



Informed Consent for Genetic Testing for Bipolar Disorder and Depression

Introduction: This form describes the benefits, risk, and limitations of two genetic tests for mood disorder (Bipolar Disorder and major depression) and therapeutic response. Read this form carefully and talk with your doctor or psychiatrist before making your decision about testing.

Psynomics offers two tests of your DNA taken from sputum or “spit” samples. These two tests are for:

- Risk of having Bipolar Disorder
- The probability that you will have a therapeutic response to the selective serotonin reuptake inhibitor (SSRI) type of antidepressant.

Purpose: For many patients, it takes many years before their psychiatric illness is correctly diagnosed as Bipolar Disorder. During this time, they may not be treated correctly and some treatments may actually make them worse. The purpose of the Bipolar test is to aid your psychiatrist in making the correct diagnoses, so the best treatment can be selected as soon as possible.

Bipolar Disorder is largely a hereditary illness. Inherited factors may explain as much as 60-70% of the incidence of this disorder. If your clinical history and DNA test indicate that you have Bipolar Disorder, this indicates that an inherited risk for Bipolar Disorder may run in your family. DNA testing presently cannot predict the level of risk for illness in relatives who have no psychiatric symptoms. However, if you are diagnosed with Bipolar Disorder, then your family members may be at higher risk. Bipolar Disorder commonly has its onset in the early 20's. Your family members, who may be having symptoms of depression or mania, should be seen by a psychiatrist for evaluation.

The purpose of the test for SSRI antidepressant response is to aid your psychiatrist in selecting the best medication. This test is useful for most patients with either Bipolar Disorder or Major Depression.

Important: These tests are not valid for everyone. The genetic basis

for Bipolar Disorder is not yet well understood. It is likely that changes in the DNA of many different genes could contribute to risk for this disorder. In addition, scientific studies have not yet been completed for all racial and ethnic groups. Your family and personal medical history must be considered along with the results of these genetic tests.

Psynomics does not report results directly to patients. One of Psynomics' psychiatrists reports your results in confidence to your psychiatrist. The Psynomics psychiatrist and your psychiatrist discuss and interpret these results in consultation.

Contingent order: Your request for genetic testing and our acceptance of your payment is contingent on meeting certain criteria, including your own history and your family history of mood disorder. In addition, you must provide the name and contact information of your psychiatrist. Placement of your order on the Psynomics website is a request to one of Psynomics' psychiatrists to review the confidential information you have submitted and then to decide if you meet the criteria to be tested. The Psynomics psychiatrist will order our laboratory to test your DNA only if you meet these criteria.

If you do not meet the criteria to be tested, then Psynomics will inform you and your money will be returned or credited back to your account. More genomics associations studies are underway and large studies are being planned. The results of these studies may broaden applicability of these tests to all racial and ethnic groups, change the predictive power, add additional genes or otherwise change the criteria for testing. Psynomics encourages you to periodically review our website for the latest information. If you did not meet the required criteria and your order was returned, you may resubmit your order at a future date.

Sampling Procedure: After you have answered the questions in your confidential session on the Psynomics website and after Psynomics receives your payment either online via our website or by mail, a Psynomics psychiatrist will review your record. If you meet certain criteria, then Psynomics will mail a sampling kit to your address.

The kit is a screw-top sample container, instructions, a copy of this consent form and a pre-addressed postage paid return mailer. Study the information on our website and talk with your psychiatrist about these tests. Your psychiatrist may call or email us with any questions or requests for more information.

You and your psychiatrist must sign this form in the spaces below.

When you are satisfied that you understand the implication of our tests for you, open the screw-top sample container, spit into the container and screw the top on. Place the sample container in the envelope with this signed consent form and mail the package back to Psynomics in the pre-addressed postage paid return mailer. No testing is done by you and no testing is done in your home. Psynomics will not test your DNA unless both you and your psychiatrist sign this form below and your psychiatrist provides their contact information, board certification and license number.

Testing Procedure: When your sample kit arrives at Psynomics, we will verify the information is in order and meets criteria, your payment is received, and we will verify that your sample container is intact. Then, one of the psychiatrists at Psynomics will review your record and order the laboratory to begin testing your samples. We obtain your DNA from the saliva you provided in the sample kit. Your tests will be run in our laboratories, which are regulated under U.S. federal regulations known as CLIA (Clinical Laboratory Improvement Act) as well as California state licensing regulations. The Psynomics lab is certified CLIA and CAP (College of American Pathologists).

New York residents: The State of New York does not allow Psynomics to provide results to residents of New York at this time. Please check our website again in the future or complete the online registration forms without payment and Psynomics will contact you when test results can be provided for New York residents.

Test Results and Interpretation: When your tests are completed in the lab, the technical data is reviewed by Psynomics' Laboratory Director, who is an M.D. as required by CLIA, CAP, federal and California regulations. The report is then reviewed again by Psynomics Chief Medical Officer who is an M.D. and board licensed psychiatrist.

Psynomics' psychiatrist prepares and sends to your psychiatrist a report on the results from your samples. The Psynomics report will identify whether your sample tested positively or negatively for the genes discussed below. We encourage your psychiatrist to speak with one of the psychiatrists at Psynomics before testing and/or after receiving the Psynomics report. The Psynomics report is our psychiatrist's method of consulting with your psychiatrist to interpret the genetic tests on your sample to assist your psychiatrist in diagnosis and treatment. Direct phone calls between your psychiatrist and one of Psynomics' psychiatrists also may be needed.

Your M.D. psychiatrist must interpret these genetic test results in view of your symptoms, medical history, and family history. This is the reason that we will only test samples from persons under the care of a psychiatrist. Psynomics does not test a-symptomatic patients.

Psychiatric diagnoses and treatment plans are made by your psychiatrist based on a review of specific symptoms in your history and a set of criteria based on behavior that define diagnoses. These criteria are described in the Diagnostic and Statistical Manual – IV (DSM-IV) which was prepared by the American Psychiatric Association.

Presently, no DNA test alone can provide a definitive diagnosis for any psychiatric disorder. Many genes act together in combination with environmental factors to increase the risk of a psychiatric disorder. In the context of your history and symptoms, DNA tests can indicate whether you have a higher or lower probability of having a given psychiatric diagnosis. Psynomics provides DNA testing, known as genotyping for two specific genes. The interpretation of these results depends on scientific studies and may change as more studies are conducted. Psynomics results on your samples should be interpreted by your psychiatrist and medical doctor in the context of your medical and family history.

Psynomics offers two genetic tests:

GRK3: (G-protein-coupled receptor kinase 3) Certain DNA sequences in this gene have been associated with an increased risk for Bipolar Disorder in some individuals of European descent. Many individuals with Bipolar Disorder will have a negative GRK3 genetic test and some individuals who do not have Bipolar Disorder will have a positive GRK3 test. Therefore, your genetic test results must be interpreted in the light of your clinical history. Your doctor is responsible for making your diagnosis and is best able to incorporate all the facts and results.

Bipolar Diagnosis Interpretation: There are four possible results for the GRK3 genetic test.

(1) If your GRK3 test is positive and if your clinical history meets the DSM-IV criteria for Bipolar Disorder, then it is more likely that you have Bipolar Disorder. Your doctor may want to consider treatments for Bipolar Disorder.

(2) If your GRK3 test is positive and if your clinical history does not meet the DSM-IV criteria for Bipolar Disorder, then you are 3 times more likely to have Bipolar Disorder. Your doctor may want to consider treatment for Bipolar Disorder.

(3) If your GRK3 test is negative and if your clinical history and symptoms meet the DSM-IV criteria for Bipolar Disorder, then you still may have Bipolar Disorder. Bipolar Disorder can result from changes in the DNA of many different genes. Genes other than GRK3 may be responsible for your illness.

(4) If your GRK3 test is negative and if your clinical history does not meet the DSM-IV criteria for Bipolar Disorders, then you do not have Bipolar Disorder.

Serotonin Transporter Test

Serotonin Transporter is a protein involved in reuptake of serotonin in the synapses between neurons. 5-HTT is a gene which codes for the serotonin transporter, located on chromosome 17. A polymorphic region (5-HTTLPR) upstream of the gene has either 14 or 16 repeated elements generating a long (l) or a short (s) variations (or alleles).

There are two possible results:

The HTTLPR marker in the serotonin transporter gene has been associated with good response to the SSRI type of antidepressants.

(1) POSITIVE: You have either the L/L or S/L variant. You are more likely to have a good response to SSRI antidepressants.

(2) NEGATIVE: You have the S/S variant. You are less likely to have a good response to SSRI antidepressants.

Important: As of this date, these gene tests have been validated only in Caucasians of European ancestry. Their meaning and interpretation in other racial and ethnic groups is unclear. Gene variants may have no effect or a different effect in different racial and ethnic groups. Results should be interpreted cautiously in other racial or ethnic groups.

Confidentiality: Psynomics keeps test results confidential and is fully in compliance with all Health Insurance Portability and Accountability Act (HIPAA) regulations. Psynomics will only release your test results to your psychiatrist, or his or her designee. Our website and internal database is encrypted and your personal information is available only to you through your login and password. Your test results will not be available to you. Your results will not be posted to your confidential session on our website. It will not be possible for our lab to identify your name with your lab results. Psynomics employees cannot identify

your name with your test results. Only Psynomics psychiatrists have access to both your name and your test results. Psynomics sends its confidential reports only to your psychiatrist.

Benefits: Bipolar Disorder is frequently difficult to diagnose because of the subtlety of the symptoms and the way in which the illness develops over time after onset of first symptoms. Genetic testing in the context of your clinical history may enable your doctor to make the correct diagnosis sooner. This in turn may lead to your being treated with the best medications faster, with resulting reduction in symptoms and suffering. Similarly, the Serotonin Transporter test for antidepressant response may help your doctor choose the best medication for you sooner and reduce the number of medications that have to be tried.

Risks: The method of collecting your DNA from your saliva has no known risks. Genetic testing may expose you to risk of discrimination by health insurance companies, making it more difficult for you to be insured. Most states and the federal government have enacted laws to prohibit genetic discrimination, and some states have enacted laws that limit use of this information by insurance companies and by employers. Broad federal legislation prohibits unauthorized disclosure of confidential personal health information.

Financial Responsibility: Genetic testing of appropriate individuals may be reimbursed by health insurance or covered by HMO's. Psynomics is not presently able to assist you in obtaining reimbursement. You are responsible for any cost of the genetic test not reimbursed by insurance.

Future Correspondence: Due to the dynamics of this field, there continues to be new information and data. It is recommended that you keep in contact with your healthcare provider and Psynomics website to learn of any new developments in mental health genetics.

Consent Statement for the Patient

By signing below, I, the patient having the test performed, acknowledge that:

- I have been offered the opportunity to ask questions and discuss with my psychiatrist the benefits and limitations of the genetic tests to be performed as indicated on the associated test request form.
- I have been previously diagnosed or treated for a psychiatric disorder, or have some symptoms of a psychiatric disorder.

- I understand Psynomics testing is for the purpose of clarifying diagnosis in symptomatic individuals.
- I understand that testing to assess the risk of future illness in someone who has never had symptoms is not currently possible.
- I have read this document in its entirety and understand that I may obtain a copy for my records.
- I consent to being tested for Bipolar Disorder and/or my response to certain antidepressant medications.

Printed Name of Person being tested

Date of Birth

Signature of Person being tested

For the Physician:

As the referring physician, I confirm that I am board certified in psychiatry and I understand the benefits and limitations of these two genetic tests and do hereby request that the above-named patient be tested. I have reviewed the above-listed information with my patient, and have answered their questions. I believe this patient understands this information and has hereby voluntarily signed this consent.

Signature of Physician

Date

Print Name of Physician

License Number

Board Certification: _____

Phone number of Physician: _____

Email of Physician: _____

Address of Physician: _____