

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:	04-23-2009
Ordering Physician:	Dr. Edward Viner		

Risk of Developing Type 2 Diabetes Based on:

- **CPMC Type 2 Diabetes Variant 1 (rs7754840)**
- **Family History**
- **Body Mass Index**

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 2 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.

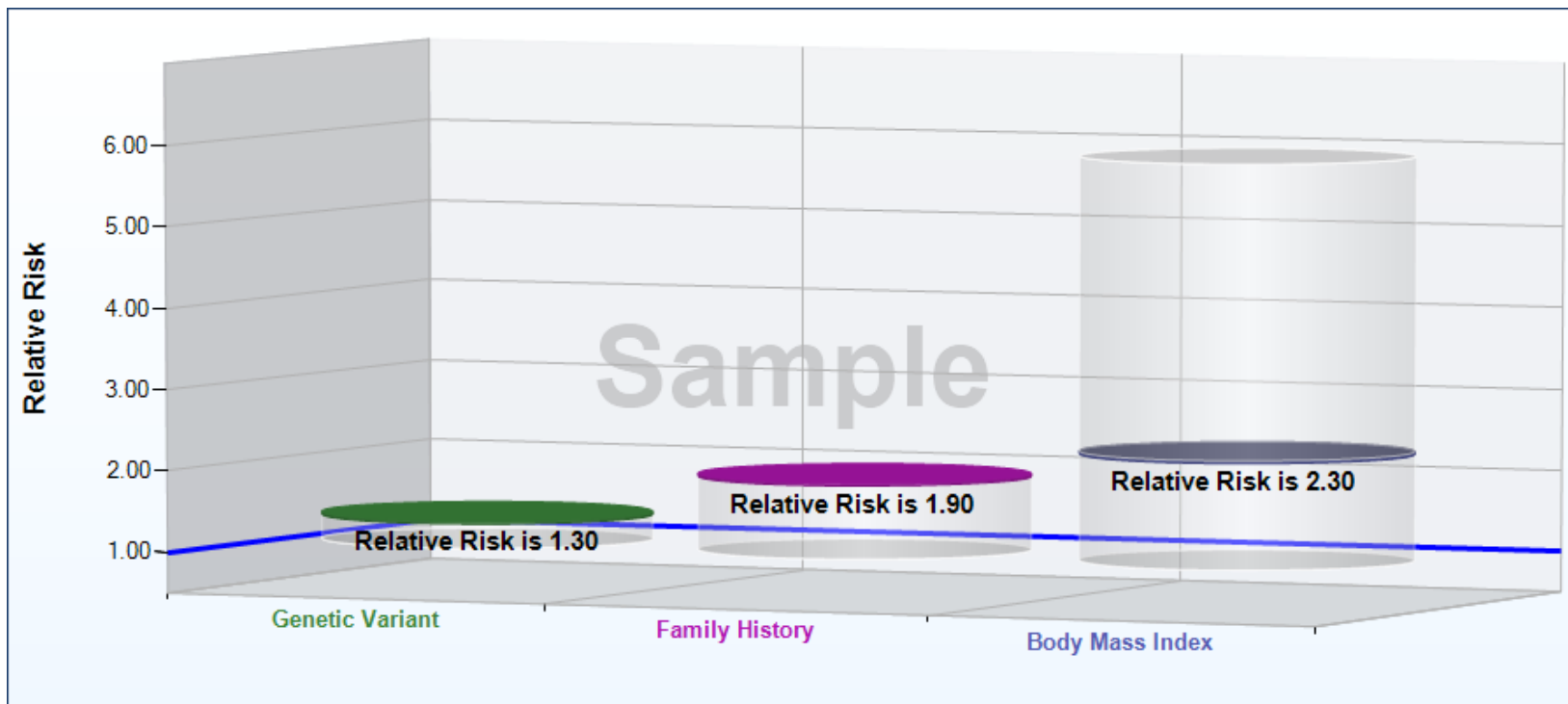
Genetic Variant Result, Details and Population Data

Type 2 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 genetic variant, family history and body mass index.

You report having been diagnosed with either type 1 or type 2 diabetes. The risk information below represents the risk of developing type 2 diabetes in people who do not have any form of diabetes. This genetic variant has only been associated with type 2 diabetes. The risk information provided is for information only.



You reported you are a Caucasian man, between 65 and 74 years old; an estimated 18 in 100 Caucasian men in your age group have type 2 diabetes.

Chart Color	Relative Risk Due To:	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	Genetic Variant	1.30	1.00	1.30	You have 2 copies of the risk variant. Based on this result, you are 30% more likely (or 1.30 times as likely) to develop type 2 diabetes as someone with no copies of this variant. <i>Having this risk variant contributes to your risk of type 2 diabetes.</i>
	Family History	1.90	1.00	1.90	Based on your family history, you are 90% more likely (or 1.90 times as likely) to develop type 2 diabetes compared to someone who does not have a mother or father with type 2 diabetes. <i>Having at least one parent with type 2 diabetes contributes to your risk of type 2 diabetes.</i>

Chart Color	Relative Risk Due To:	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	Body Mass Index	2.30	1.00	5.90	<p>Based on your BMI, you are 2.30 times as likely to develop type 2 diabetes as someone who has a BMI of less than 25 (not overweight).</p> <p><i>Being overweight (BMI of 25 or greater) contributes to your risk of type 2 diabetes.</i></p>

Type 2 Diabetes

Risk Due To Genetic Variant #1 (rs7754840)

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

Non-Risk Variant = G Risk Variant = C

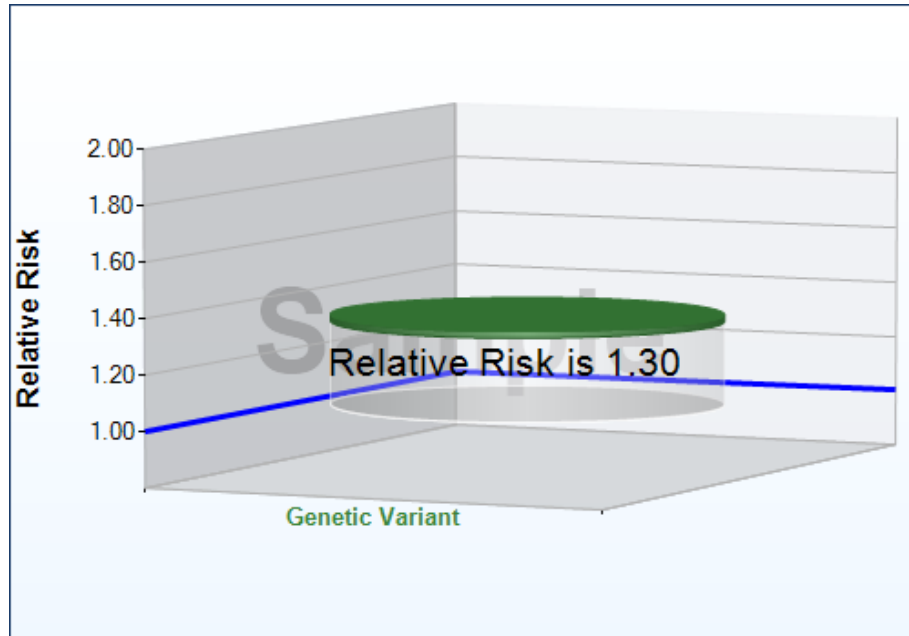
You report having been diagnosed with either type 1 or type 2 diabetes. The risk information below represents the risk of developing type 2 diabetes in people who do not have any form of diabetes. This genetic variant has only been associated with type 2 diabetes. The risk information provided is for information only.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.30	1.00	1.30	<p>You have 2 copies of the risk variant. Based on this result, you are 30% more likely (or 1.30 times as likely) to develop type 2 diabetes as someone with no copies of this variant.</p> <p><i>Having this risk variant contributes to your risk of type 2 diabetes.</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.

Type 2 Diabetes Risk Due To Family History

You reported having one or both parents with type 2 diabetes.

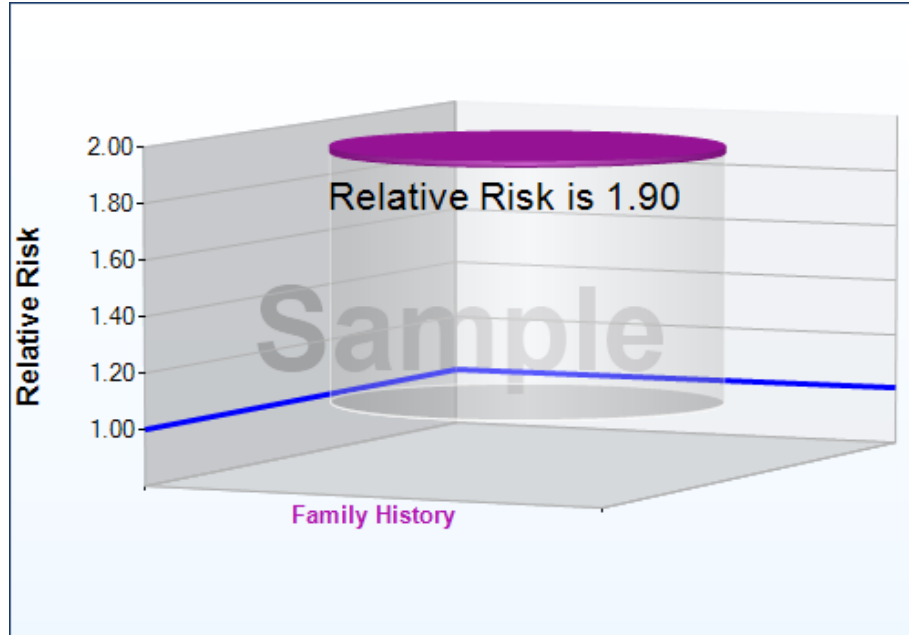
You report having been diagnosed with either type 1 or type 2 diabetes. The risk information below represents the risk of developing type 2 diabetes in people who do not have any form of diabetes. This genetic variant has only been associated with type 2 diabetes. The risk information provided is for information only.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.90	1.00	1.90	<p>Based on your family history, you are 90% more likely (or 1.90 times as likely) to develop type 2 diabetes compared to someone who does not have a mother or father with type 2 diabetes.</p> <p><i>Having at least one parent with type 2 diabetes contributes to your risk of type 2 diabetes.</i></p>

Risk is compared based on family history.

People with at least one parent with type 2 diabetes were compared to people who do not have a parent with type 2 diabetes to determine relative risk of developing type 2 diabetes.

A relative risk greater than 1.00 indicates an increased risk.



These results are based on a single study.

Type 2 Diabetes Risk Due To Body Mass Index

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

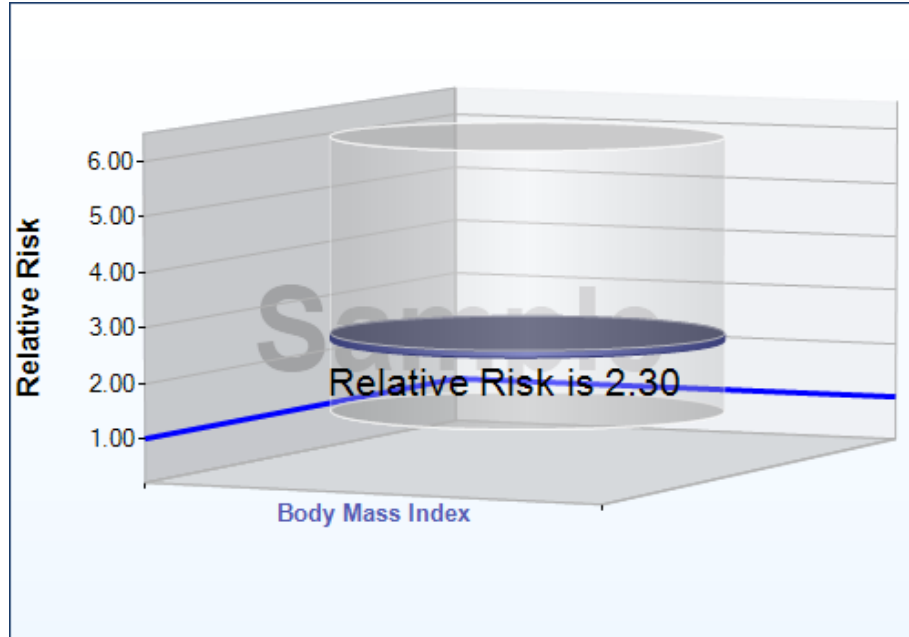
You report having been diagnosed with either type 1 or type 2 diabetes. The risk information below represents the risk of developing type 2 diabetes in people who do not have any form of diabetes. This genetic variant has only been associated with type 2 diabetes. The risk information provided is for information only.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	2.30	1.00	5.90	<p>Based on your BMI, you are 2.30 times as likely to develop type 2 diabetes as someone who has a BMI of less than 25 (not overweight).</p> <p><i>Being overweight (BMI of 25 or greater) contributes to your risk of type 2 diabetes.</i></p>

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 \geq 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 a single study.

Type 2 Diabetes - Variant #1 (rs7754840)

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 type 2 diabetes.

How Common Is This Variant?

Non-Risk Variant = G Risk Variant = C

GG - 50 in 100 people have 2 copies of the non-risk variant

GC - 37 in 100 people have 1 copy of the non-risk variant and 1 copy of the risk variant

CC - 13 in 100 people have 2 copies of the risk variant

This frequency is based on data from European populations



Gene: CDKAL1

Chromosome: 6p22.3

Causes

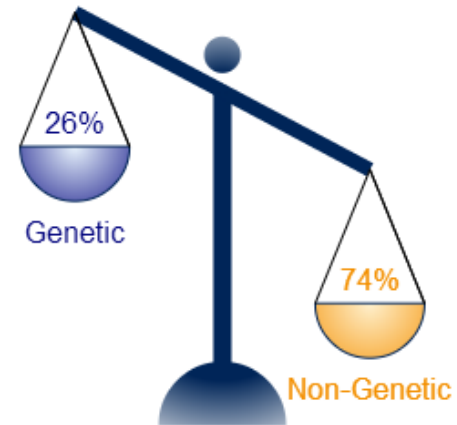
Genetic vs. Non-Genetic Risk Factors

Type 2 diabetes can be caused by both genetic factors and non-genetic (or environmental) risk factors.

It is estimated that **non-genetic** factors (like diet and exercise) account for about **74%** of the risk of type 2 diabetes.

It is estimated that **26%** of the risk for type 2 diabetes is based on **genetic** risk factors. This estimate accounts for both known and unknown gene variants.

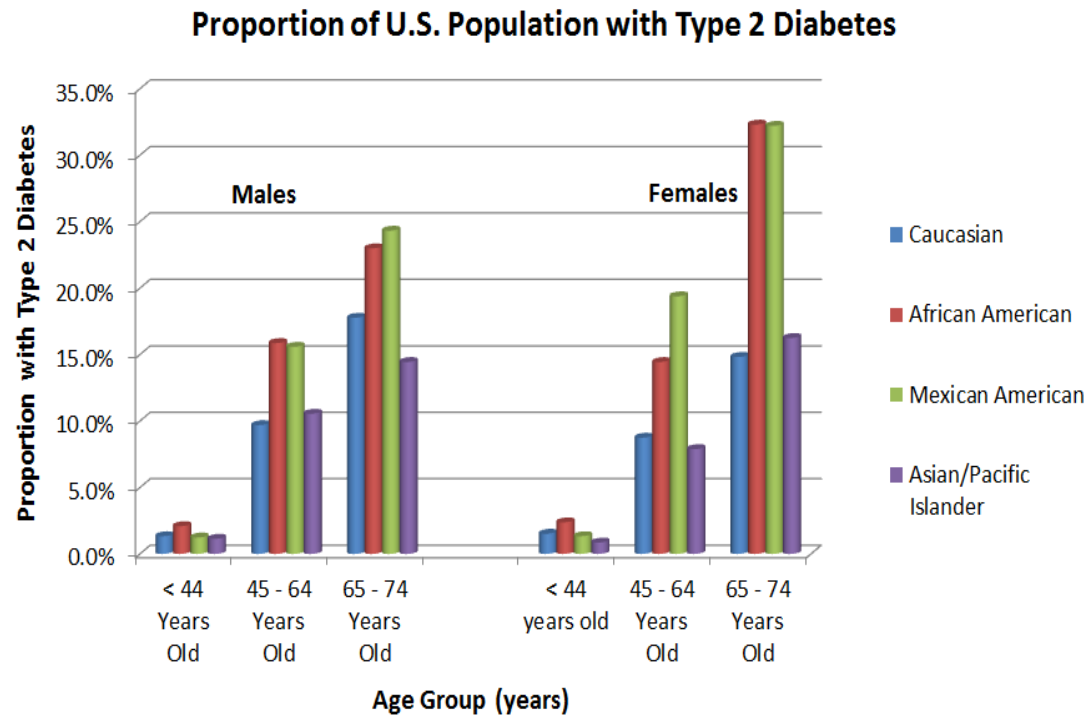
There are many different genetic and non-genetic risk factors that contribute to the risk of type 2 diabetes. We are only able to tell you about your family history risk, 1 genetic and 1 non-genetic risk factor at this time.



How Common

Age, ancestry, and gender contribute to your risk of type 2 diabetes.

You reported you are a **Caucasian man, between 65 and 74 years old**; an estimated **18 in 100 Caucasian men in your age group** have type 2 diabetes.



Limitations

Type 2 Diabetes

- This result alone does NOT diagnose type 2 diabetes. Type 2 diabetes must be diagnosed by your health care provider.
- This result does NOT mean that you have or will absolutely develop type 2 diabetes.
- This result does NOT mean that you will not develop type 2 diabetes in the future.
- This result ONLY assesses your risk for developing type 2 diabetes due to the factors presented in this report and does not mean that other genetic variants or risk factors for type 2 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 2 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 2 Diabetes

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 Type 2 Diabetes Risk Algorithm Version 1 (April 27, 2009)]

1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. *Genet Med.* 13(2):131-139.
2. Poulsen et al. (1999). Heritability of Type II (non-insulin-dependent) diabetes mellitus and abnormal glucose tolerance-a population-based twin study. *Diabetologia.* 42:139-145.
3. Centers for Disease Control and Prevention, National Center for Health Statistics, Division of Health Interview Statistics, data from the National Health Interview Survey. U.S. Bureau of the Census. Age-Specific Percentage of Civilian, Noninstitutionalized Population with Diagnosed Diabetes, by Race and Sex, United States, 2006.
4. Meigs et al. (2008). Genotype Score in Addition to Common Risk Factors for Prediction of Type 2 Diabetes. *NEJM.* 359:2208-2219.
5. Tabara et al. (2009). Replication Study of Candidate Genes Associated With Type 2 Diabetes Based on Genome-Wide Screening. *Diabetes.* 58:493-498.
6. Ng et al. (2008). Implication of Genetic Variants Near TCF7L2, SLC30A8, HHEX, CDKAL1, CDKN2A/B, IGF2BP2, and FTO in Type 2 Diabetes and Obesity in 6,719 Asians. *Diabetes.* 57:2226-2233.
7. Lewis et al. (2008). Association Analysis in African Americans of European-Derived Type 2 Diabetes Single Nucleotide Polymorphisms From Whole-Genome Association Studies. *Diabetes.* 57:2220-2225.
8. Wilson et al. (2007). Prediction of Incident Diabetes Mellitus in Middle-aged Adults: The Framingham Offspring Study. *Arch Intern Med.* 167:1068-1074.
9. 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 Type 2 Diabetes Genetic Variant 1 (rs7754840)

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:	04-23-2009
Ordering Physician:	Dr. Edward Viner		

Name of Gene/Region: CDKAL1		Chromosomal Location: 6p22.3
Variants tested	Result	Reference Genotype
rs7754840	CC	GG
Interpretation	Individuals with this result are 30% more likely (or 1.30 times as likely) to develop type 2 diabetes as someone with no copies of this 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 type 2 diabetes. For additional information on other risk factors please see the accompanying CPMC research report.	

Risk interpretation based on Coriell's Type 2 Diabetes Risk Algorithm Version 2 (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 type 2 diabetes. This test is not diagnostic for type 2 diabetes and cannot rule out the risk of developing type 2 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. Meigs, JB. et al (2008). Genotype score in addition to common risk factors for prediction of type 2 diabetes. N Engl J Med. 359(21):2208-2219.