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- 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:	01-06-2016
Ordering Physician:	Dr. Edward Viner		

Risk of Developing Migraine Based on:

- **CPMC Migraine Variant #1 (rs13208321)**
- **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 developing migraine. 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

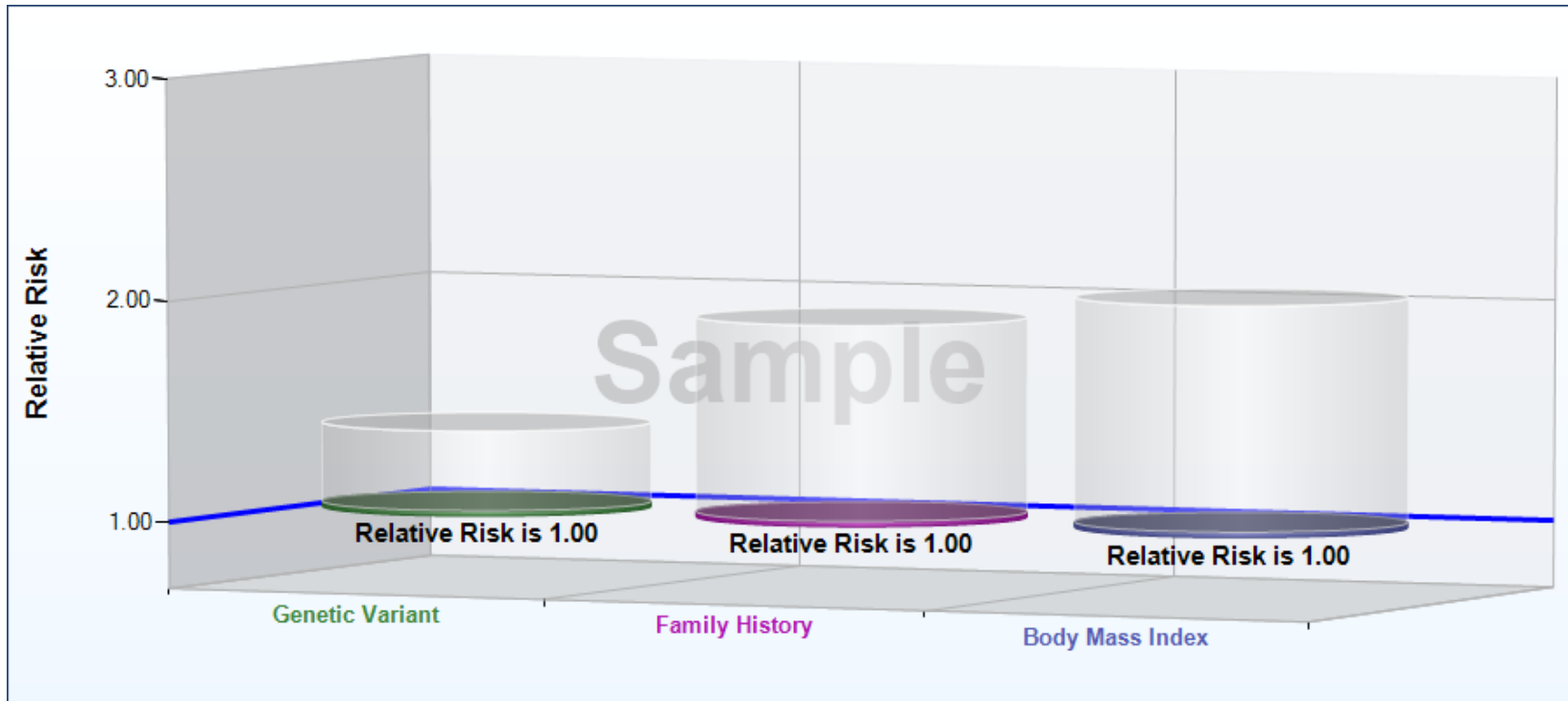
This research report includes all data included in the clinical report as well as supplemental interpretations and educational material. Please see the report that follows for the official clinical report.

Genetic Variant Result, Details and Population Data

Migraine

Risk factors may be related to each other and risk estimates cannot be combined.

This graph provides a summary of the relative risk for family history, body mass index, and one genetic variant.



You reported you are a man, 60 years old or older; 2 in 100 men in your age group have migraine headaches.

Chart Color	Relative Risk Due To:	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	Genetic Variant	1.00	1.00	1.36	You have 2 copies of the non-risk variant. Based on this result, you are at a <i>lower</i> risk to develop migraine headaches compared to someone with one or two copies of this variant.
	Family History	1.00	1.00	1.88	Based on your family history, you are at a lower risk to develop migraine headaches compared to someone with at least one first degree relative (parent, sibling, or child) with migraine headaches.
	Body Mass Index	1.00	1.00	2.01	Based on your BMI you are at a lower risk of developing migraine headaches compared to someone who is underweight (BMI <18.5) or obese (BMI ≥30).

Migraine

Risk Due To Genetic Variant #1 (rs13208321)

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

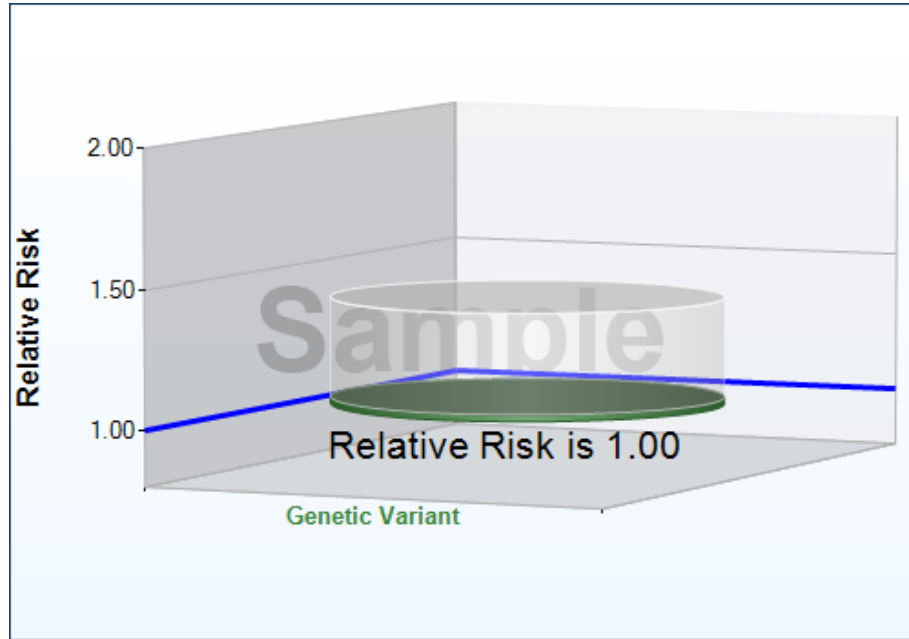
Non-Risk Variant = G Risk Variant = A

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	1.00	1.36	You have 2 copies of the non-risk variant. Based on this result, you are at a <i>lower</i> risk to develop migraine headaches compared to someone with one or two copies of this variant.

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 were 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.

Migraine

Risk Due To Family History

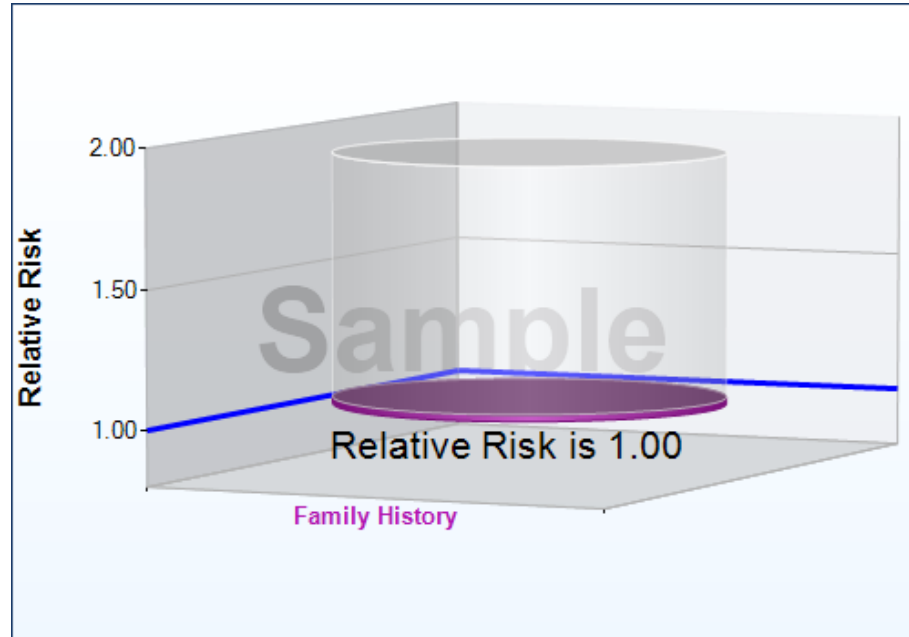
You reported that none of your first degree relatives (parents, siblings or children) have migraine headaches.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	1.00	1.88	Based on your family history, you are at a lower risk to develop migraine headaches compared to someone with at least one first degree relative (parent, sibling, or child) with migraine headaches.

Risk is compared based on family history.

People with at least one first degree relative (parent, sibling or child) with migraine headaches were compared to people with no family history of migraine headaches to determine relative risk of developing migraine headaches.

A relative risk greater than 1.00 indicates an increased risk.



These results are based on a single study.

Migraine

Risk Due To Body Mass Index

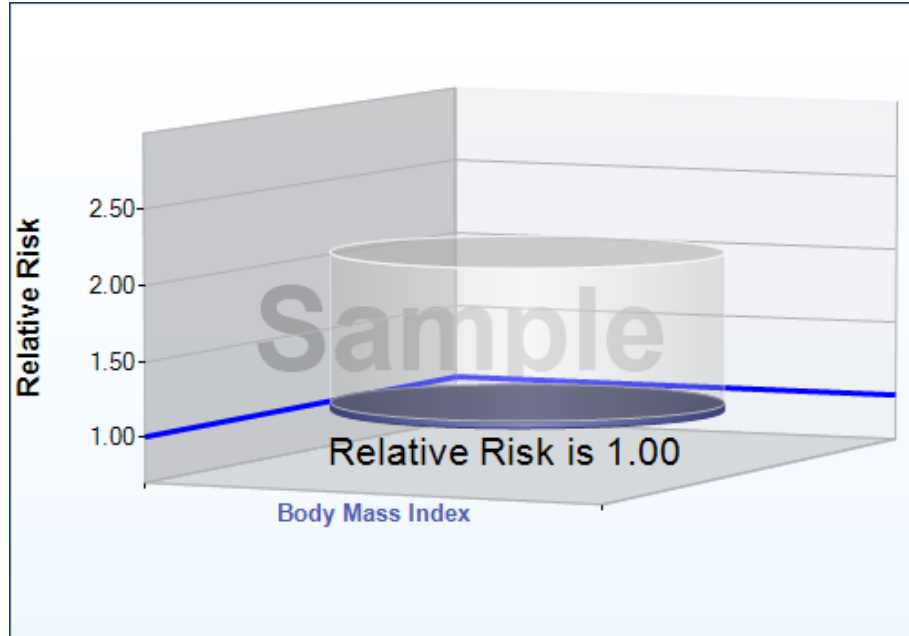
According to the height and weight you reported, you may be overweight (BMI = 25.0 - 29.9).

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	1.00	2.01	Based on your BMI you are at a lower risk of developing migraine headaches compared to someone who is underweight (BMI <18.5) or obese (BMI ≥30).

Risk is compared based on **Body Mass Index (BMI)**. BMI is used to determine if someone is underweight, overweight or obese.

People who are underweight (BMI <18.5) or obese (BMI ≥30) are compared to people who have a healthy weight (BMI >18.5 and <25) to determine relative risk.

A relative risk greater than 1.00 indicates an increased risk.



These results are based on a single study.

Migraine - Variant #1 (rs13208321)

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.

Having one or two copies of this variant **increases** your risk for migraine headaches.

How Common Is This Variant?

Non-Risk Variant = G Risk Variant = A

GG - 54 in 100 people have 2 copies of the non-risk variant

GA - 33 in 100 people have 1 copy of the non-risk variant and 1 copy of the risk variant

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

This data is based on studies in worldwide populations.



Gene: FHL5

Chromosome: 6q16.1

Causes

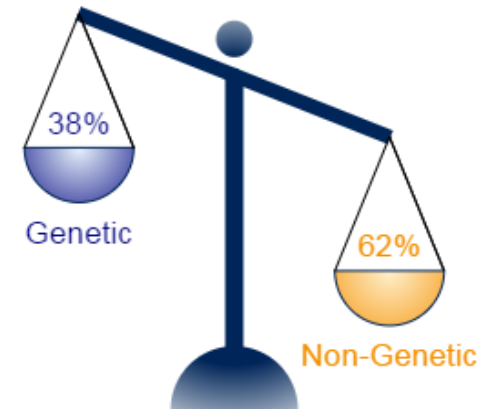
Genetic vs. Non-Genetic Risk Factors

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

It is estimated that **non-genetic** factors (like body mass index) account for about **62%** of the risk for migraine headaches.

It is estimated that **38%** of the risk for migraine headaches is based on **genetic** risk factors. This estimate accounts for both known and unknown gene variants.

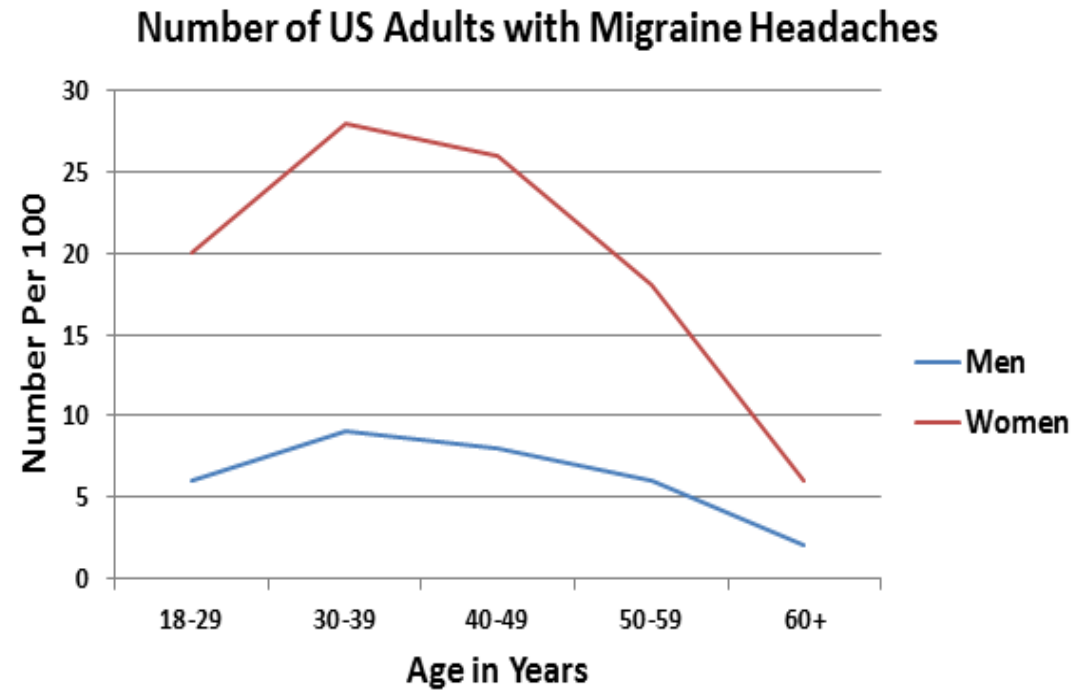
There are many different genetic and non-genetic risk factors that contribute to the risk of migraine headaches. We are only able to tell you about your family history risk, 1 non-genetic risk factor, and 1 genetic risk factor for migraine headaches.



How Common

Age and gender contribute to your risk of having migraine headaches.

You reported you are a man, 60 years old or older; 2 in 100 men in your age group have migraine headaches.



Limitations

Migraine

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

Migraine

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 Migraine Risk Algorithm Version 1 (January 12, 2016)]

1. Stack, C. et al. (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. *Genet Med.* 13(2): 131-139.
2. Ford, E.S. et al. (2008). Body mass index and headaches: Findings from a national sample of US adults. *Cephalalgia.* 28 (12): 1270-1276.
3. Misakian, A.L. et al. (2003). Postmenopausal hormone therapy and migraine headache. *J Wom Health.* 12(10): 1027-1036.
4. Svensson, D.A. et al. (2003). Shared rearing environment in migraine: Results from twins reared apart and twins reared together. *Headache.* 43(3): 235-244.
5. Stewart, W.F. et al. (2006). Familial risk of migraine: Variation by proband age at onset and headache severity. *Neurology.* 66(3): 344-348.
6. Lipton, R.B. et al. (2007). Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology.* 68(5): 343-349.
7. Anttila, V. et al. (2013). Genome-wide meta-analysis identifies new susceptibility loci for migraine. *Nat. Genet.* 45(8): 912-919.

Sample Results



Coriell Institute for Medical Research

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Clinical Report for Migraine Genetic Variant 1 (rs13208321)

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:	01-06-2016
Ordering Physician:	Dr. Edward Viner		

Name of Gene/Region: FHL5		Chromosomal Location: 6q16.1
Variants tested	Result	Reference Genotype
rs13208321	GG	GG
Interpretation	Individuals with this result are at a lower risk to develop migraine as someone with one or two copies of this genetic risk variant. These risk estimates are based on studies in European populations. 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 migraine. For additional information on other risk factors please see the accompanying CPMC research report.	

Risk interpretation based on Coriell's Migraine Clinical Risk Algorithm Version 1 (January 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 migraine. This test is not diagnostic for migraine and cannot rule out the risk of developing migraine 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. Anttila, V. et al. (2013). Genome-wide meta-analysis identifies new susceptibility loci for migraine. Nat. Genet. 45(8): 912-919.