Report Contents

1. Coriell Personalized Medicine Collaborative Research Study Report. This report includes all data included in the clinical report as well as supplemental drug specific interpretations and educational material.
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:	NATALIE DEMO	**Gender:**	Female
Date of Birth:		**Date Collected:**	
Coriell ID:	DEMONAT	**Date Received:**	
Lab Accessioning Number:	DEMONAT	**Date of Report:**	07/05/2013
Ordering Physician:			

CYP2C19 and Proton Pump Inhibitor (PPI) Response

These results were generated in a CLIA-approved laboratory as part of the Coriell Personalized Medicine Collaborative research study. Results take into account 10 genetic variants in the CYP2C19 gene, known to contribute to the metabolism of proton pump inhibitor (PPI) drugs such as omeprazole (Prilosec®, Zegerid®), lansoprazole (Prevacid®), pantoprazole (Protonix®), rabeprazole (Aciphex®), esomeprazole (Nexium®), dexlansoprazole (Kapidex®, renamed Dexilant®). This report reflects this participant's metabolism status predicted based on genetic testing but does not reflect whether they are currently taking a proton pump inhibitor drug.

The CPMC has genetic counselors available to assist with report interpretation at no charge. For questions please contact us at cpmcgc@coriell.org or by phone at 888-580-8028. Participants may schedule an appointment with one of our board certified genetic counselors by logging into their web portal account and clicking on "request an appointment". For general information about the CPMC please visit our website cpmc.coriell.org.

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

Your Genetic Result

CPMC tested multiple sites of genetic variation within the CYP2C19 gene that affect the way the body responds to PPIs.

Your combination of genetic variant results is listed below in yellow.
Your CYP2C19* result is:

CYP2C19*4/*4
(PPI Poor Metabolizer)

VARIANTS TESTED	YOUR RESULT	REFERENCE VALUE
rs4244285 (CYP2C19*2)	GG	G G
rs4986893 (CYP2C19*3)	GG	G G
rs28399504 (CYP2C19*4)	GG	A A
rs56337013 (CYP2C19*5)	CC	C C
rs72558184 (CYP2C19*6)	GG	G G
rs72558186 (CYP2C19*7)	TT	T T
rs41291556 (CYP2C19*8)	TT	T T
rs17884712 (CYP2C19*9)	GG	G G
rs6413438 (CYP2C19*10)	CC	C C
rs12248560 (CYP2C19*17)	CC	C C

[1]When your variant result for all CYP2C19 variants tested are the same as the reference, the combined genetic result is called CYP2C19*1/*1. In some cases your combined genetic result may be uncertain. Other variants, not currently included in this CPMC test may influence this result and interpretation.

Interpretation of Your Results

PPI Poor Metabolizer

CYP2C19 Result: CYP2C19*4/*4

- Your combination of genetic variants indicates you are a PPI poor metabolizer with significantly decreased CYP2C19 activity.
- Poor metabolizers process PPIs at a very slow rate and are expected to respond very well to PPI treatment. Slower processing of a PPI drug allows more time for the drug to work.
- A reduction in PPI dose may be recommended for Asian individuals.
- If you are currently taking a PPI, talk to your doctor about appropriate dosing.
- This result may also affect your response to other medications.

Share this information with your healthcare providers.

Do not make any changes to any medication without talking to your healthcare provider.

How Common

The table and picture below show the different types of PPI metabolizers and how common each is in the African Ancestry population.

Reduced CYP2C19 activity	**Poor Metabolizer** **3 out of 100 people** Expected to respond very well to a standard dose of a PPI.	
	Intermediate Metabolizer **30 out of 100 people** Expected to respond very well to a standard dose of a PPI.	
Typical CYP2C19 activity	**Extensive Metabolizer** **36 out of 100 people** Expected to respond to a standard dose of a PPI.	
Increased CYP2C19 activity	**Ultra-Rapid Metabolizer** **5 out of 100 people** Less likely to respond to a standard dose of a PPI.	
Uncertain CYP2C19 activity	**Metabolizer Status Unknown** **26 out of 100 people** Not enough data to determine expected PPI response.	

What are Proton Pump Inhibitors?

(examples include: omeprazole (Prilosec®, Zegerid®), lansoprazole (Prevacid®), pantoprazole (Protonix®), rabeprazole (Aciphex®), esomeprazole (Nexium®), dexlansoprazole (Kapidex®/Dexilant®).

Proton pump inhibitors (PPIs) are drugs that reduce the amount of acid made by the stomach.

Uses:

- Treatment of acid reflux that can cause heartburn or esophagitis (inflammation of the throat), sometimes called gastroesophageal reflux disease (GERD or GORD).
- Treatment of ulcers in the stomach and duodenum.
- To prevent stomach ulcers caused by non-steroidal anti-inflammatory drugs (NSAIDs).
- Treatment of a bacterial infection in the stomach, called *Helicobacter pylori* which can cause ulcers.

Risk Factors Affecting Response to Proton Pump Inhibitors

Genetic Risk Factors

Genetic variants, or changes, in a gene called CYP2C19 can affect the way your body metabolizes PPIs.

Some people with certain genetic variants may not benefit as much from taking a standard dose of PPIs compared to people without these variants. These people are likely to benefit from a higher than standard dose.

Non-Genetic Risk Factors

Many factors affect how your body responds to medications.

Non-genetic factors include: diet, lifestyle, medical history and interactions between medications.

Genetic Risk Factors

Some medications are metabolized (broken down or activated) by enzymes. Variants in the genes coding for these enzymes may cause your body to metabolize a medication more quickly or more slowly than normal. This change can affect how well the medication works, as well as the risk of side effects.

Genes Affecting PPI Metabolism:

CYP2C19

Types of Variants in CYP2C19

There are many variants in the CYP2C19 gene. A number system has been created to name common combinations of variants. Some variant combinations have not been assigned a number yet. Other combinations of variants cannot be assigned a number with certainty. We all have 2 copies of every gene; when possible, you will have a CYP2C19 result with two numbers.

Example: CYP2C19 *1/*2

Types of PPI Metabolizers

Each result is associated with a metabolizer status which describes how the enzyme is working.

Example: intermediate metabolizer

Drug-Drug Interactions

In addition to your genes, how your body metabolizes PPIs may prevent other medications that you take from working effectively and may increase the risk of side effects associated with these other medications.

The following medications, when taken with a PPI, may reduce the benefit of taking the other medication or may increase the risk for side effects from the other medication:

Medication	Also Known As
topotecan	Hycamtin®
clopidogrel	Plavix®
ketoconazole	Nizoral®
warfarin	Coumadin®, Athrombin®
sucralfate	Carafate®, Sulcrate®
voriconazole	VFEND®
cilostazol	Pletal®
Antiretroviral Agents	Saquinavir (Invirase®), atazanavir (Reyataz®), nelfinavir (Viracept®)

- omeprazole (Prilosec®, Zegerid®)
- lansoprazole (Prevacid®)
- pantoprazole (Protonix®)
- rabeprazole (Aciphex®)
- esomeprazole (Nexium®)
- dexlansoprazole (Kapidex®/Dexilant®)

If you are taking a PPI now, or are prescribed one in the future, talk to your healthcare providers about other medications you are taking that may interact with the PPI you are taking.

Result Limitations

- This result alone does **NOT** predict your total response to PPIs.
- Other factors such as body weight, various health conditions, and other medications may impact an individual's response to PPIs.
- There may be other genetic variants within the CYP2C19 gene which influence response to PPIs but are not included in this test.
- There may be other genetic variants in the CYP2C19 gene for which response to PPIs has not been documented and/or validated in multiple studies.
- There may be genetic variants in other genes that influence response to PPIs.
- This result reflects published data available at the time this gene-drug pair was approved by the CPMC Informed Cohort Oversight Board (November 2011). The information provided may change as new scientific information becomes available.
- Although rare, it is possible that you may receive an incorrect result; 100% accuracy of reported results cannot be guaranteed.
- Occasionally, we will be unable to interpret one or more gene variants. In this case you will not receive a result for those variants and in some cases your drug response cannot be interpreted. It is expected that you will receive results for about 95% of variants approved by the Pharmacogenetics Advisory Group (PAG) and Informed Cohort Oversight Board (ICOB).
- 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. Please see your individual results to determine which race/ethnicity the data is based on.
- In some cases, the CYP2C19 metabolizer status on your Proton Pump Inhibitor report will be different than the CYP2C19 metabolizer status on your Clopidogrel (Plavix®) report.

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. 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.

References

- Baldwin R M, et al. Br J Clin Pharmacol 2008;65(5):767-774.
- Furuta T, et al. Clin Pharmacol Ther 1999;65(5):552-561.
- Furuta T, et al. Clin Pharmacol Ther 2002;72(4):453-460.
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- Take S, et al. Am J Gastroenterol 2003;98(11):2403-2408.
- Wang H, et al. Drug Metab Dispos 2011;39(5):830-837.
- Zendehdel N, et al. Arch Iran Med 2010;13(5):406-412.

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. One microgram of the resulting DNA from each sample was used as template in the Affymetrix DMET Plus GeneChip assay. Data analysis was performed using Affymetrix DMET Console software.

To view your clinical report, click here. The clinical report contains the lab generated testing information and does not include all the content in the research study report.

[Risk interpretation based on Coriell's CYP2C19/PPI Response Genotype Translation Version 1 (June 2013)]

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CYP2C19 GENE TEST FOR PROTON PUMP INHIBITOR RESPONSE

Name:	NATALIE DEMO	**Sample Type:**	Saliva
Date of Birth:		**Gender:**	Female
Coriell ID:	DEMONAT	**Date Collected:**	
Lab Accessioning Number:	DEMONAT	**Date Received:**	
Ordering Physician:		**Date of Report:**	07/05/2013

NAME OF GENE: CYP2C19		**LOCATION OF GENE:** 10q24
Variants tested	**RESULT**	**Reference Genotype**
rs4244285 (CYP2C19*2)	GG	G G
rs4986893 (CYP2C19*3)	GG	G G
rs28399504 (CYP2C19*4)	GG	A A
rs56337013 (CYP2C19*5)	CC	C C
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rs17884712 (CYP2C19*9)	GG	G G
rs6413438 (CYP2C19*10)	CC	C C
rs12248560 (CYP2C19*17)	CC	C C
Combined Result^	**CYP2C19*4/*4**	
^ When the Result for all CYP2C19 variants tested are the same as the reference, the Combined Result is called CYP2C19 *1/*1. In some cases, due to technical limitations, your Combined Result may not be able to be determined. It may still be possible to provide an interpretation for such a result based on possible genetic outcomes (for example in rare combinations of non-reference results at more than one variant, or the presence of a "result not available" at one or more variants).		

Risk interpretation based on Coriell's CYP2C19/PPI Response Genotype Translation Version 1 (June 2013).

Interpretation

This individual is expected to be a **PPI Poor Metabolizer** based on the Combined Genetic Result: **CYP2C19*4/*4**

Individuals who are PPI poor metabolizers eliminate PPIs at a slow rate and are expected to respond very well to PPI treatment. A reduction in PPI dose may be recommended for Asian individuals.

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 in the CYP2C19 gene that are not included in this test, that influence the response to PPIs. 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.

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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 research report.

References

1. Baldwin R M, et al. Br J Clin Pharmacol 2008;65(5):767-774.
2. Furuta T, et al. Clin Pharmacol Ther 1999;65(5):552-561.
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