Report Contents

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:	NATALIE DEMO	**Gender:**	Female
Date of Birth:		**Date Collected:**	11-30-2016
Coriell ID:	DEMONAT	**Date Received:**	11-30-2016
Lab Accessioning Number:	DEMONAT	**Date of Report:**	02-08-2010
Ordering Physician:	Dr. Edward Viner		

Risk of Developing Lupus Based on:

- **CPMC Lupus Variant 1 (rs3821236)**
- **Family History**
- **Smoking**

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 lupus. 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

Lupus

Risk factors may be related to each other and risk estimates cannot be combined.
This graph provides a summary of the relative risks for genetic variant, family history, and smoking.

You reported you are an African American woman, an estimated 4 in 1,000 African American women have lupus.

Chart Color	Relative Risk Due To:	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	Genetic Variant	**2.00**	1.00	2.00	**You have 2 copies of the risk variant. Based on this result, you are 2.00 times as likely to develop lupus as someone with no copies of this variant.** *Having this risk variant contributes to your risk of lupus.*
	Smoking Status	**1.00**	1.00	1.50	**Because you are not a smoker, you are at a lower risk to develop lupus compared to current and former smokers.**
	Family History		1.00	11.30	**Risk estimates are not available. Necessary information for this risk factor was marked as “unknown” or not provided on the Family History questionnaire.**

Lupus

Risk Due To Genetic Variant #1 (rs3821236)

Your Result: 2 copies of the risk variant were detected (AA)

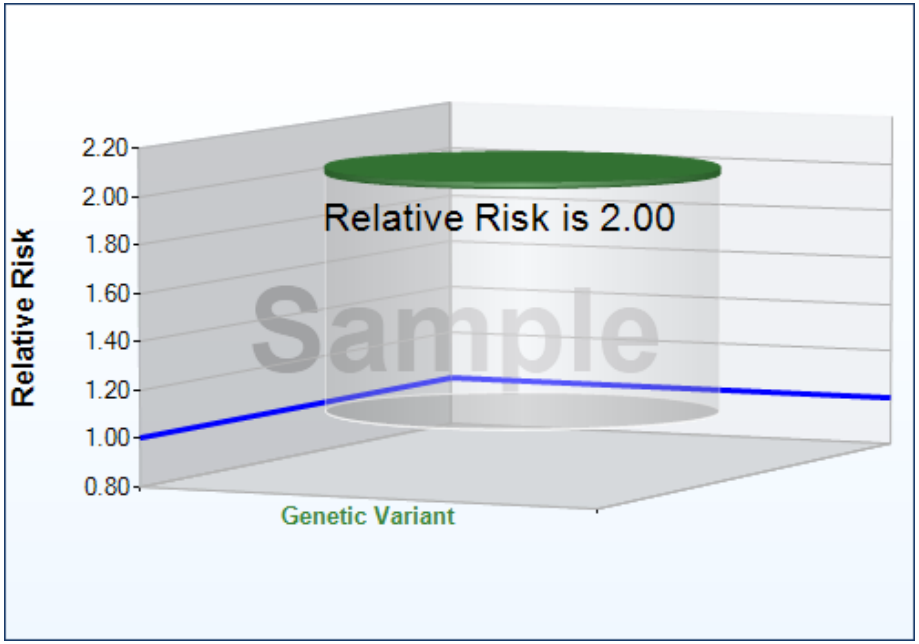
Non-Risk Variant = G Risk Variant = A

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	2.00	1.00	2.00	**You have 2 copies of the risk variant. Based on this result, you are 2.00 times as likely to develop lupus as someone with no copies of this variant.** *Having this risk variant contributes to your risk of lupus.*

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 are 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.

Lupus

Risk Due To Smoking Status

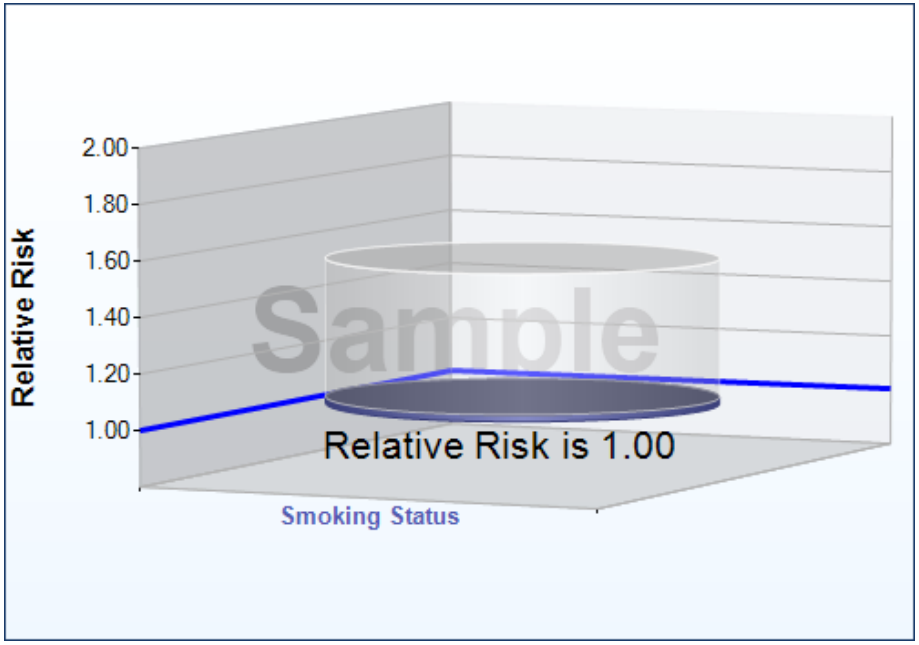
You reported that you do not smoke.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	1.00	1.50	**Because you are not a smoker, you are at a lower risk to develop lupus compared to current and former smokers.**

Risk is compared based on smoking habits.

People who are current smokers or former smokers are compared to people who have never smoked to determine relative risk.

A relative risk of greater than 1.00 indicates an increased risk.



These results are based on a single study.

Lupus

Risk Due To Family History

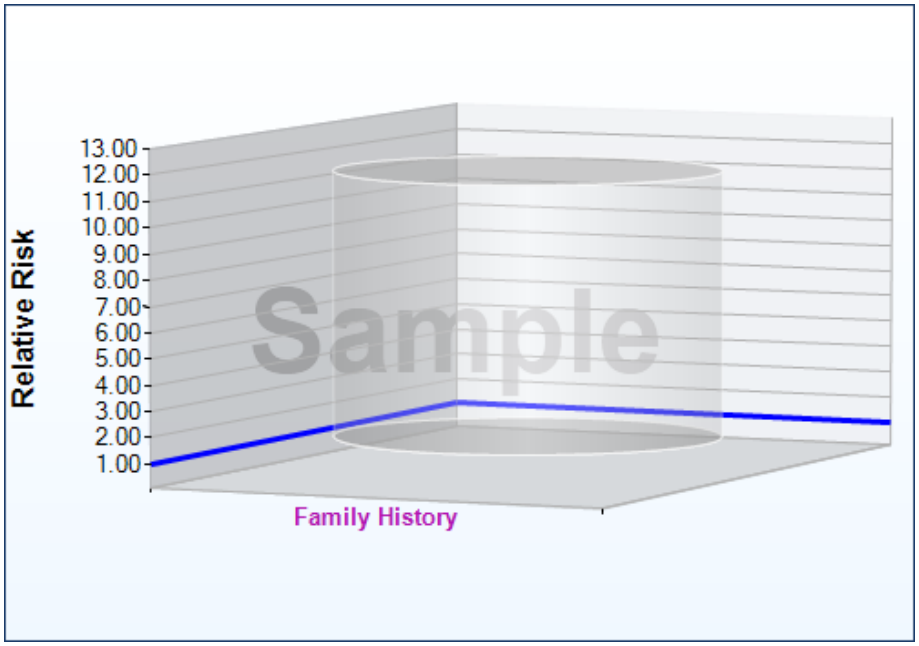
You reported that you don't know if one or more of your first degree relatives (parents, siblings, and/or children) have an autoimmune disease. Autoimmune diseases not currently included in the CPMC family history questionnaire will also impact your risk of lupus. (See Limitations for autoimmune diseases included in family history risk assessment).

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
		1.00	11.30	Risk estimates are not available. Necessary information for this risk factor was marked as "unknown" or not provided on the Family History questionnaire.

Risk is compared based on family history.

People with one or more first degree relatives (parent, sibling, or child) with an autoimmune disorder were compared to people with no first degree relatives with autoimmune disorders to determine relative risk of developing lupus.

A relative risk greater than 1.00 indicates an increased risk.



These results are based on a single study.

Lupus - Variant #1 (rs3821236)

We all have 2 copies of every gene, one from each of our parents.
Each copy may have small changes called genetic variants.
Some genetic variants are associated with an increased risk of disease.
Some genetic variants are associated with a decreased risk of disease.

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

How Common Is This Variant?

Non-Risk Variant = G **Risk Variant = A**

GG - 51 in 100 people have 2 copies of the non-risk variant

GA - 38 in 100 people have 1 copy of the non-risk variant and 1 copy of the risk variant

AA - 11 in 100 people have 2 copies of the risk variant

This frequency is based on data from African American populations.

Gene: STAT4 **Chromosome: 2q32.3**

Causes

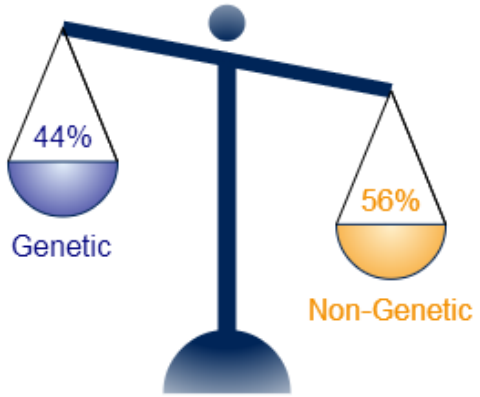
Genetic vs. Non-Genetic Risk Factors

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

It is estimated that **non-genetic** factors (like smoking) account for about **56%** of the risk of lupus.

It is estimated that **44%** of the risk for lupus is based on **genetic** risk factors. This estimate accounts for both known and unknown gene variants.

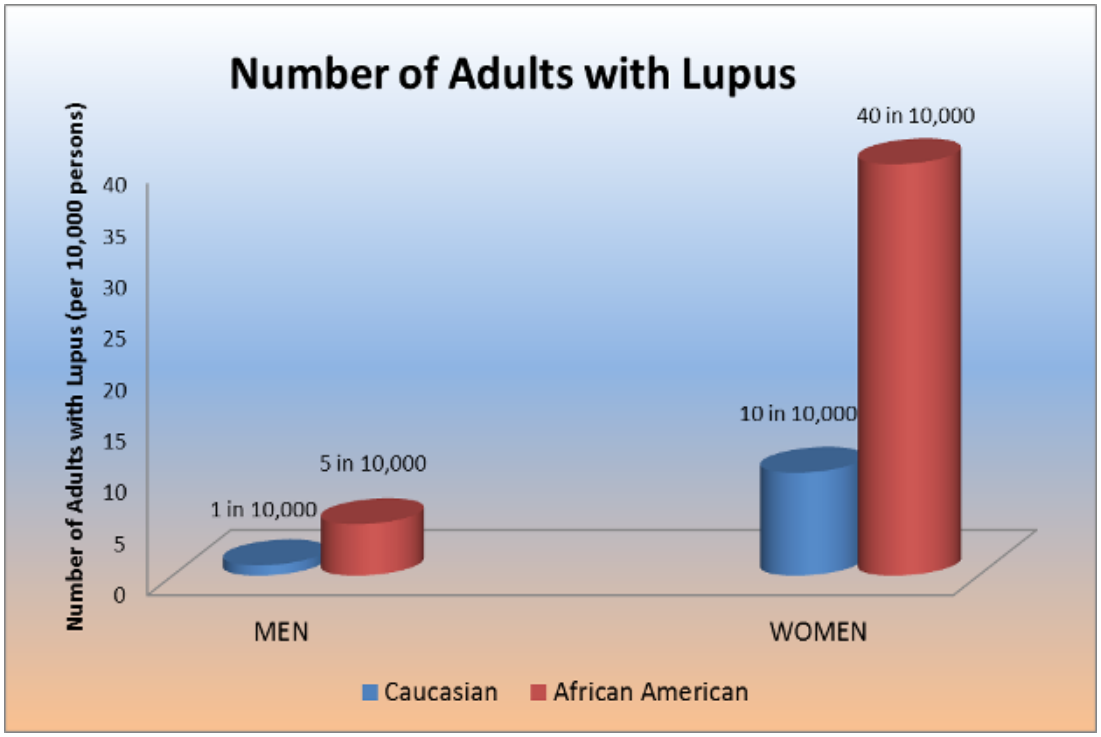
There are many different genetic and non-genetic risk factors that contribute to the risk of lupus. We are only able to tell you about your family history risk, 1 genetic and 1 non-genetic risk factors at this time.



How Common

Ancestry and gender contribute to your risk of lupus.

You reported you are an African American woman, an estimated 4 in 1,000 African American women have lupus.



Limitations

Lupus

- This result alone does NOT diagnose lupus. Lupus must be diagnosed by your health care provider.
- This result does NOT mean that you have or will absolutely develop lupus.
- This result does NOT mean that you will not develop lupus in the future.
- This result ONLY assesses your risk for developing lupus due to the factors presented in this report and does not mean that other genetic variants or risk factors for lupus are present or absent.
- Personal risk factors, such as age, family history or lifestyle, may have a greater impact on your risk to develop lupus than any individual genetic variant.
- Risk estimates are based on current available literature.
- Risk estimates for family history were based on the following autoimmune diseases captured by the CPMC family history questionnaire: lupus, rheumatoid arthritis, sjogren's, vitiligo, multiple sclerosis, celiac disease, type 1 diabetes, Grave's disease (autoimmune hyperthyroidism), Crohn's disease, ulcerative colitis and psoriasis.
- For the purposes of this report, hypothyroidism indicated in the CPMC medical and family history questionnaire is assumed to be autoimmune hypothyroidism.
- Family history of other autoimmune diseases not currently included in the CPMC family history questionnaire will also impact your risk of lupus.
- 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.
- For some risk factors data may be provided by gender. Every effort will be made to provide you with risk information based on your reported gender. However, when risk data is not available for both genders, risk results for the available gender will be provided.

Methods

Lupus

This condition and genetic variant(s) 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 Lupus Risk Algorithm Version 2 (June 1, 2014)]

1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. Genet Med. 13(2):131-139.
2. Wang, et al. (2007). Lupus: a genetic epidemiology study of 695 patients from China. Archives of Dermatology Research. 298:485-491.
3. Helmick, et al. (2008). Estimates of the Prevalence of Arthritis and Other Rheumatic Conditions in the United States. Arthritis & Rheumatism. 58:15-25.
4. Abelson, et al. (2008). STAT4 associates with SLE through two independent effects that correlate with gene expression and act additively with IRF5 to increase risk. Annals of the Rheumatic Diseases. Published online: 9 Dec 2008; doi:10.1136/ard.2008.097642.
5. Taylor, et al. (2008). Specificity of the STAT4 Genetic Association for Severe Disease Manifestations of Lupus. PLoS Genetics. 4 (5):e100084.
6. Priori, et al. (2003). Familial autoimmunity as a risk factor for Lupus and vice versa: a case-control study. Lupus. 12:735-740.
7. Costenbader, et al. (2004). Cigarette smoking and the Risk of Lupus. Arthritis & Rheumatism. 50:849-857.
8. McVean G.A. et al (2012). An integrated map of genetic variation from 1,092 human genomes. Nature. 491; 56-65.

Sample Results

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Clinical Report for Lupus Genetic Variant 1 (rs3821236)

Name:	NATALIE DEMO	**Sample Type:**	Saliva
Race/Ethnicity:	Black or African-American	**Gender:**	Female
Date of Birth:		**Date Collected:**	11-30-2016
Coriell ID:	DEMONAT	**Date Received:**	11-30-2016
Lab Accessioning Number:	DEMONAT	**Date of Report:**	02-08-2010
Ordering Physician:	Dr. Edward Viner		

Name of Gene/Region: STAT4		**Chromosomal Location:** 2q32.3
Variants tested	**Result**	**Reference Genotype**
rs3821236	AA	GG
Interpretation	**Individuals with this result are 2.00 times more likely to develop lupus as someone with no copies of this variant.** These risk estimates are based on studies in a European population. 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 lupus. For additional information on other risk factors please see the accompanying CPMC research report.	

Risk interpretation based on Coriell's Lupus Risk Algorithm Version 2 (June 1, 2014)

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 lupus. This test is not diagnostic for lupus and cannot rule out the risk of developing lupus in the future. Risk estimates are based on current available literature (see reference). 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. Taylor et al. (2008). Specificity of the STAT4 Genetic Association for Severe Disease Manifestations of Lupus. PLoS Genetics. 4 (5):e100084.