**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.
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: 05/13/2014
Ordering Physician:

ATM and Metformin Response

These results were generated in a CLIA-approved laboratory as part of the Coriell Personalized Medicine Collaborative research study. Results take into account 1 genetic variant in the ATM gene, known to influence treatment response to metformin. Metformin is sold under the brand names Fortamet®, Glucophage®, Glucophage XR®, Glumetza®, Riomet®. This report reflects this participant’s predicted treatment response based on genetic testing but does not reflect whether they are currently taking metformin.

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 for a single genetic variant within the ATM gene that can affect the likelihood of treatment success when taking metformin.

Your combination of genetic variant results is listed below in yellow.
Your ATM gene result is:

ATM-CC
(Increased Treatment Response)

<table>
<thead>
<tr>
<th>VARIANTS TESTED</th>
<th>YOUR RESULT</th>
<th>REFERENCE VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs11212617</td>
<td>CC</td>
<td>AA</td>
</tr>
</tbody>
</table>

1Other variants, not currently included in this CPMC test may influence this result and interpretation.
Interpretation of Your Results

Increased Treatment Response

ATM Result: ATM-CC

- Your genetic variant result is associated with an increased likelihood of treatment success when taking metformin.
- Individuals with at least 1 copy of the rs11212617 ‘C’ variant are more likely to reach a target HbA1c level of less than 7% when taking metformin compared to individuals who have no copies of the ‘C’ variant.
- Hemoglobin A1c (HbA1c) is a blood test that measures average level of blood sugar (glucose) over the past 3 months. This test is used to monitor diabetes control.

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 how common the predicted metformin treatment responses are in the African Ancestry population.

<table>
<thead>
<tr>
<th></th>
<th>Increased Treatment Response</th>
<th>Normal Treatment Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC or CC</td>
<td>93 out of 100 people</td>
<td>7 out of 100 people</td>
</tr>
<tr>
<td></td>
<td>Increased likelihood of treatment success when taking metformin.</td>
<td>Typical likelihood of treatment success when taking metformin.</td>
</tr>
</tbody>
</table>
**Genetic Risk Factors**

Genetic variants, or changes, in a gene called ATM can affect the likelihood that treatment with metformin will be successful. Some people with certain genetic variants may have an increased likelihood of treatment success with metformin.

**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.

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**Metformin**

*Metformin is sold under the following brand names: Fortamet®, Glucophage®, Glucophage XR®, Glumetza®, Riomet®*

This medication is used to control the amount of glucose (sugar) in your blood.

**Uses:**

- Treatment of type 2 diabetes
- Treatment of gestational diabetes
- Treatment of polycystic ovarian syndrome (PCOS)
- To prevent progression of pre-diabetes to type 2 diabetes

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**Risk Factors Affecting Response to Metformin**

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Genetic variants, or changes, in a gene called ATM can affect the likelihood that treatment with metformin will be successful. Some people with certain genetic variants may have an increased likelihood of treatment success with metformin.

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**Genetic Risk Factors**

The ATM gene is thought to be involved in insulin signaling and may also influence the function of the pancreatic cells that make insulin (beta cells). Variants in the ATM gene can affect the likelihood of treatment success when taking metformin.

**Gene Affecting Metformin Response:**

**ATM**

<table>
<thead>
<tr>
<th>ATM Gene Variant</th>
<th>Metformin Treatment Response Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>There is one common variant in the ATM gene known to influence the likelihood of treatment success with metformin. We all have 2 copies of every gene; when possible, you will have an ATM gene result with two letters (Variant=C, Reference/Normal=A).</td>
<td>Each result is associated with a predicted likelihood of treatment success.</td>
</tr>
</tbody>
</table>

Example: ATM-AC

Example: increased treatment response
Drug-Drug Interactions

In addition to your genes, other medications may affect how your body responds to metformin and may increase the risk of side effects when taking metformin.

Medication/Medication Type

- Contrast Agents (dyes used for radiologic tests like CT Scans, angiography, etc.)
- Quinolone antibiotics (gatifloxacin, ciprofloxacin, levofloxacin, norfloxacin, ofloxacin)
- Cephalexin (Keflex®)
- Cimetidine (Tagamet®)
- Buproprion (Aplenzin®, Wellbutrin®, Zyban®)

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

In addition to your genes, and other medications, your diet may affect how your body responds to metformin and may increase the risk of side effects when taking metformin.

The following foods, vitamins, and supplements are known to interact with metformin:

Alcohol

- Avoid drinking alcohol while taking metformin.
- Drinking alcohol while taking metformin increases the risk of developing a condition called lactic acidosis.
- Get help immediately if you have any of the following symptoms of lactic acidosis: weakness, increasing sleepiness, slow heart rate, cold feeling, muscle pain, shortness of breath, or stomach pain.

Gymnema sylvestre

- Avoid taking the herb gymnema sylvestre while taking metformin.
- Taking gymnema sylvestre while taking metformin may cause your blood sugar to become too low.
- Tell your doctor if you experience symptoms of low blood sugar, such as: sweating, rapid heartbeat, and dizziness.

For a list of foods, vitamins, and supplements that may interact with metformin, click here.

If you are taking metformin now, or are prescribed it in the future, talk to your healthcare providers about foods, vitamins and supplements that may interact with metformin.
Result Limitations

- This result alone does **NOT** predict your total response to metformin.
- Other factors such as body weight, various health conditions, and other medications may impact an individual’s response to metformin.
- There may be other genetic variants within the ATM gene which influence response to metformin but are not included in this test.
- There may be other genetic variants in the ATM gene for which response to metformin has not been documented and/or validated in multiple studies.
- There may be genetic variants in other genes that influence response to metformin.
- This result reflects published data available at the time this gene-drug pair was approved by the CPMC Pharmacogenetics Advisory Group (September 2013). 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. There may be other variants in the ATM gene that are not included in this test, that influence the response to metformin. 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


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 DNAAdvance 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 ATM/Metformin Activity Genotype Translation Version 1 (April 2014)]
ATM GENE TEST FOR METFORMIN RESPONSE

Name: NATAINE DEMO
Date of Birth: 
Coriell ID: DEMONAT
Lab Accessioning Number: DEMONAT
Ordering Physician: 
Sample Type: Saliva
Gender: Female

<table>
<thead>
<tr>
<th>NAME OF GENE: ATM</th>
<th>LOCATION OF GENE: 11q22.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs11212617</td>
<td>CC</td>
</tr>
<tr>
<td>Reference Genotype</td>
<td>AA</td>
</tr>
</tbody>
</table>

Risk interpretation based on Coriell’s ATM/Metformin Activity Genotype Translation Version 1 (April 2014).

**Interpretation**

Individuals with at least 1 copy of the rs11212617 ‘C’ variant in the ATM gene have an increased likelihood of reaching a target HbA1c level of less than 7% when taking metformin compared to individuals who have no copies of the ‘C’ variant.

**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 ATM gene that are not included in this test, that influence the response to metformin. 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**