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.

Coriell Institute for Medical Research
403 Haddon Avenue
Camden, New Jersey 08103 USA
Phone: 888-580-8028
Fax: 856-964-0254
cpmc.coriell.org

CPMC Research Study Report

Name:	STEVE CPMC	**Gender:**	Male
Date of Birth:		**Date Collected:**	
Coriell ID:	DEMOSTEVE	**Date Received:**	
Lab Accessioning Number:	DEMOSTEVE	**Date of Report:**	06/13/2014
Ordering Physician:			

CYP2C9 and Celecoxib Response

These results were generated in a CLIA-approved laboratory as part of the Coriell Personalized Medicine Collaborative research study. Results take into account 6 genetic variants in the CYP2C9 gene, known to contribute to the metabolism of celecoxib. This report reflects this participant's predicted metabolism status based on genetic testing but does not reflect whether they are currently taking celecoxib.

The CPMC has a genetic counselor who is 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 our board certified genetic counselor 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

The CPMC tested multiple sites of genetic variation within the CYP2C9 gene that affect the way the body responds to celecoxib.

Your combination of genetic variant results is listed below in yellow.
Your CYP2C9* result is:

CYP2C9 *3/*3
(Celecoxib Poor Metabolizer)

VARIANTS TESTED	YOUR RESULT[1]	REFERENCE VALUE
rs1799853 (CYP2C9*2)	CC	C C
rs1057910 (CYP2C9*3)	CC	A A
rs28371686 (CYP2C9*5)	CC	C C
rs9332131 (CYP2C9*6)	AA	A A
rs28371685 (CYP2C9*11)	CC	C C
rs72558189 (CYP2C9*14)	GG	G G

[1]When your variant result for all CYP2C9 variants tested are the same as the reference, the combined genetic result is called CYP2C9*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

Celecoxib Poor Metabolizer

CYP2C9 Result: CYP2C9 *3/*3

- Your combination of genetic variants indicates that you have significantly decreased CYP2C9 activity.
- Poor metabolizers process celecoxib at a very slow rate and are at an increased risk for blood clots, heart attack, or stroke when taking a standard dose of celecoxib.
- A reduction in dose or an alternative medication is recommended for poor metabolizers of celecoxib.
- If you are currently taking celecoxib, talk to your doctor about appropriate dosing.
- This result may also affect your response to other medications. For more information on other medications that are affected by variants in the CYP2C9 gene, click here.

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 celecoxib metabolizers and how common each is in the Caucasian population.

Reduced CYP2C9 activity	**Poor Metabolizer** **0 out of 100 people** Increased risk for blood clots, heart attack, or stroke when taking a standard dose of celecoxib.	
	Metabolizer Status Uncertain **33 out of 100 people** Process celecoxib at a slower rate. The impact of this slower metabolism rate on celecoxib response is not known.	
Typical CYP2C9 Activity	**Extensive Metabolizer** **67 out of 100 people** Expected to benefit from a standard dose of celecoxib.	

What is Celecoxib (Celebrex®)?

Celecoxib (Celebrex®) is a non-steroidal anti-inflammatory drug that is primarily used to treat pain.

Uses:

- Treatment of arthritis
- Treatment of pain
- Treatment of menstrual symptoms
- Treatment of colon polyps

Risk Factors Affecting Response to Celecoxib (Celebrex®)

Genetic Risk Factors

Genetic variants, or changes, in a gene called CYP2C9 can affect the way your body metabolizes celecoxib. Some people with certain genetic variants may be at an increased risk for having an adverse reaction like a blood clot, heart attack, or stroke when taking celecoxib compared to people without these variants.

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.

Gene Affecting Celecoxib Metabolism:

CYP2C9

Types of Variants in CYP2C9

There are many variants in the CYP2C9 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 CYP2C9 result with two numbers.

Example: CYP2C9*3/*5

Types of Celecoxib Metabolizers

Each result is associated with a metabolizer status which describes how the enzyme is processing celecoxib. In some cases the exact celecoxib metabolizer type is unknown because of limited published data.

Example: poor metabolizer

Drug-Drug Interactions

In addition to your genes, how your body metabolizes celecoxib 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 may interact with celecoxib:

Medication/Medication Class	Also Known As
warfarin	Coumadin®
lithium	Lithane®, Lithobid®
ACE Inhibitors	Zestril®, Prinivil®, Vasotec®, Altace®, Cozaar®
Angiotensin II Antagonists	Edarbi®, Atacand®,Teveten®, Avapro®, Cozaar®, Benicar®, Micardis®, Diovan®

- celecoxib (Celebrex®)

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

Result Limitations

- This result alone does **NOT** predict your total response to celecoxib.
- Other factors such as body weight, various health conditions, and other medications may impact an individual's response to celecoxib.
- There may be other genetic variants within the CYP2C9 gene which influence response to celecoxib but are not included in this test.
- There may be other genetic variants in the CYP2C9 gene for which response to celecoxib has not been documented and/or validated in multiple studies.
- There may be genetic variants in other genes that influence response to celecoxib.
- This result reflects published data available at the time this gene-drug pair was approved by the CPMC Informed Cohort Oversight Board (March 2012). 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.

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.

Methods

References

- Agúndez JA, et al. Curr Drug Metab. 2009 Nov;10(9):998-1008.
- Allabi AC, et al. Clin Pharmacol Ther. 2004 Aug;76(2):113-8.
- Allabi AC, et al. Pharmacogenet Genomics. 2005 Nov;15(11):779-86.
- Blaisdell J, et al. Pharmacogenetics. 2004 Aug;14(8):527-37.
- Chan AT, et al. Gastroenterology. 2009 Jun;136(7):2127-2136.
- DeLozier TC, et al. J Pharmacol Exp Ther. 2005 Dec;315(3):1085-90.
- Dickmann LJ, et al. Mol Pharmacol. 2001 Aug;60(2):382-7.
- Kidd RS, et al. Pharmacogenetics. 2001 Dec;11(9):803-8.
- Kirchheiner J, et al. Pharmacogenetics. 2003 Aug;13(8):473-80.
- Kusama M, et al. Pharm Res. 2009 Apr;26(4):822-35.
- Lundblad MS, et al. Clin Pharmacol Ther. 2006 Mar;79(3):287-8.
- Sandberg M, et al. Br J Clin Pharmacol. 2002 Oct;54(4):423-9.
- Tang C, et al. Pharmacogenetics. 2001 Apr;11(3):223-35.

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 CYP2C9/Celecoxib Activity Genotype Version 1 (June 2014)]

Coriell Institute for Medical Research
Coriell Genotyping and Microarray Center
403 Haddon Avenue Camden, NJ 08103
Phone: 856-966-7377 Fax: 856-964-0254 www.coriell.org

CYP2C9 GENE TEST FOR CELECOXIB RESPONSE

Name:	STEVE CPMC	**Sample Type:**	Saliva
Date of Birth:		**Gender:**	Male
Coriell ID:	DEMOSTEVE	**Date Collected:**	
Lab Accessioning Number:	DEMOSTEVE	**Date Received:**	
Ordering Physician:		**Date of Report:**	06/13/2014

NAME OF GENE: CYP2C9		**LOCATION OF GENE:** 10q24
Variants tested	**RESULT**	**Reference Genotype**
rs1799853 (CYP2C9*2)	CC	C C
rs1057910 (CYP2C9*3)	CC	A A
rs28371686 (CYP2C9*5)	CC	C C
rs9332131 (CYP2C9*6)	AA	A A
rs28371685 (CYP2C9*11)	CC	C C
rs72558189 (CYP2C9*14)	GG	G G
Combined Result^	**CYP2C9 *3/*3**	

^ When the Result for all tested CYP2C9 variants are the same as the reference, the Combined Result is called CYP2C9 *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 CYP2C9/Celecoxib Activity Genotype Translation Version 1 (June 2014).

Interpretation

This individual is expected to be a **Celecoxib Poor Metabolizer** based on the Combined Genetic Result: **CYP2C9 *3/*3**

Individuals who are poor metabolizers eliminate celecoxib at a very slow rate and are at an increased risk for blood clots, heart attack, or stroke when taking a standard dose. Celecoxib should be administered with caution in CYP2C9 poor metabolizers. A reduction in dose or an alternative medication is recommended for poor metabolizers of celecoxib.

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 CYP2C9 gene that are not included in this test, that influence the response to celecoxib. This test, or one or more of its components, was developed and its performance characteristics were 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. Agúndez JA, et al. Curr Drug Metab. 2009 Nov;10(9):998-1008.
2. Allabi AC, et al. Clin Pharmacol Ther. 2004 Aug;76(2):113-8.
3. Allabi AC, et al. Pharmacogenet Genomics. 2005 Nov;15(11):779-86.
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5. Chan AT, et al. Gastroenterology. 2009 Jun;136(7):2127-2136.
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