Huntington's Disease (HD)

Genetic testing for Huntington's Disease is important for confirmation of clinical diagnosis in a symptomatic individual and for pre-symptomatic testing in adults

Huntington Disease Mutation Analysis

The Huntington (IT15) gene and the huntingtin protein

- The Huntington gene directs the cell to make the huntingtin protein.
- Huntingtin protein contains a sequence in which the amino acid glutamine is repeated a number of times. These glutamine residues are encoded in the gene by the DNA trinucleotide "CAG." The number of times that "CAG" is repeated (the CAG repeatnumber) determines the number of consecutive glutamines in that segment of the huntingtin protein

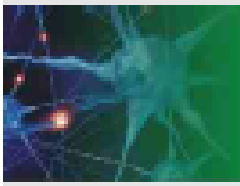
CAG repeats in the huntingtin gene

Normal huntingtin genes contain 10-35 "CAG repeats"

Implications of different repeat ranges for Individual /Patient

No. of repeats	Diagnostic test	Predictive test	Implications for family members
6-26-Normal Allele	Diagnosis of HD excluded	Will not develop HD	No increased risk for HD
27-35 Intermediate Allele	Diagnosis of HD excluded	Will not develop HD	No increased risk for HD (Few % < 10%)
36-39- Reduced Penetrance	Diagnosis of HD Confirmed in Symptomatic	May or may not develop HD; In range of reduced penetrance	Increased risk for HD
40 and over - Full Penetrance	Diagnosis of HD confirmed	Will develop HD	Increased risk for HD

NDG



CAG repeat number and age of onset

- Rough inverse correlation between CAG repeat numbers and age of onset; however the age of onset cannot be accurately predicted from CAG number alone
- CAG number also does not accurately predict what symptoms an individual will have, or how severe or rapid the course of the disease will be

Who should undergo Genetic Testing?

Diagnostic Testing

- Diagnostic genetic testing is also very useful in the evaluation of an individual who appears to have Huntington's disease but who has a negative or absent family history.
- If the clinical suspicion is strong, this may be the only diagnostic test needed.

Predictive Testing

- Patient has no symptoms but wants to know presence or absence of expanded gene
- Predictive testing should be reserved for competent adults who have participated in a careful discussion of their genetic risks and the potential risks and benefits of the test itself.

Sample Requirement : 3 ml EDTA whole blood
Test Schedule : Cut off : 7 am
Reported on : 5th day