BCM-MEDICAL GENETICS LABORATORIES

PHONE: 800-411-GENE | FAX: 713-798-6584 | www.bcmgeneticlabs.org

SHIP TO: Medical Genetics Laboratories
Baylor College of Medicine
2450 Holcombe, Grand Blvd. -Receiving Dock
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Phone: 713-798-6555

CYTOCHROME P450 2C19 (CYP2C19) GENOTYPING

INFORMED CONSENT FOR GENETIC TESTING

I, _____, understand that my physician has recommended genetic testing for myself and/or my child or children for (insert name of test) _____. I hereby voluntarily agree to submit my and/or my child's or children's sample(s) for testing as recommended by my physician. I understand that biological samples will be collected using generally accepted techniques, the risk(s) of which I have been separately informed. I understand that testing of my and/or my child's or my children's sample(s) will be limited to the test ordered by my physician. I understand that the sample(s) will be used for the purpose of attempting to determine if I and/or my family members have a mutation(s) in this disease gene(s). Results may indicate affected status, increased risk to someday be affected with and/or reproductive risk for this disease. The minor child or children for which I hereby give permission to collect biological sample(s) for this test is/are named below*:

_____ _____ Child's Gender: ☐ FEMALE ☐ MALE

Child's Name (Last, First, MI) Child's Date of Birth (MM/DD/YY)

☐ *If additional children are being tested please check this box AND list their name, date of birth, and gender on the back of this consent

I understand that:

1. There are several categories of test results that may be reported including:
   a. A clinically significant abnormality IS detected, known to be associated with a genetic disease.
   b. A clinically significant abnormality IS NOT detected, however my clinical diagnosis may still be correct. This event may be due to medical science's current lack of knowledge of all the gene(s) involved with the disease or the inability of the current technology to identify certain types of mutations in the gene(s) which cause the disease.
   c. A result of uncertain clinical significance is detected. Additional testing of the patient and/or other family members may be recommended to help determine the significance of the result.
   d. Unexpected test results may be detected. These results may occur with screening tests that evaluate many different genetic regions. From these tests, information may be learned about you, your child/children or your family that is not directly related to the clinical reason for ordering the test. This information may provide data about the risk for a different genetic disease with symptoms that may or may not be currently evident.
2. An error in the test interpretation may occur if the true biological relationships of the family members being tested are not as I have stated. For example, a sequence change or deletion or duplication detected in an affected individual but not detected in the parents may be interpreted as a clinically significant change, but this interpretation is wholly dependent on testing of the biological parents. If the stated father of an individual is not the true biological father, this interpretation may be incorrect. On rare occasions, the laboratory may obtain results that suggest non-paternity and it may be necessary to report this to the physician who ordered the testing.
3. This consent form should not be used for prenatal diagnosis. For these cases, we require that the referring professional consult directly with our laboratory regarding all the sample and paperwork requirements. Specific consent forms may also be required.
4. Genetic tests are relatively new and are being improved and expanded continuously. The tests are not considered research, but are considered to be an appropriate means of evaluation at the time of testing. This testing is complex and utilizes specialized materials so that there is always a very small possibility that the test will not work properly or that an error will occur.
5. The laboratory does not return the remaining sample to individuals or physicians; however, in some cases, it may be possible to perform additional studies on the remaining sample. The request for additional studies must be made by my referring physician or other authorized healthcare professional and there will be an additional charge. Samples will be retained in the laboratory in accordance with the laboratory retention policy. I do understand that I have the right to withdraw this consent at any time, and the entity storing the sample shall promptly destroy the sample or portions thereof that have not already been used. **PLEASE INITIAL:** _____
6. Because of the complexity of genetic testing and the implications of the test results, results will only be reported to me through the ordering healthcare professional. The results are confidential and will only be released to other medical professionals or other parties with my written consent. All laboratory raw data are confidential and will not be released unless a valid court order is received.
7. Results may have clinical or reproductive implications for my family members. In rare cases, persons with genetic diagnoses have experienced problems with insurance coverage, employment and other entities. Participation in genetic testing is completely voluntary. I understand that I may wish to obtain professional genetic counseling prior to signing this consent form.
8. I understand that a positive test result is an indication that I or the individual(s) being tested may be predisposed to or have the specific disease or condition tested for and may wish to consider further independent testing, consult my or his/her/their physician or pursue genetic counseling.
9. My signature below acknowledges my voluntary participation in this test, but in no way releases the laboratory and staff from their professional and ethical responsibility to me.
10. I have received a copy of this consent form and test information sheet. PLEASE INITIAL ON PAGE 2.

Signature: _____ Printed Name: _____

Date: _____ Relationship to Patient: _____ Witnessed by: _____

PHYSICIAN'S STATEMENT: I have explained the genetic testing specified to this individual. I have addressed the limitations outlined above, and I have answered this person's questions. I have obtained consent from the patient or the legal guardian for this testing.

Physician's Signature: _____ Date: _____

Printed Name: _____ Phone#: _____

LAST UPDATED: 10/12/2011

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DNA ANALYSIS

CYP2C19 is one of the cytochrome P450 enzymes that are responsible for much of Phase I drug metabolism. CYP2C19 metabolizes approximately 15% all prescribed drugs including clopidogrel (Plavix), mephenytoin, diazepam, propranolol, and omeprazole. Genetic variants associated with altered CYP2C19 activities have been identified and are relatively common in most populations. Individuals with nonfunctional/reduced function alleles in their CYP2C19 gene have much decreased CYP2C19 enzyme activity, which may result in adverse drug reactions or decreased drug efficacy.

The anti-platelet drug clopidogrel (Plavix) is metabolized by CYP2C19 and other enzymes in the liver to an active form. Patients with non-functional/ reduced functional alleles who were treated with clopidogrel had a higher rate of residual platelet aggregation and cardiovascular adverse events. In addition, recent studies indicate that the *17 allele is associated with increased CYP2C19 activity and increased risk for bleeding.

This analysis tests 9 different variants associated with altered CYP2C19 activity.

REASONS FOR REFERRAL

Evaluating genetic factors affecting drug metabolism for patients taking drugs metabolized by cytochrome P450 2C19, such as clopidogrel.

Limitations:

- Not all variants with known impact on enzyme expression and activity are tested in this assay.
- Non-genetic factors, variations in the other genes involving the drug metabolism are not measured by this assay.
- Rare genetic alterations at primer binding sites may result diagnostic errors.

TESTING METHODOLOGY

This analysis incorporates DNA amplification by multiplex PCR, allele specific primer extension, microarray hybridization and Fluorescence signal detection.

Variant alleles tested:

Non-functional alleles:
*2 (c.681G>A)- No activity
*3 (c.636G>A)- No activity
*4 (c.1A>G)- No activity
*6 (c.395G>A)- No activity
*7 (IVS5+2T>A)- No activity
*8 (c.358T>C)-No activity

Reduced function alleles:
*9 (c.431G>A)-Decreased activity
*10 (c.680C>T)-Decreased activity

Increased function allele:
*17 (c.-806C>T)-Increased activity

REFERENCES:

Zanger et al., Functional pharmacogenetics/genomics of human cytochromes P450 involved in drug biotransformation. Anal Bioanal Chem. (2008) 392:1093-108.

Mega J et al., Cytochrome P-450 Polymorphisms and Response to Clopidogrel. N Engl J Med. (2009) 360:354-362

Simon T et al., Genetic determinants of response to clopidogrel and cardiovascular events. N Engl J Med. (2009) 360:363-375

Sibbing D, Koch W, Gebhard D, et al: Cytochrome 2C19*17 allelic variant, platelet aggregation, bleeding events, and stent thrombosis in clopidogrel-treated patients with coronary stent placement. Circulation (2010) 121:481-483

ANALYTICAL SENSITIVITY AND SPECIFICITY: Greater than 99%

_____ (PLEASE INITIAL) I have received a copy of test information sheet. I have read these test specific information.

LAST UPDATED: 10/12/2011