

### **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

<b>Name:</b>	STEVE CPMC	<b>Gender:</b>	Male
<b>Date of Birth:</b>		<b>Date Collected:</b>	11-30-2016
<b>Coriell ID:</b>	DEMOSTEVE	<b>Date Received:</b>	11-30-2016
<b>Lab Accessioning Number:</b>	DEMOSTEVE	<b>Date of Report:</b>	11-09-2015
<b>Ordering Physician:</b>	Dr. Edward Viner		

#### Risk of Developing Hypothyroidism Based on:

- **CPMC Hypothyroidism Variant #1 (rs7850258)**

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, this report does not represent your complete genetic risk for developing hypothyroidism. These results were generated as part of this research study in a CLIA-approved laboratory.

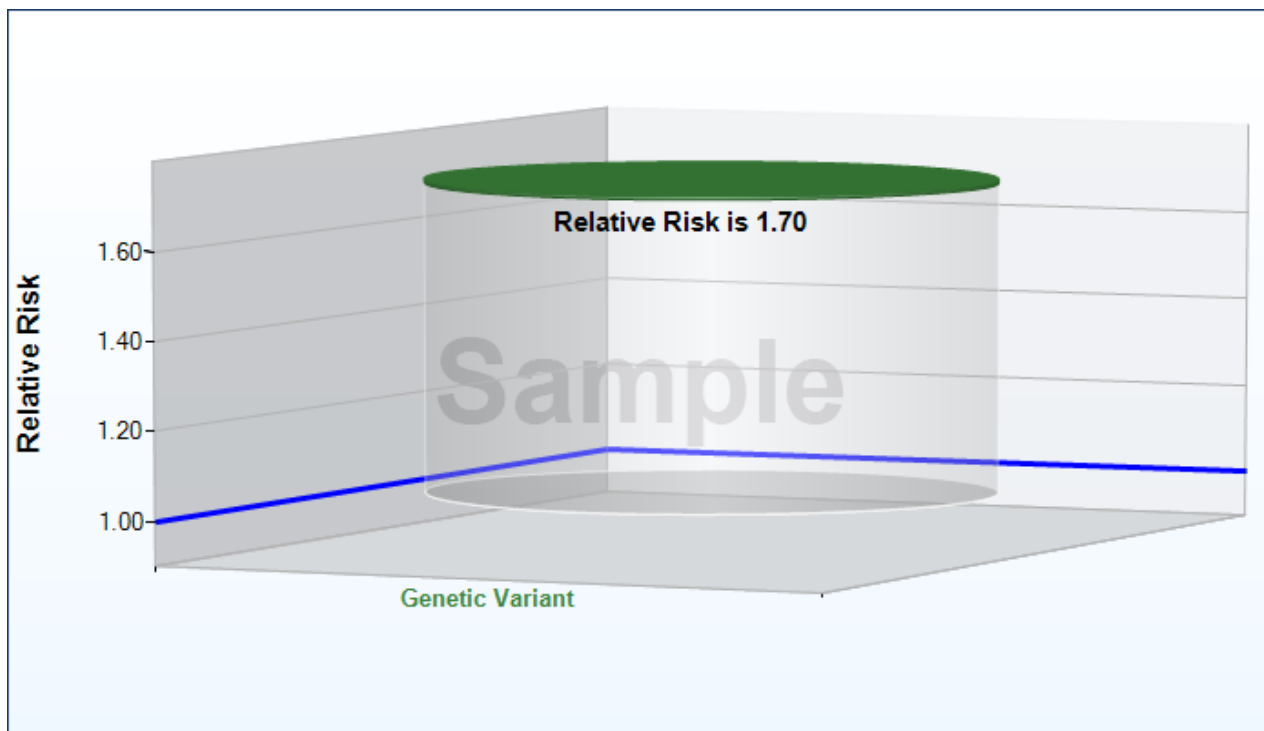
More information about the study, how to interpret CPMC results, and how we calculate risk is available on our website <http://cpmc.coriell.org> or by contacting our genetic counselor. Participants may schedule an appointment with our board-certified genetic counselor through the web portal by clicking on "request an appointment". Our genetic counselor also can be reached by email at [cpmcgc@coriell.org](mailto: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

### Hypothyroidism

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



You reported you are Caucasian and 18 years old or older; 5 in 100 people in your age group have hypothyroidism.

Chart Color	Relative Risk Due To:	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	Genetic Variant	1.70	1.00	1.70	<p>You have 2 copies of the risk variant. Based on this result, you are 70% more likely (or 1.70 times as likely) to develop hypothyroidism as someone with no copies of this variant.</p> <p><i>Having this risk variant contributes to your risk of hypothyroidism.</i></p>

# Hypothyroidism

## Risk Due To Genetic Variant #1 (rs7850258)

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

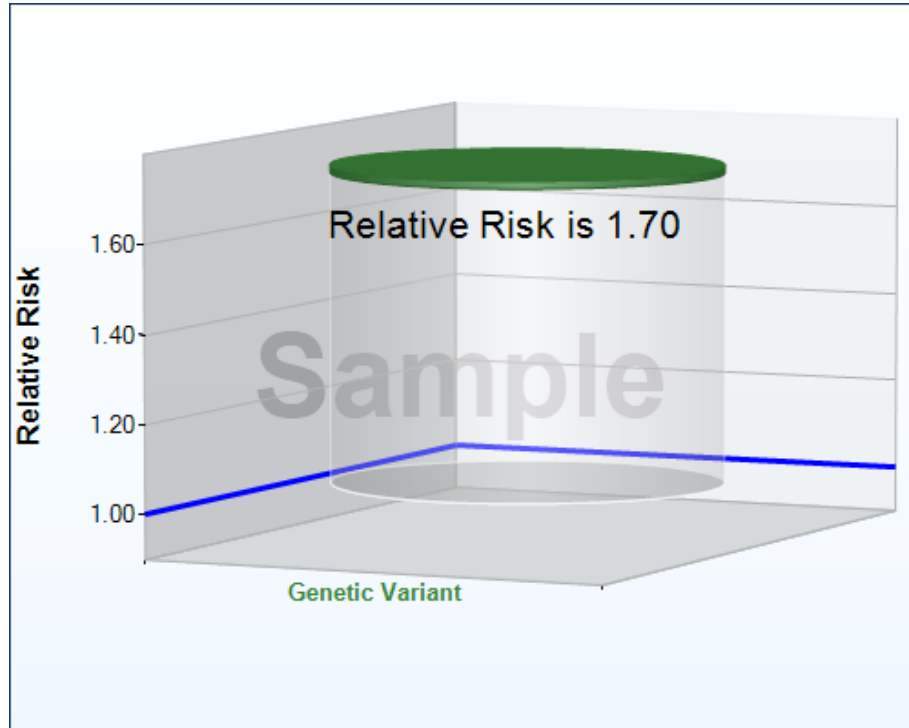
Non-Risk Variant = A Risk Variant = G

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.70	1.00	1.70	<p>You have 2 copies of the risk variant. Based on this result, you are 70% more likely (or 1.70 times as likely) to develop hypothyroidism as someone with no copies of this variant.</p> <p><i>Having this risk variant contributes to your risk of hypothyroidism.</i></p>

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.

## Hypothyroidism - Variant #1 (rs7850258)

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.

Having one or two copies of this variant **increases** your risk of hypothyroidism.

### How Common Is This Variant?

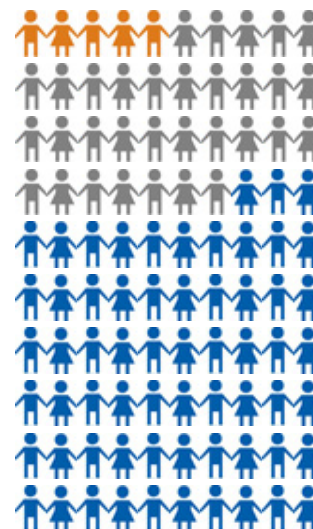
Non-Risk Variant = A    Risk Variant = G

**AA - 5 in 100 people have 2 copies of the non-risk variant**

**AG - 32 in 100 people have 1 copy of the non-risk variant and 1 copy of the risk variant**

**GG - 63 in 100 people have 2 copies of the risk variant**

**This data is based on studies in worldwide populations.**



Gene: FOXE1

Chromosome: 9q22.33

## Causes

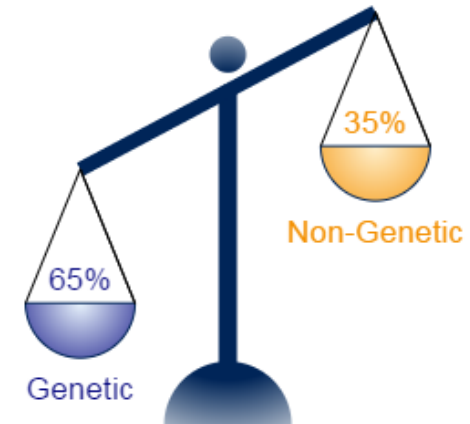
### Genetic vs. Non-Genetic Risk Factors

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

It is estimated that **non-genetic** factors (like medications) account for about **35%** of the risk for hypothyroidism.

It is estimated that **65%** of the risk for hypothyroidism 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 hypothyroidism. We are only able to tell you about one genetic risk factor for hypothyroidism at this time.**

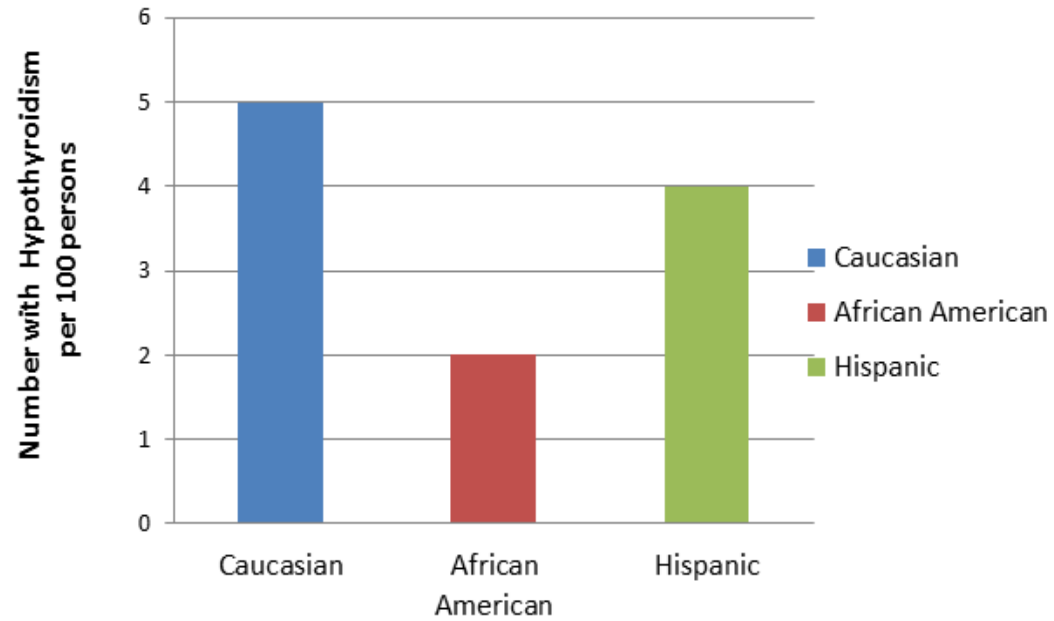


## How Common

The risk of hypothyroidism increases with age and differs across populations.

**You reported you are Caucasian and 18 years old or older; 5 in 100 people in your age group have hypothyroidism.**

## Prevalence Estimate of Hypothyroidism in 2009



## Limitations

### Hypothyroidism

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

# Hypothyroidism

**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 Hypothyroidism Risk Algorithm Version 1 (November 1, 2015)]

1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. *Genet Med.* 13(2):131-139.
2. Denny J.C. et al (2011). Variants near FOXE1 are associated with Hypothyroidism and other Thyroid conditions: Using electronic medical records for genome-and phenome-wide studies. *Am J Hum Genet.* 89: 529-542.
3. Panicker, V. (2011). Genetics of thyroid function and disease. *Clin Biochem Rev.* 32 (4): 165-175.
4. Golden, S.H. et al (2009). Prevalence and incidence of endocrine and metabolic disorders in the United States: A comprehensive review. *J Clin Endocrinol Metab,* 94(6): 1853-1878.

## Sample Results



### Coriell Institute for Medical Research

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#### Clinical Report for Hypothyroidism Genetic Variant 1 (rs7850258)

<b>Name:</b>	STEVE CPMC	<b>Sample Type:</b>	Saliva
<b>Race/Ethnicity:</b>	White (Caucasian)	<b>Gender:</b>	Male
<b>Date of Birth:</b>		<b>Date Collected:</b>	11-30-2016
<b>Coriell ID:</b>	DEMOSTEVE	<b>Date Received:</b>	11-30-2016
<b>Lab Accessioning Number:</b>	DEMOSTEVE	<b>Date of Report:</b>	11-09-2015
<b>Ordering Physician:</b>	Dr. Edward Viner		

Name of Gene/Region: FOXE1		Chromosomal Location: 9q22.33
Variants tested	Result	Reference Genotype
rs7850258	GG	AA
<b>Interpretation</b>	<b>Individuals with this result are 70% more likely (or 1.70 times as likely) to develop hypothyroidism as someone with no copies of this variant.</b> 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.	
<b>Other Risks</b>	Other genetic variants and other risk factors including co-morbidities, lifestyle and family history may contribute to the risk of hypothyroidism. For additional information on other risk factors please see the accompanying CPMC research report.	

Risk interpretation based on Coriell's Hypothyroidism Clinical Risk Algorithm Version 1 (November 1, 2015)

#### 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 hypothyroidism. This test is not diagnostic for hypothyroidism and cannot rule out the risk of developing hypothyroidism 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

1. Denny J.C. et al (2011). Variants near FOXE1 are associated with Hypothyroidism and other Thyroid conditions: Using electronic medical records for genome-and phenome-wide studies. *Am J Hum Genet.* 89: 529-542.