Informed Consent for Molecular Pathology Testing

Medical condition being evaluated: _____

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MOLECULAR TEST REQUEST (Check off **EACH** test to be ordered)**:**

- ☐ **Factor V Leiden (Venous Thrombosis/Coagulopathy)**
- ☐ **Factor II (Prothrombin) Mutation (Venous Thrombosis/Coagulopathy)**
- ☐ **MTHFR (c.677C>T & c.1298A>C) Mutation (Venous Thrombosis/Coagulopathy)**
- ☐ **HEMOCHROMATOSIS Gene (C282Y and H63D) Mutation**
- ☐ **IL28B GENOTYPING (rs12979860 and rs8099917) (HCV infection treatment)**
- ☐ **HLA-DQ2/DQ8 GENOTYPING (Celiac Disease Genotyping)**
- ☐ **OTHER**_____

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Informed Consent for Molecular Pathology Testing

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This form must be completely filled out and signed by the patient, parent/legal guardian or legal next of kin.

Please read carefully and discuss with your doctor and/or the person obtaining the consent before signing.

1. The condition stated above has been described to you/your legal guardian in detail and all questions related to testing have been answered.
2. When testing shows a mutation or change in a gene, then the result may indicate 1) you are affected with the condition, predisposition or disease above, 2) confirm a clinical diagnosis of the condition or disease above, 3) you are a carrier of the condition or disease above or 4) may have uncertain significance. A positive test result will help determine if you have the specified condition or if you may develop the condition with a level of certainty, which has been discussed with you/your legal guardian. Consulting a doctor or counselor is recommended to learn the full meaning of the results. Counseling is available prior to your consent for testing and signature of this form as well as after the test result(s) is/are available. Testing and counseling of family members is available and may also be requested.
3. When the testing does not show a known mutation, the chance that you are a carrier or are affected is reduced. However, there is still a chance that you may be a carrier or be affected because the current testing may not be able to find all the possible mutations and changes within a gene.
4. The decision to consent or to refuse the above testing is entirely your or your legal guardian's choice.
5. The results of this test will be reported to your physician and will become part of your medical record. Under New York State Public Health Law this information is confidential. The results may be made available to a health care facility (hospital or clinical laboratory) or a health care provider who may need the information to provide health care for you or a person whom you have specifically authorized by signing a written release.
6. No other tests than the tests specifically authorized above will be performed on your sample. The sample will not be used in any identifiable manner for research purposes. Your sample (tissue, blood, fluid and/or DNA) shall be discarded 60 days after testing.
7. The patient/legal guardian has read or has been read the above and fully understands the significance, risk and benefits of having the test completed.

MOLECULAR PATHOLOGY TESTING QUICK FACTS

FACTOR V LEIDEN MUTATION

- Clinical indications for test include: family history of venous thromboembolism (deep vein thrombosis and pulmonary embolism), unprovoked thrombotic event at < 45 years of age, women with multiple stillbirths or spontaneous abortions
- Women who are placed on oral contraceptives or estrogen replacement at the time of menopause and have had venous thrombotic events have an increased risk of having the Factor V Leiden mutation
- Presence of the Factor V Leiden mutation increases the risk of venous thrombosis seven-fold in heterozygotes and 80-fold in homozygotes
- 3%-7% of the general Caucasian population and 1.2% of the African-American population have the Factor V Leiden mutation
- This test is performed on DNA extracted from patient blood using a real-time PCR method (Roche's FDA-approved LightCycler assay).

FACTOR II (PROTHROMBIN) MUTATION

- Clinical indications for test include: family history of venous thromboembolism (deep vein thrombosis and pulmonary embolism), unprovoked thrombotic event at < 45 years of age, women with multiple stillbirths or spontaneous abortions
- Individuals with one or more episodes of venous thrombosis at a young age, family history of early thrombotic episodes or diagnosis of arterial thrombosis, including myocardial infarction and stroke have an increased risk of having the Prothrombin mutation .
- Presence of the Factor II mutation increases the risk of venous thrombosis three-fold in heterozygotes. Patients with both the Factor II and Factor V Leiden mutations have a 20-foldincreased risk for recurrent VTE.
- The Factor II mutation has an allele frequency of 1.2% in the general US population, 3.0% in southern European populations, and 1.7% in northern European populations. The mutation is rare in individuals of Asian and African descent
- This test is performed on DNA extracted from patient blood using a real-time PCR method (Roche's FDA-approved LightCycler assay).

5,10-METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR, C677T & A1298C)

- Clinical indications for test include: asses thrombotic risk, increased risk factors for cerebrovascular, peripheral vascular and coronary heart disease as well as hyperhomocysteinemia, a condition which may cause up to a 10-fold rick for venous thrombosis.
- Individuals who are compound heterozygous for MTHFR C677T/A1298C have an associated increase homocysteine levels in blood and an increased risk for coronary artery disease and venous thrombosis.
- Individuals who are homozygous for C677T or compound heterozygous for C677T/A1298C (*in trans)* is associated with an increased risk of venous thromboembolism and premature atherosclerotic disease. Heterozygous C677T is not associated with an increase of homocysteine levels in blood and venous thrombosis.
- The MTHFR C677T mutation varies widely with ethnicity, ranging from 1% in Afro-Americans to 30% or more in Caucasians and Asians. The allelic frequency of the MTHFR A1298C mutation is about 27% in Ashkenazi Jews.
- This test is performed on DNA extracted from patient blood using the Invader assay (Hologic).

HEMOCHROMATOSIS GENE (C282Y AND H63D) MUTATION

- Clinical indications for the test include: histologic and/or biochemical evidence of iron overload, clinically suspected hereditary hemochromatosis and family history of hereditary hemochromatosis.
- The C282Y and H63D hemochromatosis gene (HFE) mutations are the major cause of hereditary hemochromatosis (HH). The homozygous C282Y mutation is the most prevalent mutation and occurs in 60-90% of individuals affected by HH. Individuals with HH may also be H63D homozygous (4%), C282Y/H63D compound heterozygous (6.7%), C282Y heterozygous (4.3%), or H63D heterozygous (8.5%).
- Individuals homozygous for C282Y exhibit a more severe clinical presentation of HH and greater iron overload than C282Y/H63D compound heterozygotes, who exhibit a milder clinical presentation of the disease.
- This test is performed on DNA extracted from patient blood using PCR followed by digestion of PCR products with restriction endonucleases and agarose gel electrophoresis.

IL28B GENOTYPING (rs12979860 and rs8099917)

- Clinical indications for the test include: to identify the determinants of therapeutic response (such as, sustained virological response (SVR)) to peg-interferon alfa and ribavirin as well as to protease inhibitor triple therapy in individuals with chronic hepatitis C virus (HCV) infection).
- Approximately 70% of Caucasians, 40% of African-Americans and 95% of Asians carry at least one copy of the rs12979860C polymorphism near the IL28B gene.
- IL28B rs12979860 is the most useful SNP predictor for SVR in individuals chronically infected with HCV genotype 1. SVR rates are more than twofold higher in IL28B rs12979860 C/C patients as compared with patients with the unfavorable non-C/C genotype. IL28B rs8099917 T/G also correlates with SVR and TT genotype responds favorably to the treatment as compared to GG or TG genotypes.
- This test is performed on DNA extracted from blood using PCR followed by an allele specific primer extension assay analyzed on the Luminex LX 200 instrument.

HLA-DQ2/DQ8 GENOTYPING

- Clinical indications for the test include: to predict the genetic risk for celiac disease. Although 20-30% of the general population shows the HLA-DQ2 and/or DQ8 haplotype, their absence essentially excludes a diagnosis of celiac disease.
- 90-95% celiac disease patients carry a variant of human leukocyte antigen (HLA)-DQ2 haplotype (DQ2.2/DQ2.5), encoded by DQA1*0501/DQB1*0201 and DQA1*0201/DQB1*0202. Other 5-10% patients carry HLA-DQ8 haplotype, encoded by DQA1*03/DQB1*0302.
- The genetic risk is different among different genotypes with DQ2 Homozygous being highest and DQ2/other low risk alleles being lowest.
- This test is performed on DNA extracted from blood using PCR followed by an allele specific primer extension assay analyzed on the Luminex LX 200 instrument. The assay only detects HLA-DQ2 (HLA-DQA1*0501, DQA1*0201, DQB1*0201, DQB1*0202) and HLA-DQ8 (HLA-DQA1*03 and DQB1*0302). Alleles other than these genetic variants will not be identified. Other genetic and non genetic factors that influence celiac disease are not evaluated.

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YES: I REQUEST and CONSENT to have my DNA tested for genetic test listed above. I fully understand and accept the consequences of this decision.

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Patient/Legal Guardian Signature Date Printed Name

NO: I DECLINE and DO NOT CONSENT to have my DNA tested for the genetic test listed above. I fully understand and accept the consequences of this decision.

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Patient/Legal Guardian Signature Date Printed Name