



Huntington Disease (HD)

Huntington Disease (HD) is an autosomal dominant, progressive neurodegenerative disorder characterized by motor disturbance, cognitive loss, and psychiatric manifestations, which usually manifests after 40. It has an incidence of 1 in 10,000 individuals of European descent. In 5-10% of cases, HD is seen in juveniles, typically with more severe symptoms and a more rapid disease course. The gene, Huntingtin, which causes HD was first mapped to 4p16.3 in the 1980s and definitively identified in 1993 by The Huntington Disease Collaborative Research Group.

This gene contains a normally polymorphic trinucleotide CAG repeat region in the first exon. Normal individuals have between 6 to 35 copies of this repeat in their genes, usually fewer than 20 repeats. Affected individuals have demonstrated expansions ranging from 36 to over 101 CAG repeats. The penetrance of expansions in the range of 36 to 41 repeats is not complete, especially in the 26-28 range. Individuals with CAG repeat sizes of 30 to 35 have not manifested Huntington's Disease but bear a modestly increased risk of transmitting to offspring expansions (and occasionally contractions) of the repeat region including expansion into the disease-causing range. This effect is more likely in paternal transmission of the Huntingtin gene.

The test is performed by PCR amplification of DNA from a patient's white blood cells targeting a region in the first exon of the Huntingtin gene which contains the CAG repeat sequence. The resulting products from each chromosome 4 are analyzed, and the size of the CAG repeat region calculated based on their size. A customized report is generated which takes into account family history (if provided) and the inheritance pattern of this disorder. The use of a healthcare professional experienced in genetic counseling for Huntington Disease is strongly recommended both to obtain informed consent for HD testing as well as for disclosure of test results.

Detection of an expanded trinucleotide CAG repeat can be used to confirm a clinical diagnosis of Huntington's Disease. Testing is also used for presymptomatic screening in individuals at risk (having a parent or sibling who has been previously diagnosed with Huntington Disease). Testing is potentially applicable to prenatal diagnosis. At the present, there is no treatment effective in delaying or preventing the onset and progression of the disease.

Turnaround Time: 30 days.

Specimen Requirements: See Oncology/Genetics Specimen Handling Protocol or Molecular Diagnostics Genetics Requisition Form.

Informed Consent: The laboratory REQUIRES a copy of the signed informed consent document before presymptomatic testing is performed. If you would like a copy of a blank consent form, please check our website at <http://path.upmc.edu/divisions/mdx/diagnostics.html> or call the laboratory at (412) 648-8519.