

Your Genes and You: Perspectives on Huntington's Disease from a Genetic Counselor

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History of HD gene testing

- 1983 – Marker linked to HD gene identified
- 1986 – Linkage analysis available in some families
- 1993 – HD gene and CAG repeat as mechanism for HD identified

Impact of Test Availability

- Did everyone rush into a genetics clinic to be tested?
- No
- Why not?
- It's complicated...

Predictive vs. Diagnostic Testing

- Predictive testing
 - > Person with NO symptoms of HD
 - > Person at-risk for HD based on family history
 - > Also referred to as pre-symptomatic testing
- Diagnostic testing
 - > Person with symptoms of HD
 - > Used to confirm a diagnosis (possible impact on management)
 - > Molecular confirmation to allow family members to be tested with more certainty

Predictive Testing Process

- Psychological Evaluation
- Neurological Evaluation
- Initial Genetic Counseling
- Blood draw
- Results visit



Predictive Testing Process

- Psychological Evaluation
 - > Meet with psychologist and/or social worker for a mental health assessment
 - > Goal is to determine state of mind and identify any stressors or factors that would affect decision-making
 - > Help identify those who may need greater emotional support during and after testing

Predictive Testing Process

- Neurological Evaluation

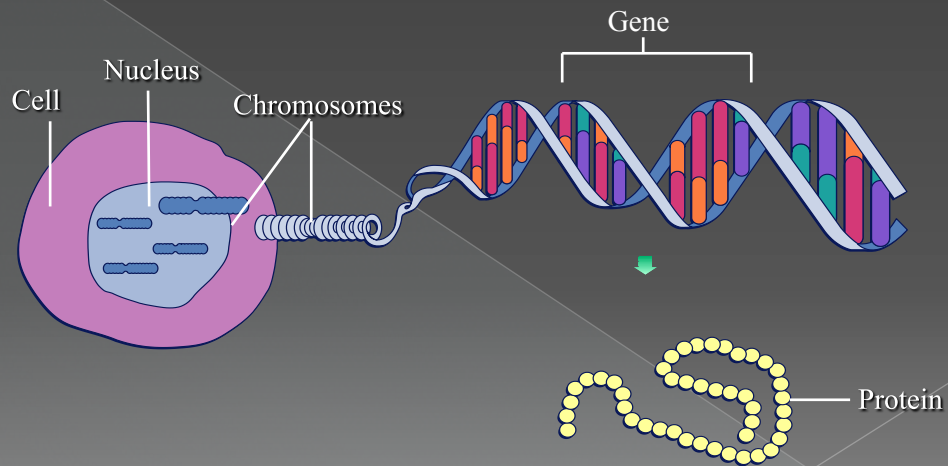
- > HDSA guidelines state that a neurological evaluation should be offered to any applicant who is concerned about or suspicious of HD symptoms
- > If someone is having symptoms of HD, it may provide needed information and render genetic testing unnecessary
- > In some cases, it may alleviate concern about symptoms that are not related to HD

Predictive Testing Process

- Initial Genetic Counseling

- > Collect detailed personal and family history information
- > Review some basic genetics
- > Discuss the inheritance of HD
- > Discuss the testing options
- > Try to address patient specific concerns
- > Explore motivations, preconceptions, expectations, support system, coping strategies, etc.

Genes



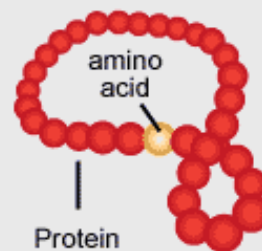
Protein Formation



Which proteins a cell makes is determined by genes that are organized in series of 3 base pairs, called "codons"

GCCTAGTTACTGC
CGGATCAATGACG
codon

Every codon codes a specific amino acid in a specific order



Reading the DNA Code

- The sequence of letters in the genetic code (A, T, G, and C) directs the formation of a protein
 - > Each set of 3 letters corresponds to an amino acid
 - > Amino acids are the basic building blocks of proteins

Figure A-1: DNA Language

C-A-T =



G-G-C =

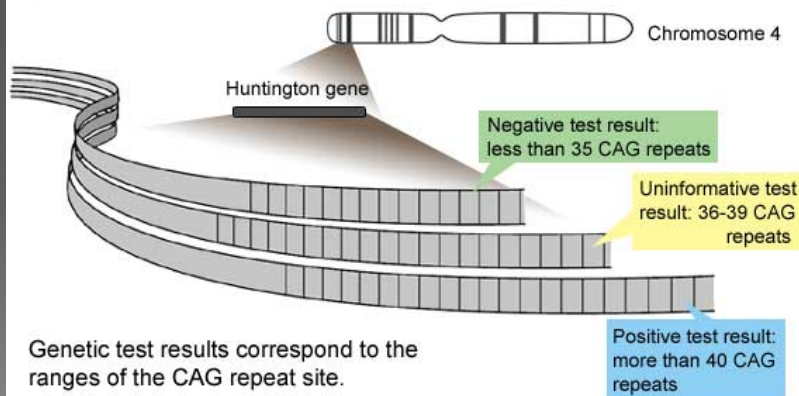


(proline)

Just as English words represent certain images, DNA "words" (codons) represent certain amino acids.

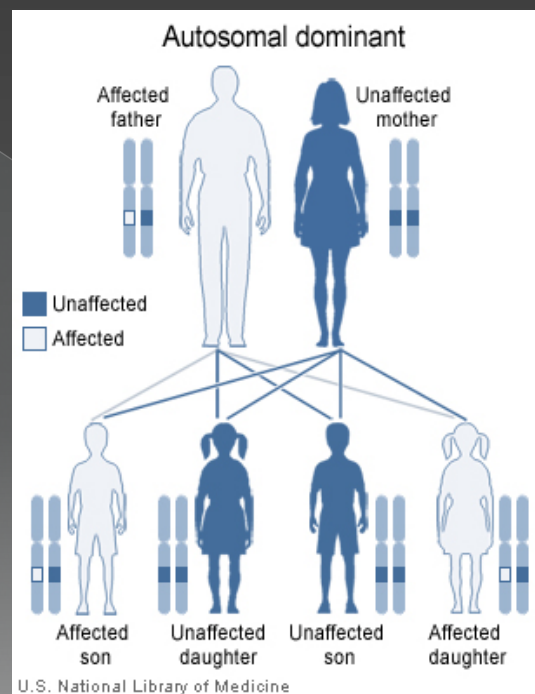
CAG Repeats

Figure S-3: CAG Repeat Counts on the Huntington gene



CAG Trinucleotide Repeat

| <u>Results</u> | <u>Repeat #</u> |
|--------------------------------------|-----------------|
| Normal | < 26 |
| Normal but potentially unstable | 27-35 |
| Abnormal with variable penetrance | 36-39 |
| HD | > 40 |



Predictive Testing Process

- Blood Test

- > One tube of blood
- > ~\$256 (but prices vary tremendously)
- > May choose to pay for test or go through insurance
- > 3-4 weeks turn around time
- > Results indicate the number of CAG repeats

- Results visit

- > Results are disclosed in person
- > Must bring a support person

Predictive Testing

- Genetic testing does not tell us when some will develop symptoms or which symptoms they will have
- The decision of whether or not to have predictive testing for HD is a very complex and personal one
- There are no right or wrong choices
- Everyone must make their decision based on their own experiences and beliefs
- It is important that those seeking this testing receive adequate support, education and assessment of readiness for this information

Insurance Concerns

- State and federal laws that protect us from genetic discrimination
 - > Several KY laws
 - > HIPAA
 - > GINA - Genetic Information Nondiscrimination Act passed in 2007 and states that an employer or health insurance company cannot treat you differently based on a genetic test result
- Not as many protections with respect to life and/or disability insurance

Things to Think About

- What would I do differently if the test were positive?
- What would I do differently if the test were negative?

Things to Think About

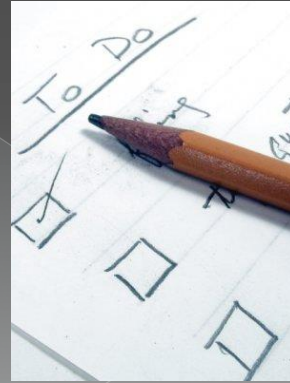
- Motivations
 - › Knowledge
 - › Financial planning
 - › Family planning
- Relationships and support
- Perceptions or exposure
- Family influences
- Financial concerns
- Timing

The Big Cloud

- Some at-risk individuals become consumed with thinking about whether or not to undergo testing
- May be useful to make a decision about timing
 - › Ex: I am not going to be tested this year.
 - › Ex: I am not going to think about it until...

Make a Plan

- Need to have a pre-arranged plan
 - > Do you tell people you are getting it done?
 - > Who?
 - > When and how to tell?
 - > Do you tell them what day you will get the results?
 - > Time off of work



Coping with the Results

- Studies have shown that both carriers and non-carriers have challenges coping with, and adjusting to, their new knowledge of their genetic status
- Issues facing carriers
- Issues facing non-carriers

Coping with the Results

- Decruyenaere M, et al. Psychological distress in the 5-year period after predictive testing for Huntington's disease. (2003) Eur J Hum Genet. Jan;11(1):30-8
 - Studied distress in 24 carriers and 33 non-carriers
 - Five years after the test, mean distress scores of both carriers and non-carriers were within the normal range. Carriers did not differ from non-carriers with regard to mean general distress.
- Crozier S, et al. The psychological impact of predictive genetic testing for Huntington's disease: a systematic review of the literature. (2015) J Genet Couns. 2015 Feb;24(1):29-39
 - Review article that compiled data from 8 studies on psychological impact of predictive HD testing
 - No significant difference in distress between groups at 5 or 10 year follow-up

Take Home Message...

- To Test or Not to Test
 - Complex and personal decision
 - Many factors to consider (timing, motivations, support network, etc.)
 - See a genetic counselor if you want to learn more
- If you test, please have it done through a center that understands the delicate nature of the test and respects confidentiality



Questions?