

INFORMED CONSENT FOR CEREBRAL AUSTOSOMAL DOMINANT ARTERIOPATHY WITH SUBCORTICAL INFARCTS AND LEUKOENCEPHALOPATHY (CADASIL) DNA TESTING

Patient Name _____ Date of Birth _____ Sex F M
 Physician _____ Physician Phone _____
 Practice Specialty _____ Physician Fax _____
 Genetic Counselor _____ Counselor Phone _____

Does the patient have symptoms of CADASIL? Yes No

If yes, describe: _____

Who is the patient's closest relative with CADASIL? _____

Age the relative's symptoms began: _____ Was this relative's diagnosis confirmed by DNA testing? Yes No

Please list the specific *NOTCH3* gene variant, if known: _____

- Participation in genetic testing is completely voluntary. Genetic counseling is highly recommended prior to and following genetic testing for CADASIL. See www.nsgc.org to find a medical genetics professional. The ordering health care provider or genetic counselor should explain the test results in person and be available for follow-up genetic counseling. Patients undergoing presymptomatic testing should be accompanied by a support person, who is not at risk for CADASIL, when receiving results.
- CADASIL is an inherited condition that typically presents with transient ischemic attacks (TIAs) and strokes. Symptoms may include problems with thinking, dementia, migraines, psychiatric and mood disorders, and epilepsy. There is currently no cure or effective treatment for CADASIL. This blood test involves extracting DNA and sequencing the *NOTCH3* gene. It is able to detect disease-causing DNA variants in 95 percent of affected individuals. A causative variant cannot be identified in 5 percent of affected individuals. The accuracy of an affected DNA test result is 99 percent. Possible sources of error include: sample mislabeling or contamination, transfusion, bone marrow transplantation, and maternal cell contamination of prenatal or cord blood samples.
- There are three possible test results:
 - 1) **Negative:** No pathogenic variants were identified in the *NOTCH3* gene. This individual is neither at risk for developing CADASIL nor having affected offspring.
 - 2) **Uncertain:** A variant of uncertain significance was identified in the *NOTCH3* gene. This individual may or may not be affected with CADASIL depending on whether the variant is disease-causing or benign.
 - 3) **Positive:** One disease-causing variant was identified in the *NOTCH3* gene; therefore, this individual will be expected to develop symptoms of CADASIL within a normal lifespan. Offspring of this individual have a 50 percent risk for developing CADASIL. The age of symptom onset and disease progression is highly variable.
- Test results may reveal non-paternity or that other family members may be affected with, or at risk for developing, CADASIL.
- There are psychological risks associated with CADASIL testing. A result that indicates an individual will be unaffected can produce feelings of guilt as well as joy. An uncertain test result, indicating the patient may or may not develop symptoms, can be frustrating. A result that indicates an individual will be affected could lead to serious psychological consequences including feelings of depression, futility, and severe stress.
- If a disease causing *NOTCH3* gene variant is identified, insurance rates, the ability to obtain disability and life insurance, and employability could be affected. The Genetic Information Nondiscrimination Act of 2008 extends some protections against genetic discrimination (<http://www.genome.gov/10002328>). All test results are released to the ordering health care provider and those parties entitled to them by federal, state, and local laws.
- Because ARUP is not a storage facility, most samples are discarded after testing is completed. Some samples may be stored indefinitely for test validation or education purposes after personal identifiers are removed. All New York samples are discarded 60 days following test completion. You may request disposal of your sample by calling ARUP Laboratories at (800) 242-2787 ext. 3301.

Patient, Legal Guardian, Power of Attorney (POA): I have the legal authority to request ARUP Laboratories to test this sample for CADASIL. I am the patient, his/her legal guardian, or POA. I have been counseled regarding the risks, benefits, and limitations of this test and carefully considered the psychological impact the results may have on the patient and his/her family.

 Patient/Legal Guardian/POA Printed Name Signature Date

Ordering Healthcare Provider or Genetic Counselor: I have explained CADASIL genetic testing, its risks, benefits, limitations, and alternatives to the patient or legal guardian and addressed all their questions.

 Healthcare Provider Printed Name Signature Date