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:	NATALIE DEMO	**Gender:**	Female
Date of Birth:		**Date Collected:**	11-30-2016
Coriell ID:	DEMONAT	**Date Received:**	11-30-2016
Lab Accessioning Number:	DEMONAT	**Date of Report:**	12-01-2009
Ordering Physician:	Dr. Edward Viner		

Risk of developing Coronary Artery Disease based on:

- **CPMC Coronary Artery Disease Variant 1 (rs1333049)**
- **Family History**
- **Smoking**
- **Type 2 Diabetes**

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 coronary artery disease. 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.

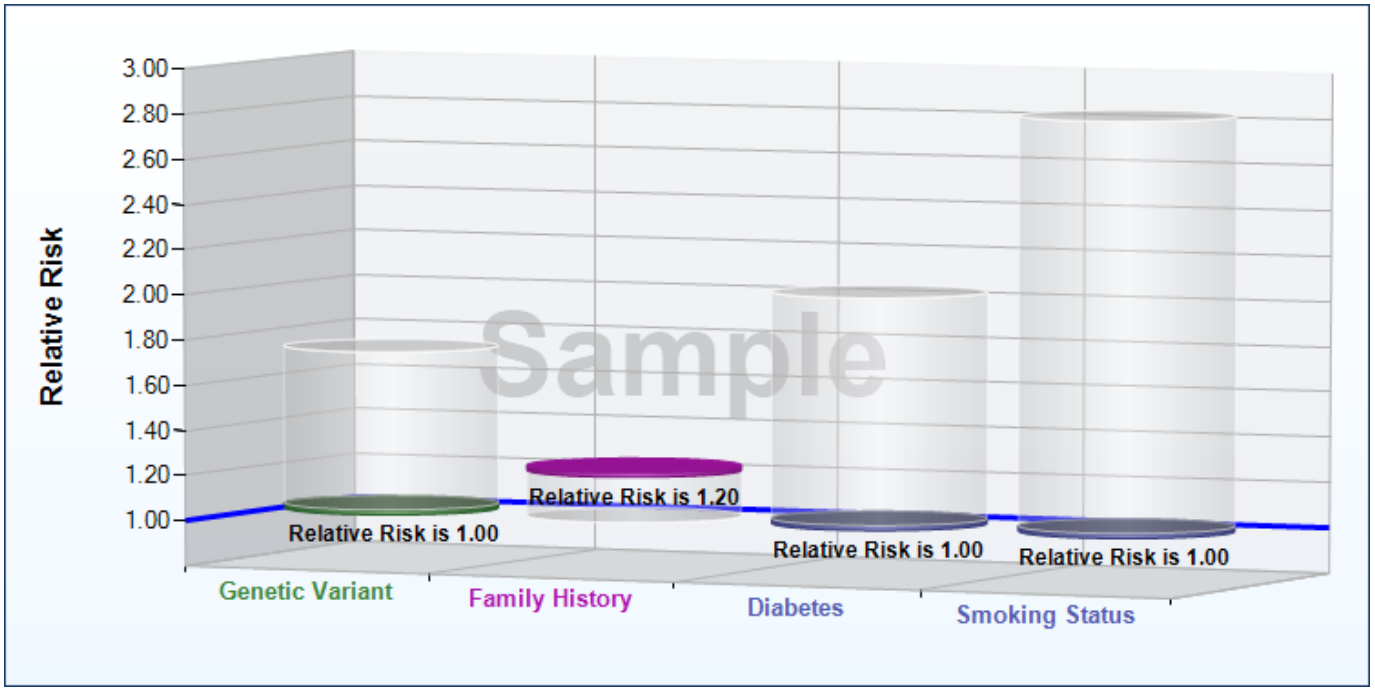
This research report includes all data included in the clinical report as well as supplemental interpretations and educational material. Please see the report that follows for the official clinical report.

Genetic Variant Result, Details and Population Data

Coronary Artery Disease

Risk Summary

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, diabetes and smoking status.



You reported you are a woman, between 20 and 39 years old; an estimated 1 in 100 women in your age group have coronary artery disease.

Chart Color	Relative Risk Due To:	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	Genetic Variant	**1.00**	1.00	1.70	**You have 2 copies of the non-risk variant. Based on this result, you are at lower risk to develop coronary artery disease compared to someone with one or two copies of this variant.**
	Family History	**1.20**	1.00	1.20	**Based on your family history, you are 20% more likely (or 1.20 times as likely) to develop coronary artery disease compared to a woman who does not have at least one parent with coronary artery disease.** *Having at least one parent with coronary artery disease contributes to your risk of coronary artery disease.*
	Diabetes	**1.00**	1.00	2.00	**Because you reported that you do not have diabetes, you are at a lower risk of coronary artery disease compared to women who have diabetes.**
	Smoking Status	**1.00**	1.00	2.80	**Because you are not a smoker, you are at a lower risk to develop coronary artery disease compared to current smokers.**

Coronary Artery Disease

Risk Due To Genetic Variant #1

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

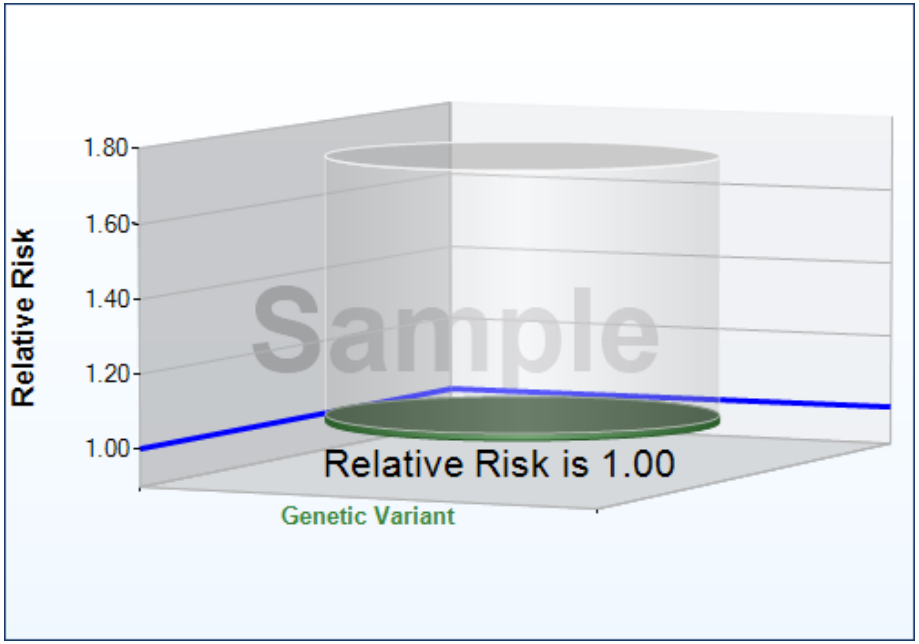
Non-Risk Variant = G Risk Variant = C

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	1.00	1.70	**You have 2 copies of the non-risk variant. Based on this result, you are at lower risk to develop coronary artery disease compared to someone with one or two copies of this variant.**

Genetic Variant Risk is based on the number of copies of this 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.



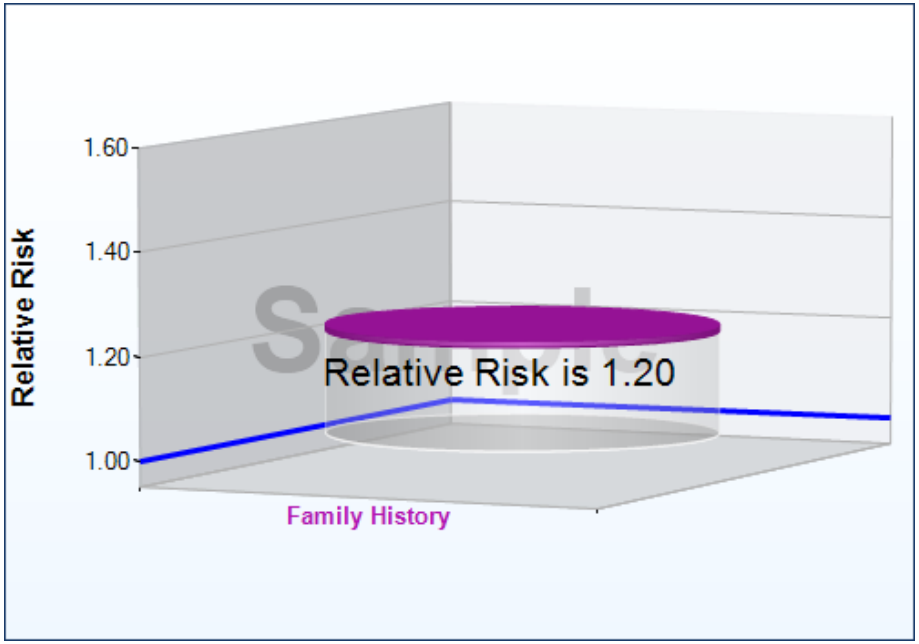
These results are based on a single study.

Coronary Artery Disease

Risk Due To Family History

You reported having one or both parents with coronary artery disease.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.20	1.00	1.20	**Based on your family history, you are 20% more likely (or 1.20 times as likely) to develop coronary artery disease compared to a woman who does not have at least one parent with coronary artery disease.** *Having at least one parent with coronary artery disease contributes to your risk of coronary artery disease.*



Risk is compared based on family history.

Women with at least one parent with coronary artery disease were compared to women whose parents did not have coronary artery disease to determine relative risk of developing coronary artery disease.

A relative risk greater than 1.00 indicates an increased risk.

These results are based on a single study.

Coronary Artery Disease

Risk Due To Diabetes

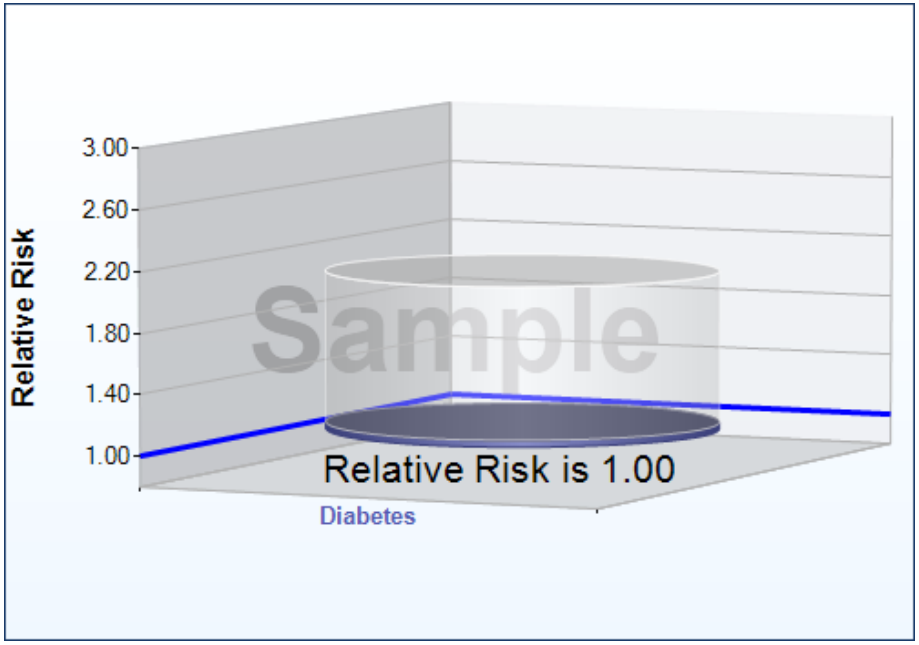
You reported that you do not have diabetes.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	1.00	2.00	**Because you reported that you do not have diabetes, you are at a lower risk of coronary artery disease compared to women who have diabetes.**

Risk is compared based on diagnosis of diabetes.

Women who have diabetes are compared to women who do not have diabetes to determine relative risk.

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



These results are based on multiple studies.

Coronary Artery Disease

Risk Due To Smoking Status

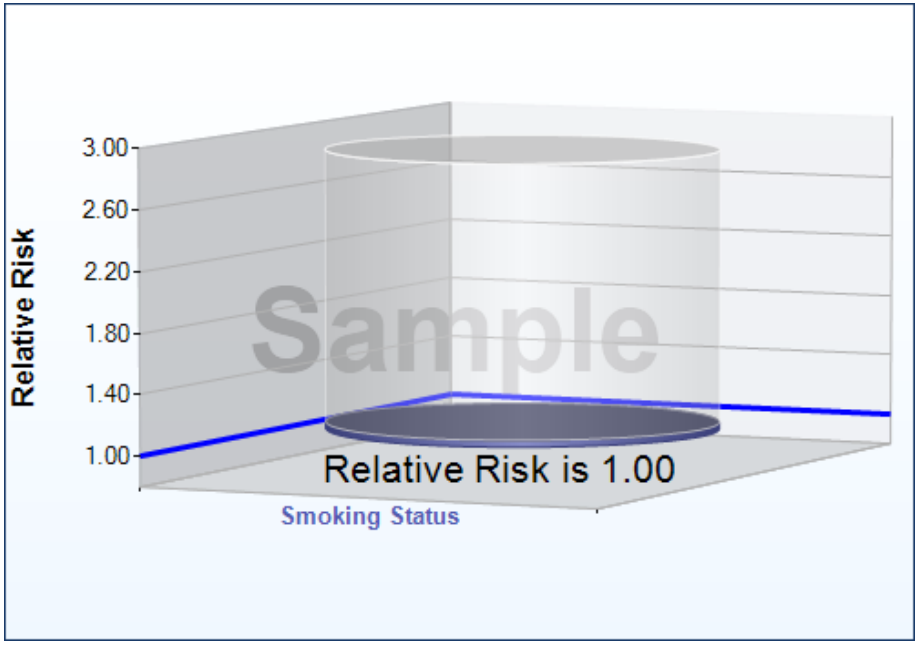
You reported that you do not smoke.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	1.00	2.80	**Because you are not a smoker, you are at a lower risk to develop coronary artery disease compared to current smokers.**

Risk is compared based on smoking habits.

Women who are current smokers were compared to women who have never smoked to determine relative risk.

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



These results are based on a single study.

Coronary Artery Disease - Variant #1 (rs1333049)

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 coronary artery disease.

How Common Is This Variant?

Non-Risk Variant = G **Risk Variant = C**

CC - 7 in 100 people have 2 copies of the risk variant

GC - 42 in 100 people have 1 copy of the non-risk variant and 1 copy of the risk variant

GG - 51 in 100 people have 2 copies of the non-risk variant

This frequency is based on data from African American populations.

Gene: CDKN2A/CDKN2B **Chromosome: 9p21.3**

Causes

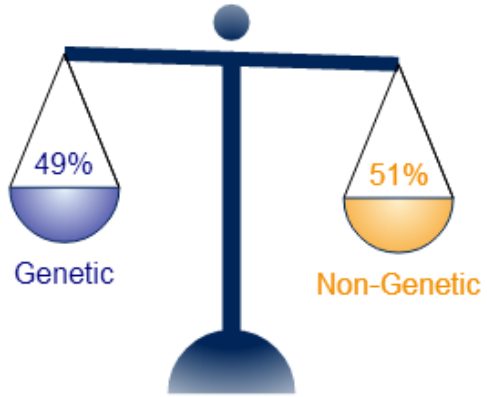
Genetic vs. Non-Genetic Risk Factors

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

It is estimated that **non-genetic** factors (like smoking and diabetes) account for about **51%** of the risk of coronary artery disease.

It is estimated that about **49%** of the risk for coronary artery disease is based on **genetic** risk factors. This estimate accounts for both known and unknown gene variants.

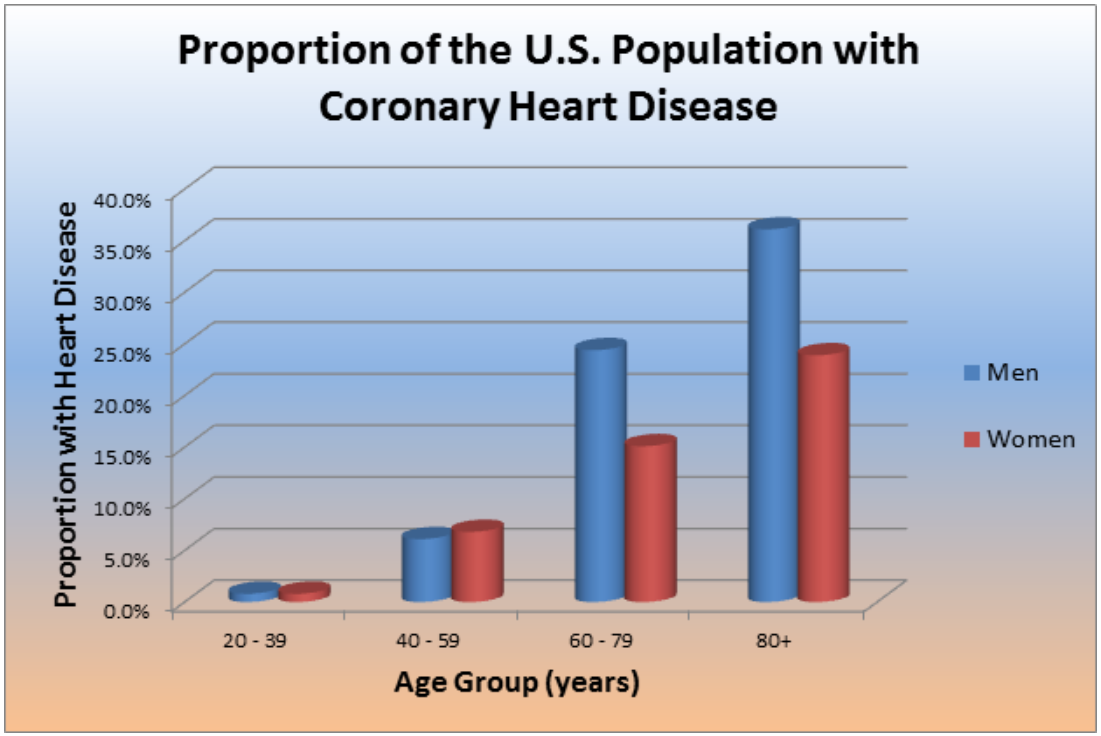
There are many different genetic and non-genetic risk factors that contribute to the risk of coronary artery disease. We are only able to tell you about your family history risk, 1 genetic and 2 non-genetic risk factors at this time.



How Common

Age and gender contribute to your risk of coronary artery disease.

You reported you are a woman, between 20 and 39 years old; an estimated 1 in 100 women in your age group have coronary artery disease.



Limitations

Coronary Artery Disease

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

Coronary Artery Disease

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 Coronary Artery Disease Risk Algorithm Version 1 (April 2, 2009)]

1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. Genet Med. 13(2):131-139.
2. Lango et. al. (2008). What will whole genome searches for susceptibility genes for common complex disease offer to clinical practice? J Intern. Med. 263: 16-27.
3. Lloyd-Jones, D. et al (2009). Heart Disease and Stroke Statistics 2009 Update: A Report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 119:e21 - e181.
4. Schunkert, H. et al (2008). Repeated replication and a prospective meta-analysis of the association between chromosome 9p21.3 and coronary artery disease. Circulation 117:1675-1684.
5. Honohara, K. et al (2008). Replication of the association between a chromosome 9p21 polymorphism and coronary artery disease in Japanese and Korean populations. J Hum. Genet. 53: 375-359.
6. McVean G.A. et al (2012). An integrated map of genetic variation from 1,092 human genomes. Nature. 491; 56-65.
7. D'Agostino, R.B. Sr. et al (2001). Validation of the Framingham coronary heart disease prediction score: results of a multiple ethnic group investigation. JAMA. 286: 180-187.
8. Myers, R.H. et al (1990). Parental history is an independent risk factor for coronary artery disease: the Framingham Study. Am. Heart J. 120: 963-969.

Sample Results

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Clinical Report for Coronary Artery Disease Genetic Variant (rs1333049)

Name:	NATALIE DEMO	**Sample Type:**	Saliva
Race/Ethnicity:	Black or African-American	**Gender:**	Female
Date of Birth:		**Date Collected:**	11-30-2016
Coriell ID:	DEMONAT	**Date Received:**	11-30-2016
Lab Accessioning Number:	DEMONAT	**Date of Report:**	12-01-2009
Ordering Physician:	Dr. Edward Viner		

Name of Gene/Region: CDKN2A/CDKN2B		**Chromosomal Location:** 9p21.3
Variants tested	**Result**	**Reference Genotype**
rs1333049	GG	GG
Interpretation	**Individuals with this result are at a lower risk to develop coronary artery disease compared to someone with one or two copies of this genetic risk variant.** These risk estimates are based on studies involving multiple populations that include individuals with European and Japanese 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 coronary artery disease. For additional information on other risk factors please see the accompanying CPMC research report.	

Risk interpretation based on Coriell's Coronary Artery Disease Risk Algorithm Version 1 (April 2, 2009)

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 coronary artery disease. This test is not diagnostic for coronary artery disease and cannot rule out the risk of developing coronary artery disease 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. Schunkert, H. et al (2008). Repeated replication and a prospective meta-analysis of the association between chromosome 9p21.3 and coronary artery disease. Circulation 117:1675-1684.
2. Honohara, K. et al (2008). Replication of the association between a chromosome 9p21 polymorphism and coronary artery disease in Japanese and Korean populations. J Hum. Genet. 53: 375-359.