## 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:** | 10-08-2014 |
| **Ordering Physician:** | Dr. Edward Viner | | |

**Risk of Developing Asthma Based on:**

- **CPMC Asthma Variant 1 (rs1837253)**
- **Family History**
- **Body Mass Index**
- **Smoking Status**

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

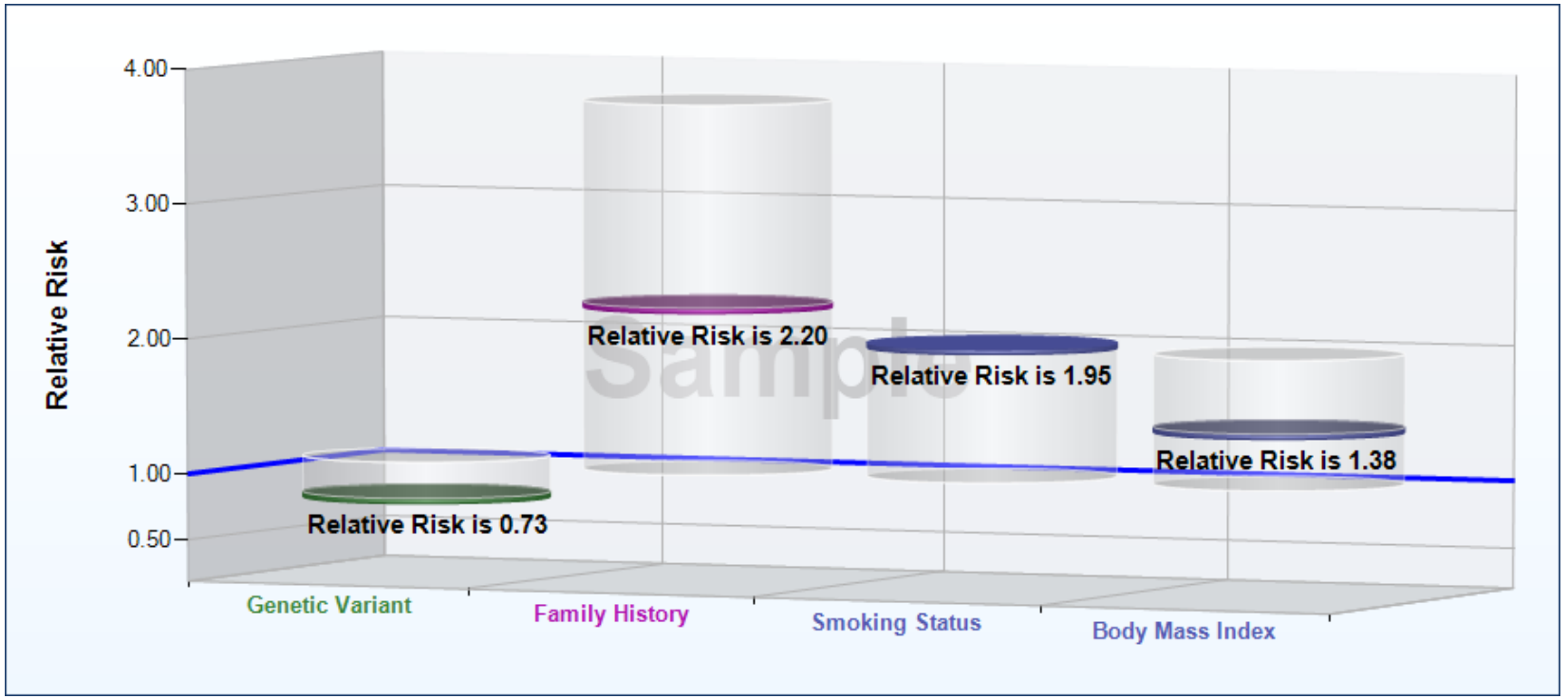
More information about the study, how to interpret CPMC results, and how we calculate risk is available on our website http://cpmc.coriell.org or by contacting our genetic counselor. Participants may schedule an appointment with our board-certified genetic counselor through the web portal by clicking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

# Asthma

**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, family history, body mass index, and smoking status.**




You reported you are a Caucasian man 65 years old or older; an estimated 6 in 100 Caucasian men in your age group have asthma.

| Chart Color | Relative Risk Due To: | Your Risk | Minimum Risk | Maximum Risk | Interpretation |
|---|---|---|---|---|---|
| | **Genetic Variant** | **0.73** | 0.73 | 1.00 | **You have 2 copies of the protective variant. Based on this result, your risk to develop asthma is 27% *lower* (or 0.73 times less likely) than someone with no copies of this protective genetic variant.**<br><br>***Having this protective genetic variant lowers your risk of asthma.*** |
| | **Family History** | **2.20** | 1.00 | 3.70 | **Based on your family history, you are 2.20 times more likely to develop asthma than someone who has no family history of asthma or only one second degree relative with asthma.**<br><br>***Having a first degree relative (parent, sibling or child) with asthma contributes to your risk of asthma.*** |
| | **Smoking Status** | **1.95** | 1.00 | 1.95 | **Because you are a current smoker you are 95% more likely (or 1.95 times as likely) to develop asthma compared to people who do not smoke.**<br><br>***Being a current smoker contributes to your risk of asthma.*** |

| Chart Color | Relative Risk Due To: | Your Risk | Minimum Risk | Maximum Risk | Interpretation |
|---|---|---|---|---|---|
| | **Body Mass Index** | **1.38** | 1.00 | 1.92 | **Based on your BMI you are 38% more likely (or 1.38 times as likely) to develop asthma as someone who has a BMI of less than 25 (not overweight).**<br><br>***Being overweight (BMI of 25 or greater) contributes to your risk of asthma.*** |

# Asthma

## Risk Due To Genetic Variant #1 (rs1837253)

**Your Result: 2 copies of the protective variant were detected (TT)**

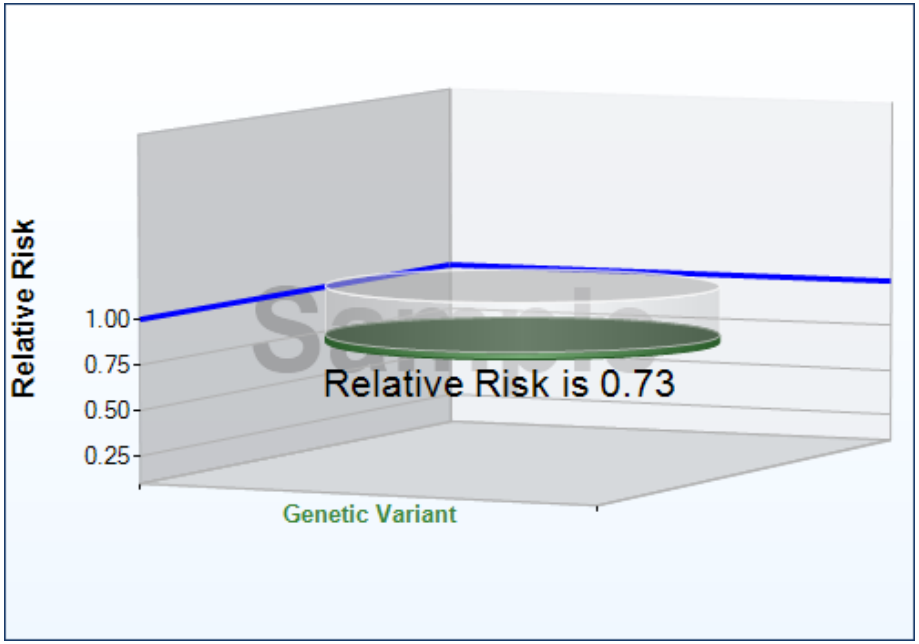
**Non-Protective Variant = C  Protective Variant = T**

| Chart Color | Your Risk | Minimum Risk | Maximum Risk | Interpretation |
|---|---|---|---|---|
| | **0.73** | 0.73 | 1.00 | **You have 2 copies of the protective variant. Based on this result, your risk to develop asthma is 27% *lower* (or 0.73 times less likely) than someone with no copies of this protective genetic variant.**<br><br>***Having this protective genetic variant lowers your risk of asthma.*** |

**Genetic Variant Risk is based on the number of copies of this protective genetic variant.**

**People with one or two copies of the protective variant are compared to people with no copies of the protective variant to determine relative risk.**

**A relative risk less than 1.00 indicates a decreased risk.**



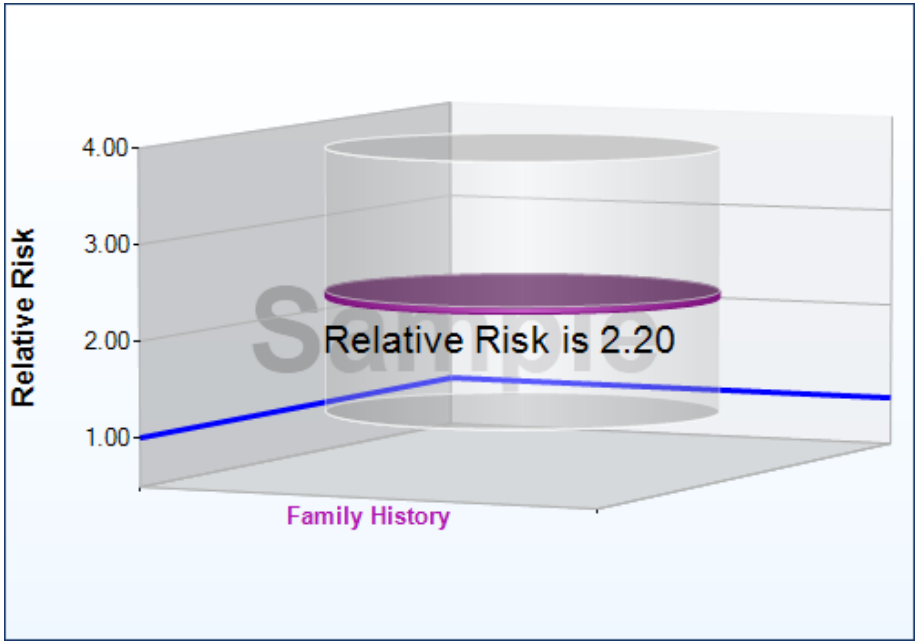

**These results are based on a single study.**

# Asthma

## Risk Due To Family History

**You reported that a first degree relative (parent, sibling or child) has asthma.**

| Chart Color | Your Risk | Minimum Risk | Maximum Risk | Interpretation |
|---|---|---|---|---|
| | **2.20** | 1.00 | 3.70 | **Based on your family history, you are 2.20 times more likely to develop asthma than someone who has no family history of asthma or only one second degree relative with asthma.**<br><br>***Having a first degree relative (parent, sibling or child) with asthma contributes to your risk of asthma.*** |




**Risk is compared based on family history.**

**People with first and/or second degree relatives with asthma were compared to people with no family history of asthma or only one second degree relative with asthma to determine relative risk of developing asthma.**

**First degree relatives include parents, siblings and children. Second degree relatives include aunts, uncles and grandparents.**

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

**These results are based on a single study.**

# Asthma

## Risk Due To Smoking Status

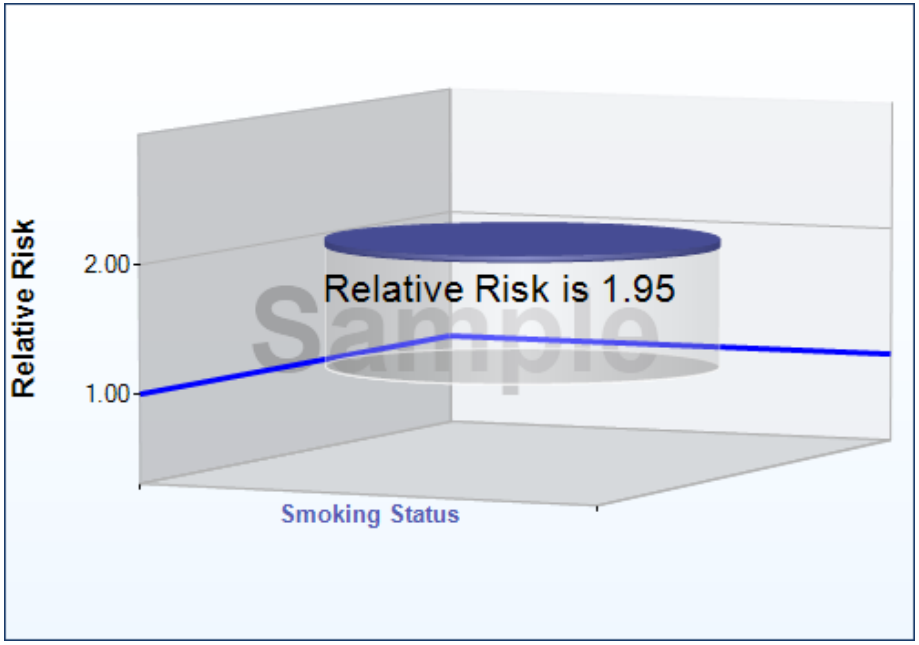
**You reported that you are a current smoker.**

| Chart Color | Your Risk | Minimum Risk | Maximum Risk | Interpretation |
|---|---|---|---|---|
| | **1.95** | 1.00 | 1.95 | **Because you are a current smoker you are 95% more likely (or 1.95 times as likely) to develop asthma compared to people who do not smoke.**<br><br>***Being a current smoker contributes to your risk of asthma.*** |

**Risk is compared based on smoking habits.**

**People who are current smokers were compared to people who do not smoke to determine relative risk.**

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




**These results are based on a single study.**

# Asthma

## Risk Due To Body Mass Index

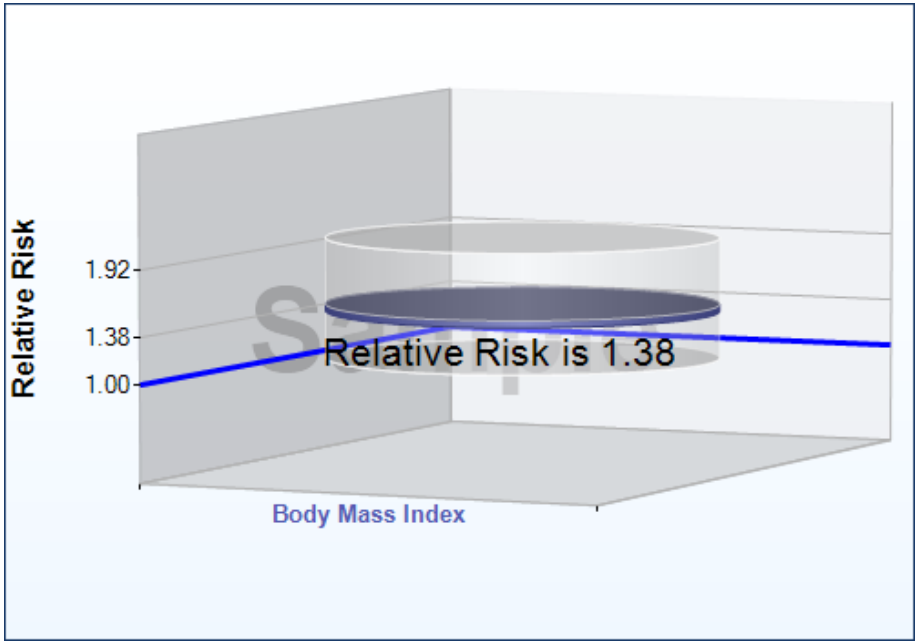
**According to the height and weight you reported, you may be overweight (BMI = 25.0-29.9).**

| Chart Color | Your Risk | Minimum Risk | Maximum Risk | Interpretation |
|---|---|---|---|---|
| | **1.38** | 1.00 | 1.92 | **Based on your BMI you are 38% more likely (or 1.38 times as likely) to develop asthma as someone who has a BMI of less than 25 (not overweight).**<br><br>***Being overweight (BMI of 25 or greater) contributes to your risk of asthma.*** |

**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.**

# Asthma

In addition to body mass index, smoking status, family history and genetic variants, there are other risk factors for asthma that are not captured by our questionnaires.

The following risk factor may increase your risk of developing asthma:

**Allergic rhinitis** is a group of symptoms affecting the nose. These symptoms occur when you breathe in something that you are allergic to, such as dust, animal dander, or pollen. Symptoms can also occur when you eat a food that you are allergic to. Symptoms of allergic rhinitis include:

- Itchy nose, mouth, eyes, throat, or skin
- Impaired sense of smell
- Runny nose
- Sneezing
- Watery eyes
- Stuffy nose
- Coughing

## People who have been diagnosed with allergic rhinitis are 4.90 times as likely to develop asthma compared to people who have not been diagnosed with allergic rhinitis.

# Asthma - Variant #1 (rs1837253)

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 asthma.

## How Common Is This Variant?

**Non-Protective Variant = C** **Protective Variant = T**

**CC - 56 in 100 people have 2 copies of the non-protective variant**

**CT - 38 in 100 people have 1 copy of the non-protective variant and 1 copy of the protective variant**

**TT - 6 in 100 people have 2 copies of the protective variant**

**This frequency is based on data from Caucasian populations**

**Gene: TSLP** **Chromosome: 5q22.1**

**Causes**

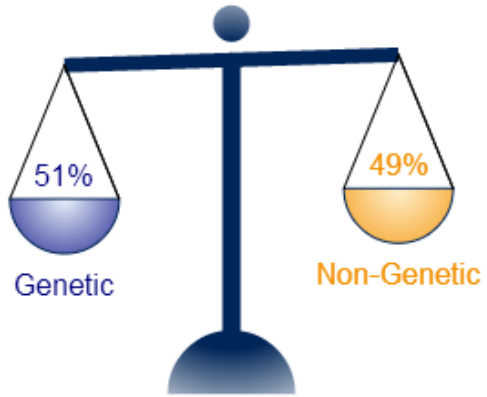
# Genetic vs. Non-Genetic Risk Factors

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

It is estimated that **non-genetic** factors (like obesity and smoking) account for about **49%** of the risk of asthma.

It is estimated that **51%** of the risk for asthma is based on **genetic** risk factors. This estimate accounts for both known and unknown gene variants.

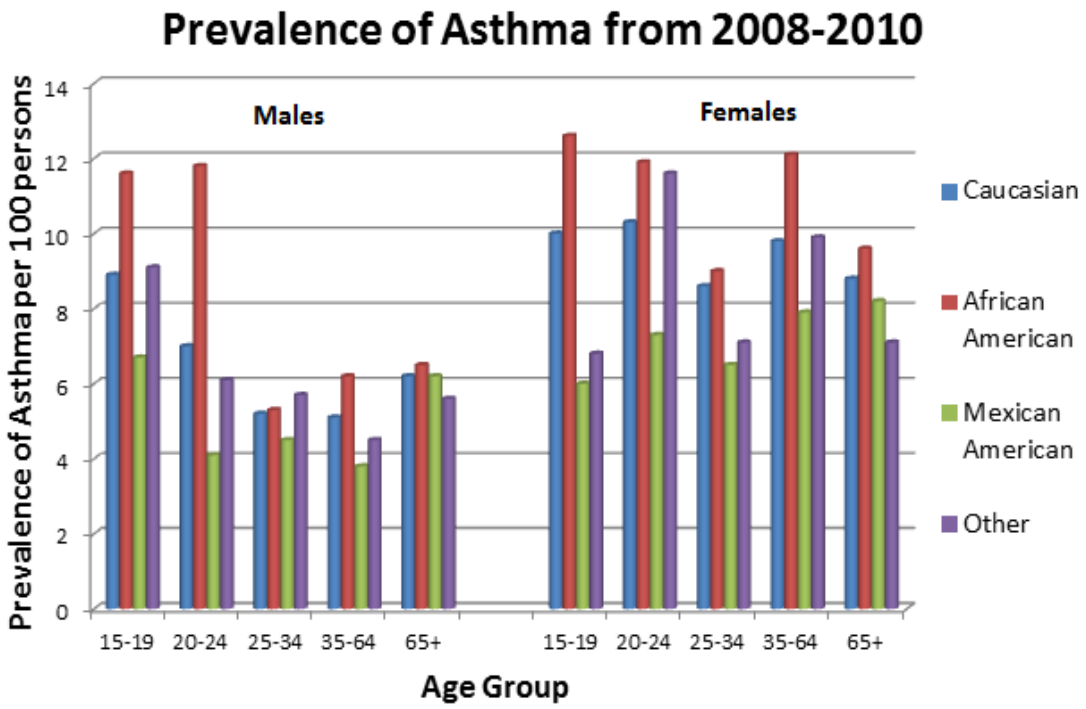
**There are many different genetic and non-genetic risk factors that contribute to the risk of asthma. We are only able to tell you about your family history risk, 1 genetic and 2 non-genetic risk factors at this time.**



**How Common**

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

**You reported you are a Caucasian man 65 years old or older; an estimated 6 in 100 Caucasian men in your age group have asthma.**



## Limitations

# Asthma

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

# Asthma

**This condition and genetic variant was 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 Asthma Risk Algorithm Version 1 (September 5, 2014)]


1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. Genet Med. 13(2):131-139.
2. Torgerson, DG. et al (2011). Meta-analysis of genome-wide association studies of asthma in ethnically diverse North American populations. Nat Genet 43(9): 887-892.
3. Beuther, DA. et al (2007). Overweight, Obesity, and Incident Asthma: A Meta-analysis of Prospective Epidemiologic Studies. Am J Respir. Crit. Care Med. 175:661-666.
4. Vignoud, L. et al (2011). Smoking and Asthma: Disentangling the mutual influences using a longitudinal approach. Respir Med 105(12):1805-1814.
5. Liu, T. et al (2009). The association between family history of asthma and the prevalence of asthma among US adults: National Health and Nutrition Examination Survey, 1999-2004. Genet Med. 11(5):323-328.
6. Thomsen, SF. et al (2010). Estimates of asthma heritability in a large twin sample. Clin Exp Allergy. 40(7): 1054-1061.
7. Moorman, JE. et al (2012). National Surveillance of Asthma: United States, 2001-2010. National Center for Health Statistics. Vital Health Stat. 3(35).
8. van den Nieuwenhof, L. et al (2010). Is physician-diagnosed allergic rhinitis a risk factor for the development of asthma? Allergy. 65:1049-1055.
9. United States of America. U.S National Library of Medicine. National Institutes of Health. Allergic Rhinitis. By A.D.A.M. Editorial Board. U.S. National Library of Medicine, 27 May 2013. Web. 10 Sept. 2013. http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001816/.
10. McVean G.A. et al (2012). An integrated map of genetic variation from 1,092 human genomes. Nature. 491; 56-65.

**Sample Results**

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## Clinical Report for Asthma Genetic Variant 1 (rs1837253)

| | | | |
|---|---|---|---|
| **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:** | 10-08-2014 |
| **Ordering Physician:** | Dr. Edward Viner | | |

| **Name of Gene/Region:** TSLP | | **Chromosomal Location:** 5q22.1 |
|---|---|---|
| **Variants tested** | **Result** | **Reference Genotype** |
| rs1837253 | TT | CC |
| **Interpretation** | **Individuals with this result are 27% less likely (or 0.73 times as likely) to develop asthma as someone with no copies of this protective variant.**<br>These risk estimates are based on studies involving multiple populations that include individuals with African-American, African-Caribbean, European, and Latin-American ancestry. 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 asthma. For additional information on other risk factors please see the accompanying CPMC research report. | |

Risk interpretation based on Coriell's Asthma Risk Algorithm Version 1 (September 5, 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 asthma. This test is not diagnostic for asthma and cannot rule out the risk of developing asthma 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. Torgerson, DG. et al (2011). Meta-analysis of genome-wide association studies of asthma in ethnically diverse North American populations. Nat Genet 43(9): 887-892.