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.

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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:**	07-06-2010
Ordering Physician:	Dr. Edward Viner		

Risk of Developing Type 1 Diabetes Based on:

- **CPMC Type 1 Diabetes Variant 1 (rs9272346)**
- **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 type 1 diabetes. 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

Type 1 Diabetes

Risk factors may be related to each other and risk estimates cannot be combined.
This graph provides a summary of the relative risks for both the genetic variant and family history.
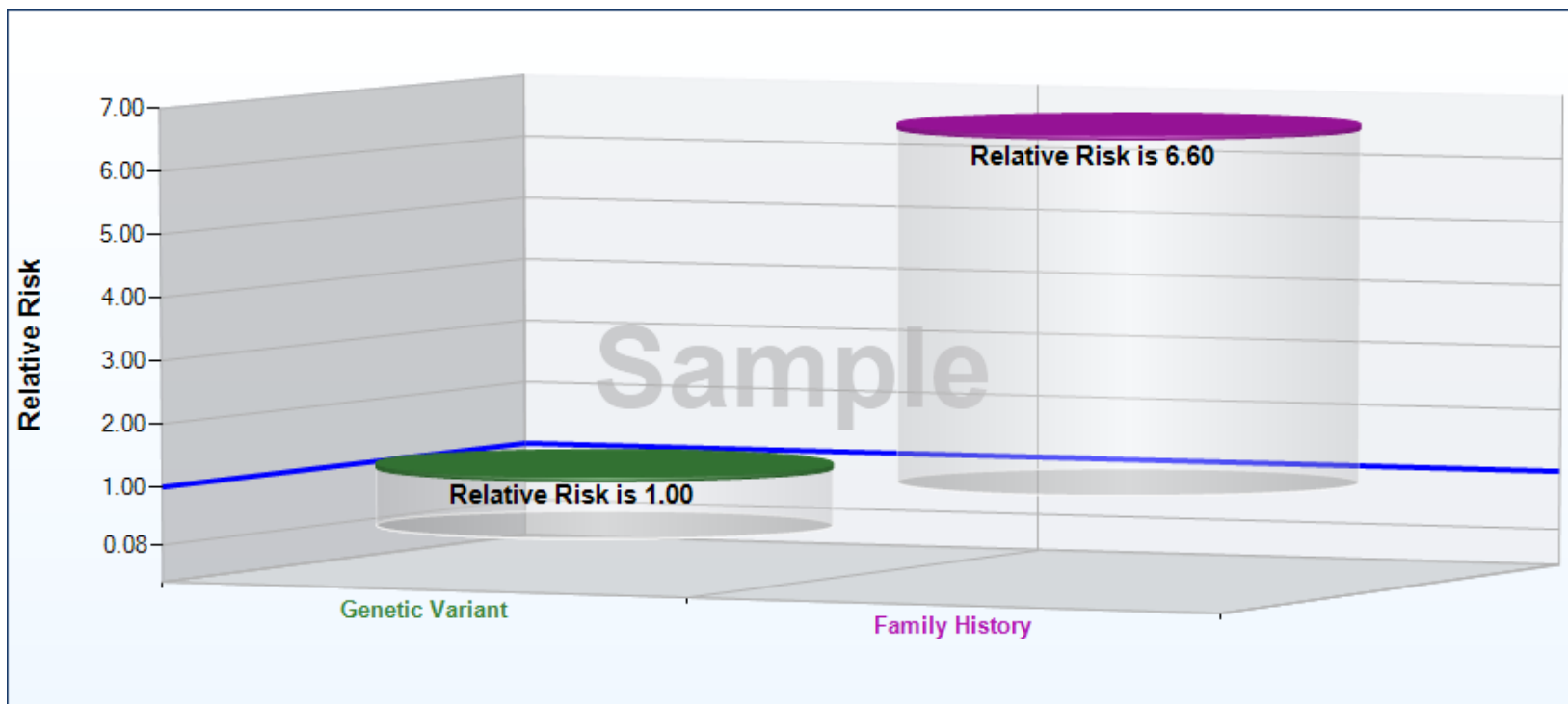
You reported that you are between 30 and 74 years old; an estimated 3 in 1,000 adults between 30 and 74 years old in the United States have adult onset type 1 diabetes.

Chart Color	Relative Risk Due To:	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	Genetic Variant	1.00	0.08	1.00	You have 2 copies of the non-protective variant. Based on this result, you are at a *higher* risk to develop type 1 diabetes compared to someone with one or two copies of this protective genetic variant.
	Family History	6.60	1.00	6.60	Based on your family history, you are 6.60 times more likely to develop type 1 diabetes than someone who does not have a first degree relative (parent, sibling, or child) with either type 1 or type 2 diabetes. *Having more than one first degree relative with either type 1 or type 2 diabetes contributes to your risk of type 1 diabetes.*

Type 1 Diabetes
Risk Due To Genetic Variant #1 (rs9272346)
**Your Result: 2 copies of the non-protective variant were detected (AA)**
Non-Protective Variant = A   Protective Variant = G

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	0.08	1.00	You have 2 copies of the non-protective variant. Based on this result, you are at a *higher* risk to develop type 1 diabetes compared to someone 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.

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.

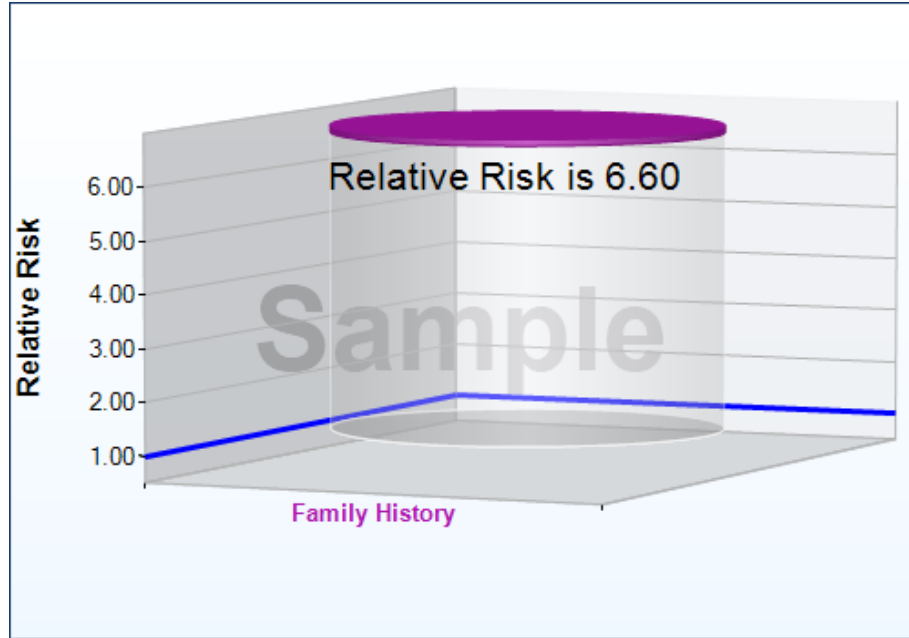**A relative risk less than 1.00 indicates a decreased risk.**
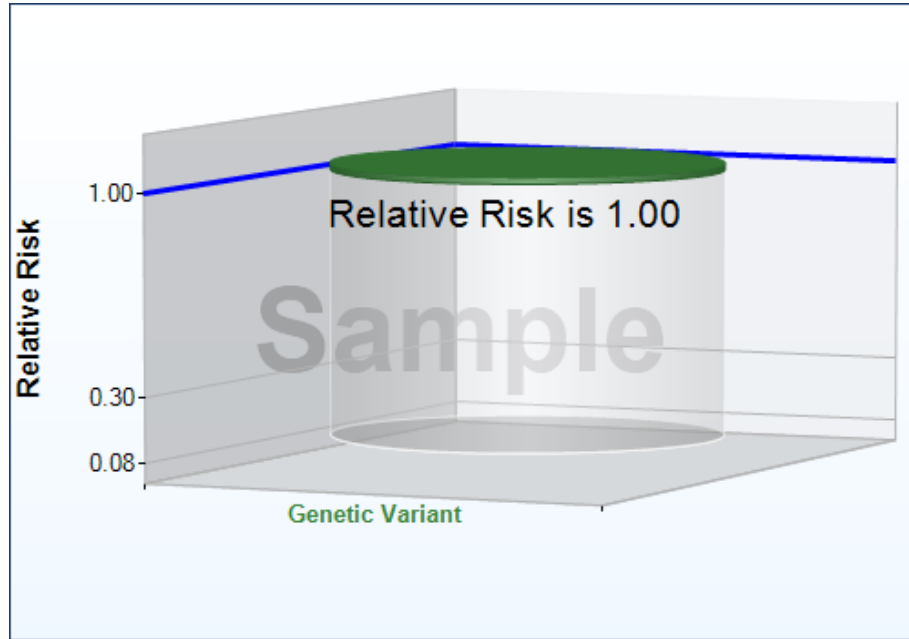
These results are based on a single study.

Type 1 Diabetes
Risk Due To Family History
You reported that more than one first degree relative (parent, sibling, or child) has either type 1 or type 2 diabetes.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	6.60	1.00	6.60	Based on your family history, you are 6.60 times more likely to develop type 1 diabetes than someone who does not have a first degree relative (parent, sibling, or child) with either type 1 or type 2 diabetes. *Having more than one first degree relative with either type 1 or type 2 diabetes contributes to your risk of type 1 diabetes.*

Risk is compared based on family history.

People with at least one first degree relative (parent, sibling, or child) with type 1 or type 2 diabetes are compared to people with no first degree relatives with type 1 or type 2 diabetes to determine relative risk of developing type 1 diabetes.

A relative risk greater than 1.00 indicates an increased risk.

These results are based on a single study.

Type 1 Diabetes - Variant #1 (rs9272346)

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 type 1 diabetes.

How Common Is This Variant?

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

AA - 36 in 100 people have 2 copies of the non-protective variant

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

GG - 26 in 100 people have 2 copies of the protective variant

This frequency is based on data from European populations

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Gene: HLA-DQA1   Chromosome: 6p21.3

Causes

Genetic vs. Non-Genetic Risk Factors

Type 1 diabetes can be caused by both genetic factors and non-genetic (or environmental) risk factors.

It is estimated that **non-genetic** factors (such as virus exposure) account for about **12%** of the risk of type 1 diabetes.

It is estimated that **88%** of the risk for type 1 diabetes 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 type 1 diabetes. We are only able to tell you about your family history risk and 1 genetic risk factor at this time.
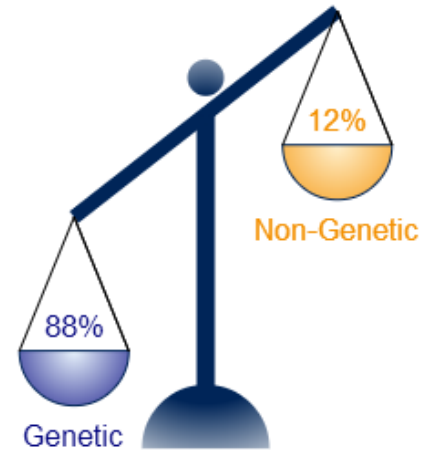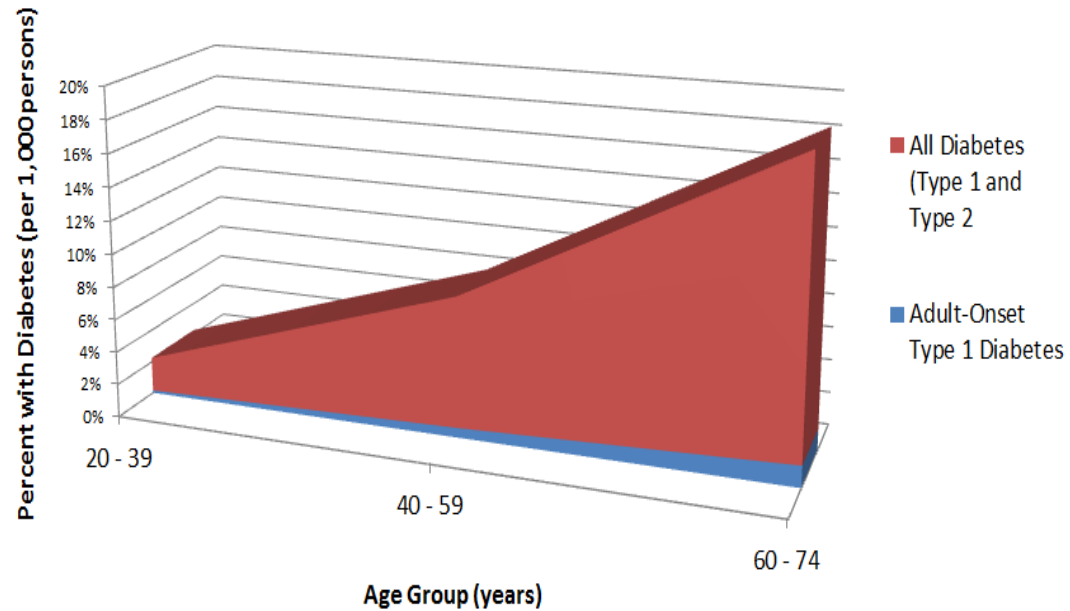
How Common

Type 1 diabetes is usually diagnosed in children and young adults, but can occur at any age.

Type 1 diabetes is less common than type 2 diabetes. Only about 5-10% of all cases of diabetes are type 1 diabetes.

About 3 out of every 1,000 adults (age 30 to 74 years of age) in the United States have adult-onset type 1 diabetes.

You reported that you are between 30 and 74 years old; an estimated 3 in 1,000 adults between 30 and 74 years old in the United States have adult onset type 1 diabetes.

Proportion of U.S. Adults with Diagnosed Diabetes

Percent with Diabetes (per 1,000 persons)

20%
18%
16%
14%
12%
10%
8%
6%
4%
2%
0%

20 - 39

40 - 59

60 - 74

Age Group (years)

■ All Diabetes (Type 1 and Type 2

■ Adult-Onset Type 1 Diabetes

Type 1 Diabetes

- This result alone does NOT diagnose type 1 diabetes. Type 1 diabetes must be diagnosed by your health care provider.
- This result does NOT mean that you have or will absolutely develop type 1 diabetes.
- This result does NOT mean that you will not develop type 1 diabetes in the future.
- This result ONLY assesses your risk for developing type 1 diabetes due to the factors presented in this report and does not mean that other genetic variants or risk factors for type 1 diabetes are present or absent.
- Personal risk factors, such as age, family history or lifestyle, may have a greater impact on your risk to develop type 1 diabetes 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

Type 1 Diabetes

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 Type 1 Diabetes Risk Algorithm Version 1 (July 6, 2009)]

1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. Genet Med. 13(2):131-139.

2. Harris, M.I. et al (1994). Prevalence of Adult-Onset IDDM in the U.S. Population. Diabetes Care 17(11): 1337-1340.

3. Liese, A.D. et al (2006). The Burden of Diabetes Mellitus Among US Youth: Prevalence Estimates From the SEARCH for Diabetes in Youth Study. Pediatrics 118(4): 1510-1518.

4. Hyttinen, V. et al (2003). Genetic Liability of Type 1 Diabetes and the Onset Age Among 22,650 Young Finnish Twin Pairs. Diabetes 52:1052-1055.

5. Cooper, J.D. et al (2008). Meta-analysis of genome-wide association study data identifies additional type 1 diabetes loci. Nature Genetics 40(12): 1399-1401.

6. Carlsson, S. et al (2007). Influence of Family History of Diabetes on Incidence and Prevalence of Latent Autoimmune Diabetes of the Adult. Diabetes Care 30:3040-3045.

7. McVean G.A. et al (2012). An integrated map of genetic variation from 1,092 human genomes. Nature. 491; 56-65.

Sample Results

Clinical Report for Type 1 Diabetes Genetic Variant 1 (rs9272346)

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:**	07-06-2010
Ordering Physician:	Dr. Edward Viner		

Name of Gene/Region: HLA-DQA1		Chromosomal Location: 6p21.3	
Variants tested	**Result**	**Reference Genotype**	
rs9272346	AA	AA	
Interpretation	**Individuals with this result are at a higher risk to develop type 1 diabetes 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 European 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 type 1 diabetes. For additional information on other risk factors please see the accompanying CPMC research report.		

Risk interpretation based on Coriell's Type 1 Diabetes Risk Algorithm Version 2 (August 14, 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 type 1 diabetes. This test is not diagnostic for type 1 diabetes and cannot rule out the risk of developing type 1 diabetes 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. Cooper, J.D. et al (2008). Meta-analysis of genome-wide association study data identifies additional type 1 diabetes loci. Nature Genetics 40(12): 1399-1401.