical, family, and lifestyle questionnaire. If answers were not provided or if a “do not know” response was given, risk estimates for some factors may not be available.
- Risk information for non-genetic factors is based on information provided in the medical, family, and lifestyle questionnaire and may not be reflective of current risk if any of these factors have changed. Participants will be given the opportunity to update medical, family and lifestyle questionnaire responses periodically.
- Every effort will be made to provide participants with risk information based on their reported race/ethnicity. However, data may not be available for all races/ethnicities for all risk factors. Results will indicate which race/ethnicity the data given is based upon.

Methods

Testicular 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 Testicular Cancer Risk Algorithm Version 1 (June 11, 2013)]

1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. Genet Med. 13(2):131-139.
2. Rapley, EA. et al (2009). A genome-wide association study of testicular germ cell tumor. Nat Genet. 41(7):807-810.
3. Nordsborg, RB. et al (2011). Cancer in first-degree relatives and risk of testicular cancer in Denmark. Int J Cancer. 129(10):2485-2491.
4. Jack, RH. et al (2007). Testis and prostate cancer incidence in ethnic groups in South East England. Int J Androl. 30:215-221.
5. Dieckmann, KP. et al (2008). Tallness is associated with risk of testicular cancer: evidence for the nutrition hypothesis. Br J Cancer. 99:1517-1521.
6. Cook, MB. et al (2010). A systematic review and meta-analysis of perinatal variables in relation to the risk of testicular cancer – experiences of the son. Int J Epidemiol. 39:1605-1618.
7. Czene, K. et al. (2002). Environmental and heritable causes of cancer among 9.6 million individuals in the Swedish family-cancer database. Int J Cancer. 99:260-266.
8. Howlader, N. et al. SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations), National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2009_pops09/, based on November 2011 SEER data submission, posted to the SEER web site, April 2012.

Sample Results

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Phone: 856-966-7377 Fax: 856-964-0254 www.coriell.org

Clinical Report for Testicular Cancer Genetic Variant 1 (rs995030)

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:**	08-08-2013
Ordering Physician:	Dr. Edward Viner		

Name of Gene/Region: KITLG		**Chromosomal Location:** 12q21.32
Variants tested	**Result**	**Reference Genotype**
rs995030	GG	GG
Interpretation	**Men with this result are at a higher risk to develop testicular cancer compared to men with one or two copies of the protective variant.** These results 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 testicular cancer. For additional information on other risk factors please see the accompanying CPMC research report.	

Risk interpretation based on Coriell's Testicular Cancer Risk Algorithm Version 1 (June 11, 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 testicular cancer. This test is not diagnostic for testicular cancer and cannot rule out the risk of developing testicular 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 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

References

1. Rapley, EA et al (2009). A genome-wide association study of testicular germ cell tumor. Nat Genet. 41(7):807-810.

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