## 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:** | 03-08-2016 |
| **Ordering Physician:** | Dr. Edward Viner | | |

**Risk of Developing Glaucoma Based on:**

- **CPMC Glaucoma Variants**
  - **rs7049105**
  - **rs7518099**
- **Family History**
- **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 two genetic variants, but does not represent your complete genetic risk for developing glaucoma. These results were generated as part of this research study in a CLIA-approved laboratory.

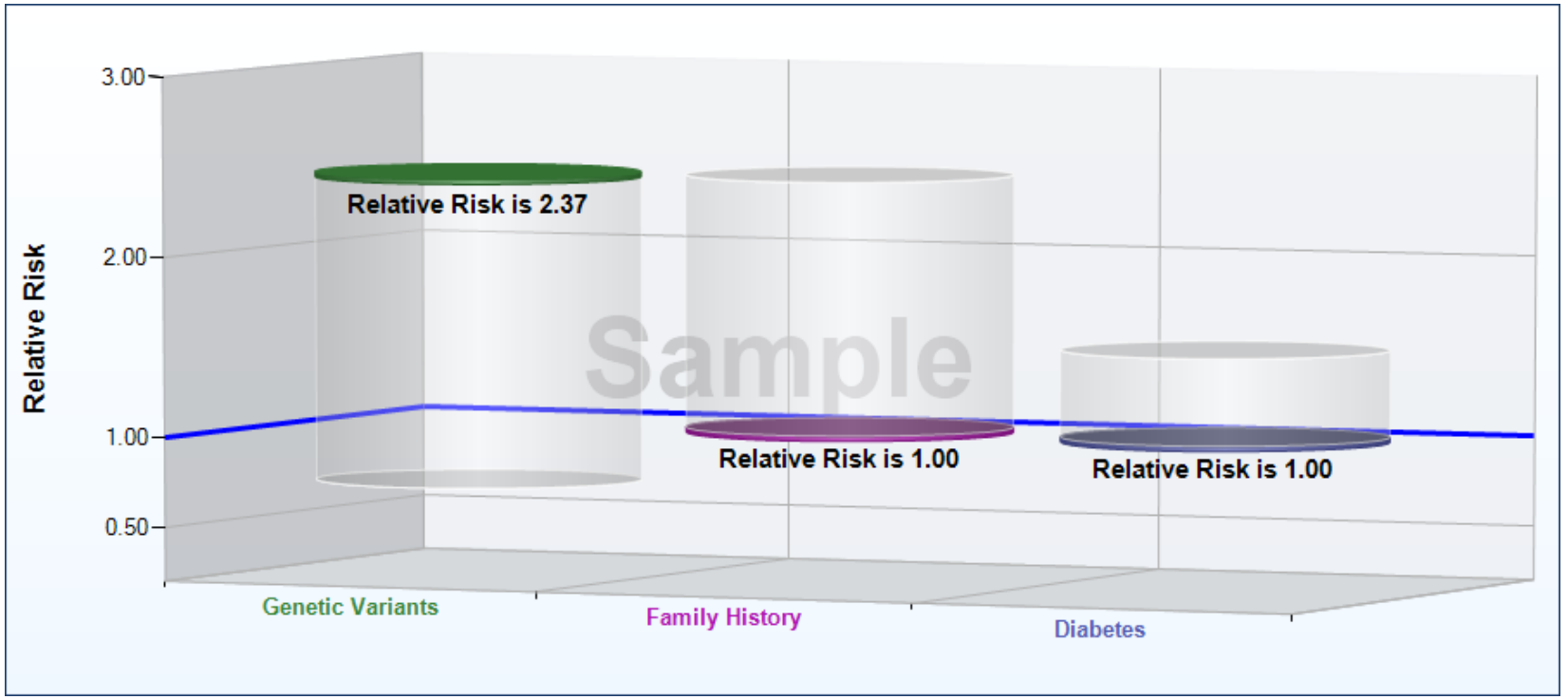
More information about the study, how to interpret CPMC results, and how we calculate risk is available on our website http://cpmc.coriell.org or by contacting our genetic counselor. Participants may schedule an appointment with our board-certified genetic counselor through the web portal by clicking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

# Glaucoma

**Risk factors may be related to each other and risk estimates cannot be combined.**
**This graph provides a summary of the relative risk for 2 genetic variants, family history, and diabetes.**




You reported you are an African American woman, less than 40 years old. Data are not available for your age group; however, an estimated 2 in 100 African American women between the ages of 40 and 49 have glaucoma.

| Chart Color | Relative Risk Due To: | Minimum Risk | Maximum Risk | Your Risk | Interpretation |
|---|---|---|---|---|---|
| | **Genetic Variants** | 0.68 | 2.37 | **2.37** | **Based on your combination of genetic variants, you are 2.37 times as likely to develop glaucoma as compared to an average individual.**<br><br>***Having this combination of genetic variants increases your risk of glaucoma.*** |
| | **Family History** | 1.00 | 2.40 | **1.00** | **Based on your family history, you are at a lower risk to develop glaucoma compared to someone with at least one first degree relative (parent, sibling, or child) with glaucoma.** |
| | **Diabetes** | 1.00 | 1.48 | **1.00** | **Because you do not have diabetes, you are at a lower risk to develop glaucoma compared to individuals who have been diagnosed with diabetes.** |

**How Common**

# Glaucoma (Multi-variant Version #1)

**The table and picture below show how many individuals will fall into each of the genetic risk categories for glaucoma based on 2 genetic variants.**

| | |
|---|---|
| **Reduced Risk** | **20 in 100 people** |
| **Average Risk** | **75 in 100 people** |
| **Elevated Risk** | **5 in 100 people** |

## Your Genetic Results

# Glaucoma

## Multi-variant Genetic Risk

**The CPMC tested 2 sites of genetic variation in 2 genes associated with glaucoma.**
**Your result for each genetic variant tested is shown below in yellow.**

| Variants Tested | Reference Value | Your Result |
|---|---|---|
| rs7049105 | TT | CC |
| rs7518099 | TT | CC |

# Glaucoma

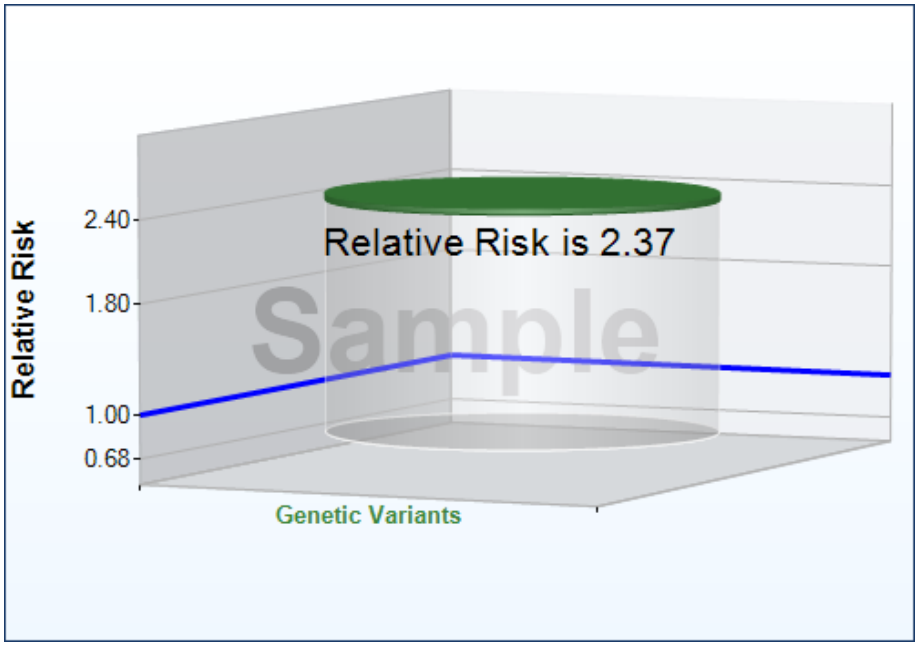
## Multi-variant Genetic Risk

| Chart Color | Genetic Risk Score | Risk Category | Interpretation |
|---|---|---|---|
| | **2.37** | Elevated | **Based on your combination of genetic variants, you are 2.37 times as likely to develop glaucoma as compared to an average individual.**<br><br>***Having this combination of genetic variants increases your risk of glaucoma.*** |

**The CPMC tested 2 sites of genetic variation in 2 genes associated with glaucoma.**

**Your risk due to the genetic variants tested was estimated and compared to the genetic risk of an average individual.**

**Other genetic variants, not currently included in this CPMC test, may also influence your risk to develop glaucoma.**




**These results are based on multiple studies.**

# Glaucoma

## Risk Due To Family History

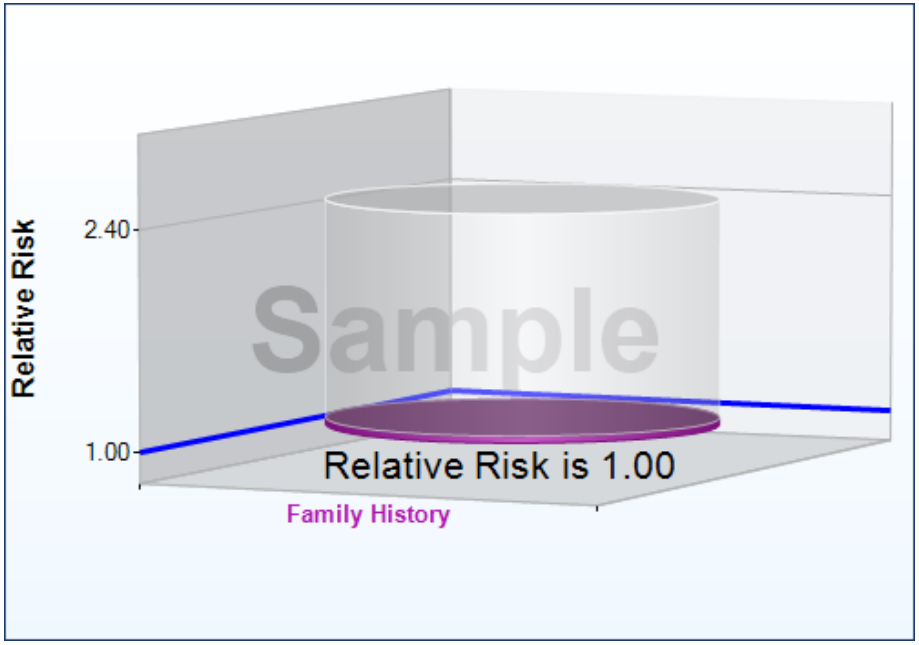
**You reported that none of your first degree relatives (parents, siblings or children) have glaucoma.**

| Chart Color | Minimum Risk | Maximum Risk | Your Risk | Interpretation |
|---|---|---|---|---|
| | 1.00 | 2.40 | **1.00** | **Based on your family history, you are at a lower risk to develop glaucoma compared to someone with at least one first degree relative (parent, sibling, or child) with glaucoma.** |

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

**People with at least one first degree relative with glaucoma were compared to people with no family history of glaucoma to determine relative risk of developing glaucoma.**

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




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

# Glaucoma

## Risk Due To Diabetes

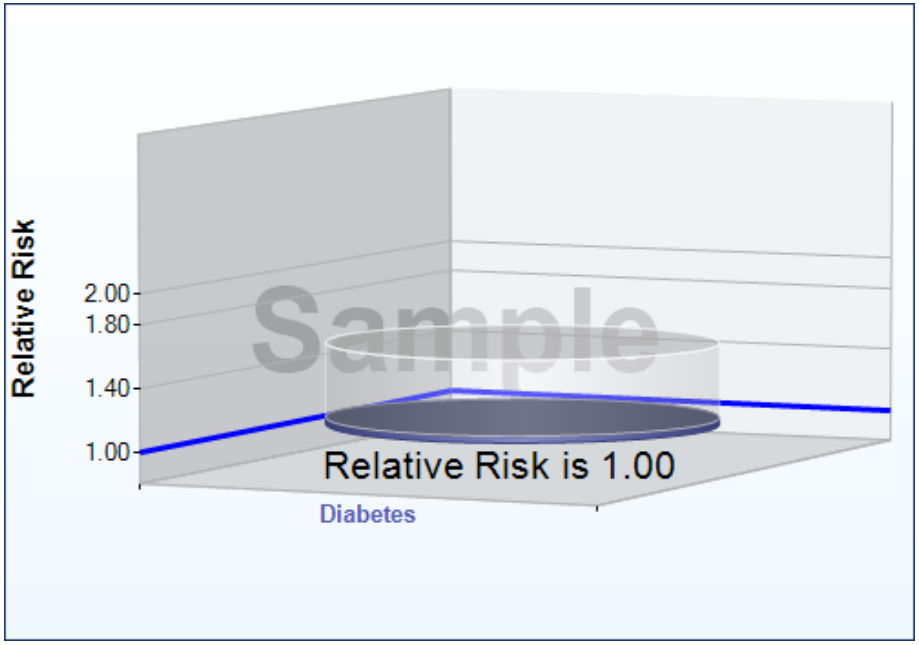
**You reported that you have not been diagnosed with diabetes.**

| Chart Color | Minimum Risk | Maximum Risk | Your Risk | Interpretation |
|---|---|---|---|---|
| | 1.00 | 1.48 | **1.00** | **Because you do not have diabetes, you are at a lower risk to develop glaucoma compared to individuals who have been diagnosed with diabetes.** |

**Risk is compared based on having a diagnosis of diabetes.**

**Those who have been diagnosed with diabetes were compared to those who have not been diagnosed with diabetes to determine relative risk.**

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




**These results are based on multiple studies.**

# Glaucoma (Multi-variant Version #1)

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.

The CPMC tested 2 sites of genetic variation in 2 genes associated with glaucoma.
Background information about each genetic variant tested is shown below.

| Genetic Variants | Variant Type | Gene | Chromosomal Location |
|---|---|---|---|
| **rs7049105** | T = non-risk<br>C = risk | *CDKN2B-AS1* | 9p21.3 |
| **rs7518099** | T = non-risk<br>C = risk | *TMCO1* | 1q24.1 |

**Causes**

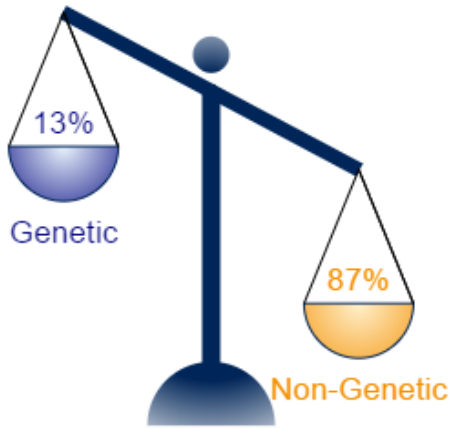
# Genetic vs. Non-Genetic Risk Factors

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

It is estimated that **non-genetic** factors (like diet and diabetes) account for about **87%** of the risk for glaucoma.

It is estimated that **13%** of the risk for glaucoma is based on **genetic** risk factors. This estimate accounts for both known and unknown gene variants.

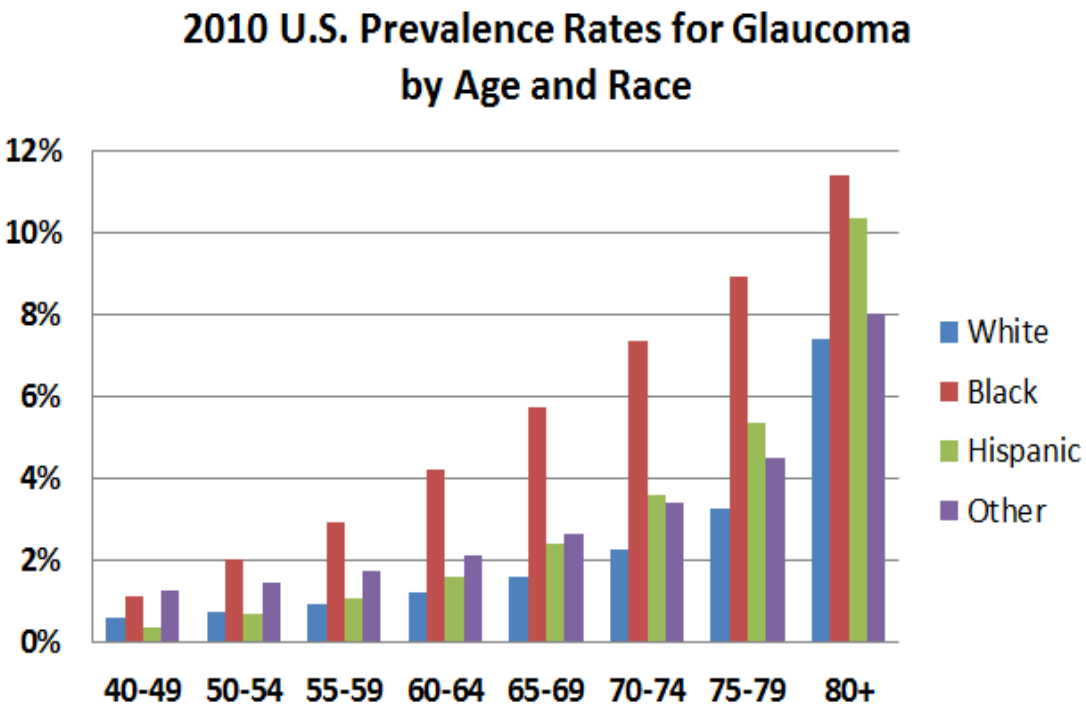
**There are many different genetic and non-genetic risk factors that contribute to the risk of glaucoma. We are only able to tell you about your family history risk, 2 genetic risk factors, and 1 non-genetic risk factor for glaucoma.**



**Prevalence**

The risk of glaucoma increases with age and is more common among African Americans.

**You reported you are an African American woman, less than 40 years old. Data are not available for your age group; however, an estimated 2 in 100 African American women between the ages of 40 and 49 have glaucoma.**



## Limitations

# Glaucoma

- These results alone do NOT diagnose glaucoma. Glaucoma must be diagnosed by your health care provider.
- This result does NOT mean that you have or will absolutely develop glaucoma.
- This result does NOT mean that you will not develop glaucoma in the future.
- This result ONLY assesses your risk for developing glaucoma due to the factors presented in this report and does not mean that other genetic variants or risk factors for glaucoma are present or absent.
- Personal risk factors, such as age, family history or lifestyle, may have a greater impact on your risk to develop glaucoma than any individual or multiple genetic variant(s).
- Our method of estimating genetic risk due to multiple genetic variants requires complete data. If data are missing for any individual genetic variant included in our analysis, we will not be able to provide you a genetic risk estimate.
- 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

# Glaucoma

**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 Glaucoma Research Risk Algorithm Version 1 (July 12, 2016)]


1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. Genet Med. 13(2):131-139.
2. Goddard, G.H. et al (2010). Risk categorization for complex disorders according to genotype relative risk and precision in parameter estimates. Genet Epidemiol. 34(6):624-32.
3. Crouch, D.J. et al (2012). REGENT: a risk assessment and classification algorithm for genetic and environmental factors. Eur J Hum Genet. 21(1):109-11.
4. Leske, M.C. et al (2008). Risk factors for incident open-angle glaucoma: The Barbados eye studies. Ophthalmol. 115(1):85–93.
5. Zhao, D. et al (2015). Diabetes, fasting glucose, and the risk of glaucoma: A meta-analysis. Ophthalmol. 122(1):72-78.
6. The National Eye Institute. (2010). 2010 U.S. age-specific prevalence rates for glaucoma by age and race/ethnicity. National Institutes of Health. Retrieved from: https://nei.nih.gov/eyedata/glaucoma/tables
7. Wiggs, J. L. et al (2012). Common variants at 9p21 and 8q22 are associated with increased susceptibility to optic nerve degeneration in glaucoma. PLoS Genet. 8(4):e1002654.
8. Burdon, K.P. et al (2011). Genome-wide association study identifies susceptibility loci for open-angle glaucoma TMCO1 and CDKN2B-AS1. Nat Genet. 43(6):574-580.

**Sample Results**

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## Clinical Report for Glaucoma (Multi-variant)

| | | | |
|---|---|---|---|
| **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:** | 03-08-2016 |
| **Ordering Physician:** | Dr. Edward Viner | | |

| Gene/Region | Variant Tested | Reference Genotype | Your Result | Interpretation |
|---|---|---|---|---|
| CDKN2B-AS1 | rs7049105 | TT | CC | Without considering other genetic variants, individuals with this result are 80% more likely (1.80 times as likely) to develop glaucoma as someone with no copies of this variant. These risk estimates are based on studies involving individuals with European ancestry.* |
| TMCO1 | rs7518099 | TT | CC | Without considering other genetic variants, individuals with this result are 95% more likely (or 1.95 times as likely) to develop glaucoma as someone with no copies of this variant. These risk estimates are based on studies involving individuals with European ancestry.* |
| **Other Risks** | | Other genetic variants and other risk factors including co-morbidities, lifestyle and family history may contribute to the risk of glaucoma. For additional information on other risk factors please see the accompanying CPMC research report. | | |

*When race/ethnicity specific risk estimates are not available, risk estimates based on European populations are provided.

Risk interpretation based on Coriell's Glaucoma Clinical Risk Algorithm Version 1 (July 12, 2016)

### 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 glaucoma. This test is not diagnostic for glaucoma and cannot rule out the risk of developing glaucoma 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. Wiggs, J. L. et al (2012). Common variants at 9p21 and 8q22 are associated with increased susceptibility to optic nerve degeneration in glaucoma. PLoS Genet. 8(4):e1002654.
2. Burdon, K.P. et al (2011). Genome-wide association study identifies susceptibility loci for open-angle glaucoma TMCO1 and CDKN2B-AS1. Nat Genet. 43(6):574-580.