Healthy Woman DNA Insight®

PERSONAL GENETIC REPORT

Protected Health Information
Personal Details
Name: SAMPLE PATIENT
DOB: Jan 1, 19XX
Gender: Female
Ethnicity: Caucasian
Report Date: Nov 12, 2015
Received Date: Nov 2, 2015

Test Performed / Method
Genotyping by array-based evaluation of multiple molecular probes

Ordering Healthcare Professional
Nilesh Dharajiya, M.D.
4755 Nexus Center Drive
San Diego, CA 92121 US

Laboratory Info
Accession #: F7715016
Activation Code: ABCDE-BABAB
Specimen Type: Saliva
Collected Date: Oct 29, 2015
Test Results Reviewed & Approved by Laboratory Director:
Nilesh Dharajiya, M.D.

SCIENTIFIC STRENGTH RATING SYSTEM
The genetic markers and studies selected for this report represent the best and most recent genetic research in diet, nutrition, exercise, weight-related health conditions and medication response. Some research can be described as stronger than others based on the size of the population studied and whether the outcome has been replicated. Due to the current state of scientific research on the genetics of diet, exercise and nutrition, most of the studies referenced in your report are based on individuals of Caucasian ethnicity. While we all have the same genes, there are genetic and non-genetic factors in different ethnicities that might yield different outcomes for non-Caucasian populations. Your report includes a star system (in applicable sections), described below, to rate the strength of the research evidence for the genetic marker and the associated result. The star rating is not applicable for your health conditions and drug response sections. However, the genetic markers and studies used to report these conditions are based on the most accepted scientific information in the field.

★★★★ Results derived from a large study of approximately 2,000 or more people, with at least one additional study showing the same results (replication study).

★★★★ Results derived from a moderately-sized study of at least 400 people, with or without a replication study.

★★★★ Small study of less than 400 people in some cases, with other small replicated studies. Results in this category are preliminary, but pass our criteria for statistical significance.

★★★★ Results in this category should be considered extremely preliminary.

Disclaimer
This test was developed and its performance characteristics determined by Pathway Genomics Corporation. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research.

If you have any questions about this report or wish to speak with one of Pathway Genomics’ genetic counselors, please call (877) 505.7374.
YOUR METABOLIC HEALTH CAN BE INFLUENCED BY MANY GENES

Your report includes genetic variants that measure your likelihood for having decreased HDL cholesterol levels, as well as elevated LDL cholesterol, blood sugar and triglyceride levels. All of these are indicators of adverse metabolic health, which are precursors to various health conditions, including coronary artery disease, stroke and type 2 diabetes. Your genetic results for these metabolic health factors are summarized below.

› YOUR PROBABILITIES ›

- **ELEVATED LDL CHOLESTEROL**
  - Page: 31
  - Above Average

- **DECREASED HDL CHOLESTEROL**
  - Page: 32
  - Above Average

- **ELEVATED TRIGLYCERIDES**
  - Page: 33
  - Above Average
YOUR HEALTH RECOMMENDATIONS

✓ You have a higher than average genetic likelihood for elevated LDL cholesterol levels. Regular monitoring of your cholesterol by your physician is recommended.

✓ Your genetic profile shows a higher than average likelihood for decreased HDL (good) cholesterol. HDL levels can sometimes be improved through aerobic exercise and a healthy diet.

✓ You have a higher than average genetic likelihood for elevated triglyceride levels. Therefore, regular monitoring by your physician is recommended. You can help manage triglyceride levels by maintaining a healthy weight, reducing saturated fat and sugar intake, and increasing your consumption of omega-3 fatty acids (fish or seafood).

METABOLIC HEALTH FACTORS

ELEVATED LDL CHOLESTEROL

Low-density lipoprotein (LDL) is the type of cholesterol that can become dangerous if you have too much of it. Like gunk clogging up your kitchen drain, LDL cholesterol can form plaque and build up in the walls of your arteries. This can make your arteries narrower and less flexible, putting you at risk for conditions like a heart attack or stroke. Optimally, LDL levels should be less than 100 mg/dl. Near-optimal levels range from 100 to 129 mg/dl and borderline high from 130 to 159 mg/dl. A score greater than 160 mg/dl is high and greater than 190 mg/dl is very high. Your physician can measure your cholesterol levels.

A genetic result of “High” or “Above Average” does not mean you have elevated LDL cholesterol levels, but tells you that you may have a genetic propensity for elevated LDL cholesterol levels. On the other hand, a result of “Low” or “Below Average,” tells you that you have a lower than average genetic likelihood for elevated LDL cholesterol levels. However, you could still develop problems with your LDL levels as a result of your diet and other factors. This report is based on genetic variants studied in over 19,000 individuals. A genetic result of “High” means that you share a similar genetic profile with individuals from the Framingham Heart Study who had elevated LDL cholesterol levels measuring, on average, above 139 mg/dl with approximately 25% of individuals measuring above 160 mg/dl. A genetic result of “Above Average” means that you share a similar genetic profile with individuals measuring, on average, above 130 mg/dl LDL with approximately 17% of individuals measuring above 160 mg/dl LDL cholesterol. A genetic result of “Average” means that you share a similar genetic profile with individuals measuring, on average, near-optimal LDL cholesterol levels. Diet plays an important part in LDL levels. Processed foods and foods high in trans fat contribute to elevated LDL levels.

YOUR RELATED GENES

<table>
<thead>
<tr>
<th>Gene Tested</th>
<th>Genotype</th>
<th>Scientific Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABCG8-rs6544713</td>
<td>C/T</td>
<td>★★★★★</td>
</tr>
<tr>
<td>APOB-rs515135</td>
<td>G/A</td>
<td>★★★★★</td>
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<tr>
<td>CELSR2-rs12740374</td>
<td>G/G</td>
<td>★★★★★</td>
</tr>
<tr>
<td>HMGCR-rs3846663</td>
<td>C/T</td>
<td>★★★★★</td>
</tr>
<tr>
<td>HNF1A-rs2650000</td>
<td>A/C</td>
<td>★★★★★</td>
</tr>
<tr>
<td>INTERGENIC-rs1501908</td>
<td>G/G</td>
<td>★★★★★</td>
</tr>
<tr>
<td>LDLR-rs6511720</td>
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<td>★★★★★</td>
</tr>
<tr>
<td>MAFB-rs6102059</td>
<td>C/T</td>
<td>★★★★★</td>
</tr>
<tr>
<td>NCAN-rs10401969</td>
<td>T/T</td>
<td>★★★★★</td>
</tr>
<tr>
<td>PCSK9-rs11206510</td>
<td>T/T</td>
<td>★★★★★</td>
</tr>
</tbody>
</table>

ABOVE AVERAGE
You share a similar genetic profile with individuals who exhibit borderline-high LDL cholesterol levels. Therefore, you have a higher than average likelihood for elevated LDL (bad) cholesterol levels.
MEDICATION RESPONSE
SIMVASTATIN-INDUCED MYOPATHY

Simvastatin is a member of the statins, a class of cholesterol-lowering drugs whose major potential adverse effect is skeletal muscle toxicity. Approximately 5% to 10% of patients taking statins experience muscle pain\(^93\). A small portion of patients, (1.5% to 5.0%) may develop more severe symptoms indicating muscle degradation (myopathy)\(^93\). In rare cases (0.1 to 0.2 cases per 1,000 person-years), severe muscle damage leads to acute, potentially lethal kidney failure\(^93,94\). A result of “increased risk” should be discussed with your physician to guide the choice of drug and drug dosing. A result of “typical risk” indicates that the likelihood of adverse effects due to simvastatin is similar to the overall population. Our test uses the genetic variant most commonly associated with statin-caused muscle damage. However, rarer variants may also affect the likelihood of statin-related complications. In addition to genetic effects, your risk of simvastatin-induced myopathy varies with your age, gender, body mass index, ethnicity and other clinical factors\(^95\).

YOUR RESULT
INCREASED RISK
Based on your genetic profile you have an increased likelihood of developing a myopathy in response to simvastatin.

YOUR RELATED GENES

<table>
<thead>
<tr>
<th>Gene Tested</th>
<th>Your Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLCO1B1-rs4149056</td>
<td>T/C</td>
</tr>
</tbody>
</table>

MEDICATION RESPONSE
WARFARIN

Warfarin is the most frequently used oral anticoagulant worldwide, prescribed for indications such as venous thrombosis, pulmonary embolism, atrial fibrillation and cardiac valve replacement. Warfarin is highly efficacious, but its narrow therapeutic window and large interindividual dosing variability lead to a high incidence of adverse events\(^96,97\). Customizing initial warfarin dose based on genetic results may decrease your risk of bleeding complications and may reduce the time required to achieve a stable, therapeutic effect\(^98,99,100\). A result of “Substantially Increased Sensitivity” or “Increased Sensitivity” should be discussed with your physician for decisions around initial drug dosing. A genetic result of “Typical Sensitivity” indicates that probably standard doses of warfarin are appropriate for you. However, consult your physician for appropriate drug dosing and potential drug-drug interactions.

YOUR RESULT
TYPICAL SENSITIVITY
Based on your genetic profile you have an average sensitivity to warfarin.

YOUR RELATED GENES

<table>
<thead>
<tr>
<th>Gene Tested</th>
<th>Your Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP2C9-rs1057910</td>
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</tr>
<tr>
<td>CYP2C9-rs1799653</td>
<td>C/C</td>
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<tr>
<td>CYP2C9-rs9332131</td>
<td>A/A</td>
</tr>
<tr>
<td>VKORC1-rs9923231</td>
<td>G/G</td>
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</tbody>
</table>
The scientific studies referenced in this report are provided below and can be referenced at www.pubmed.gov. All of these papers were published in peer-reviewed journals. PubMed is a service managed by the National Institutes of Health (NIH), a part of the U.S. Department of Health and Human Services, and it tracks more than 19 million citations for biomedical articles and scientific research.


Risks & Limitations

Risks

Risk of Laboratory Error

Pathway is a certified laboratory under the federal Clinical Laboratory Improvement Amendments of 1988 (CLIA) with standard and effective procedures in place for handling samples. However, laboratory error can occur, which might lead to incorrect results. Examples include, but are not limited to, a sample or DNA mislabeling or contamination, failure to obtain an interpretable report, and any other operational laboratory error. I understand that sometimes Pathway’s laboratory may need a second sample to complete my testing.

Risk of laboratory technical problems

Pathway’s CLIA-certified laboratory also has standard and effective procedures in place to protect against technical and operational problems. However, such problems may still occur and examples include, but are not limited to, failure to obtain an interpretable result for a particular SNP. Sometimes it is not possible to obtain a testing result for a particular mutation or marker due to circumstances beyond Pathway’s control, in which case it may not be possible for Pathway to conclusively report on a genetic change that might cause or be predictive of a condition. This may mean that Pathway cannot report my results for a particular health trait or condition, carrier status result, drug response, or other phenotype. Pathway may re-test my sample in order to obtain these results, but upon re-testing the results may still not be obtained. As with all medical laboratory testing, there is a small chance that the laboratory could report false positive or false negative results. A false positive result means that a genotype is reported as being present when it is actually not present. A false negative result means that a genotype is not reported as being present when it actually is present. A tested individual may wish to pursue further testing to verify any results.

Limitations

The purpose of this test is to provide information about how a tested individual’s genes affect their metabolism, weight, exercise, energy use, eating behavior, diet and nutritional choices. Tested individuals should not change their diet, physical activity, or any medical treatments they are currently using based on genetic testing results without consulting their personal health care provider.

Tested individuals may find that their experience is not consistent with Pathway’s selected peer-reviewed scientific research findings of relative improvement for the study group(s). The science in this area is still developing and many personal health factors affect diet and health. Since subjects in the scientific studies referenced in this report may have had personal health and other factors different from those of tested individuals, results from these studies may not be representative of the results experienced by tested individuals. Further, some recommendations may or may not be attainable, depending on the tested individual’s physical ability or other personal health factors. A limitation of this testing is that most scientific studies have been performed in Caucasian populations only. The interpretations and recommendations are done in the context of Caucasian studies, but the results may or may not be relevant to tested individuals of different or mixed ethnicities.

The association between genetic mutations and the information within this report is an active area of scientific research, and future scientific discoveries might alter our understanding of how this information is related to your diet, nutrition, and exercise.

Based on test results and other medical knowledge of the tested individual, health care providers might consider additional independent testing, or consult another health care provider or genetic counselor.
### Result Status Definitions

<table>
<thead>
<tr>
<th>Status</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amended</td>
<td>Test results and/or patient information that have been revised in a way that does not impact the clinical significance of the result(s) and/or patient diagnosis, treatment or management.</td>
</tr>
<tr>
<td>Corrected</td>
<td>Test results and/or patient information that have been revised in a way that may impact the clinical significance of the result(s) and/or patient diagnosis, treatment or management.</td>
</tr>
<tr>
<td>Final</td>
<td>Test results that are available at the time of report issue or have been revised from pending status to final status.</td>
</tr>
<tr>
<td>Pending</td>
<td>Test results that are not available at the time of report issue. All pending results will be specified in the report.</td>
</tr>
</tbody>
</table>
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