



# Reproductive Options and Huntington Disease

# Michelle Fox, MS, LCGC

## Genetic Counselor



The information provided by speakers in workshops, forums, sharing/networking sessions and any other educational presentation made as part of the 2015 HDSA Convention program is for informational use only.

HDSA encourages all attendees to consult with their primary care provider, neurologist or other healthcare provider about any advice, exercise, medication, treatment, nutritional supplement or regimen that may have been mentioned as part of any presentation.

# Presenter Disclosures

**Michelle Fox, MS, LCGC**

**The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:**

Michelle is an independent genetics consultant working for Invitae, a genetic information and testing laboratory which does not provide Huntington Disease testing.



# Overview

- HD Basics
- Reproductive Options
- Issues to consider
- Family stories

# Huntington's Disease: Overview

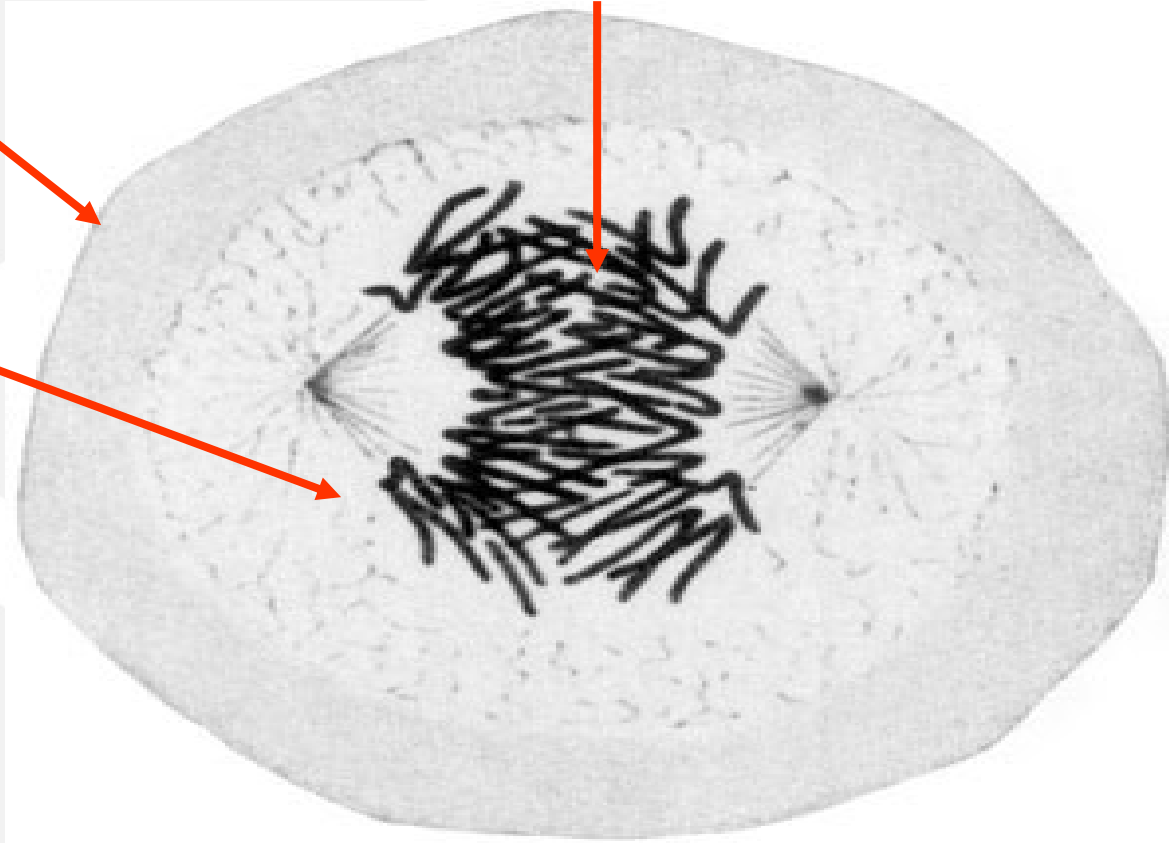
- Autosomal dominant
- Adult-onset (late 30's-40's)
  - As early as age 1 or as late as age 90
  - 6% present before the age of 20 (Juvenile HD)
- Prevalence 7-10 per 100,000
  - Likely underestimated
- 15-20 year duration
- Triad of clinical findings: Motor, Cognitive and Psychiatric

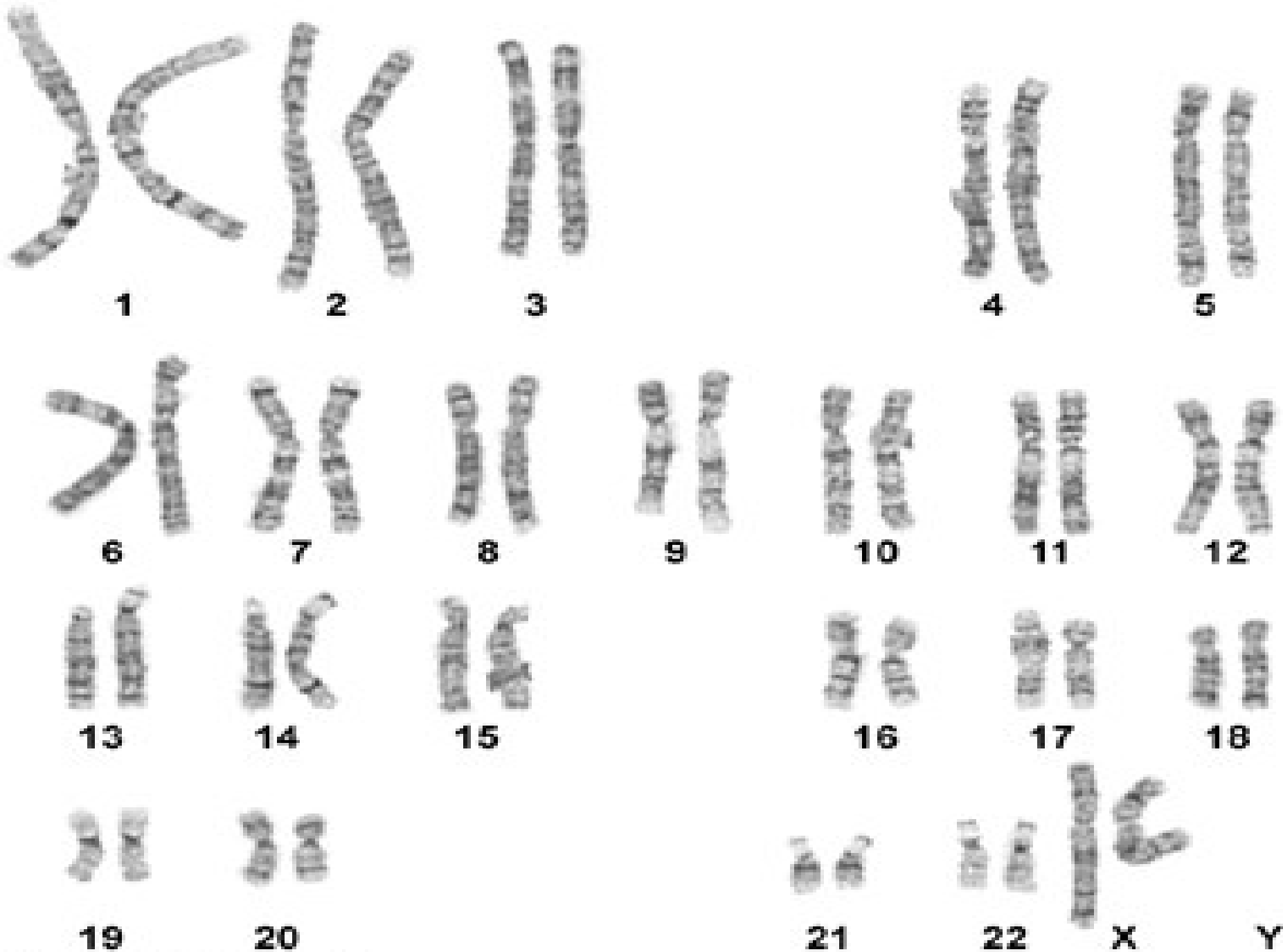
# Where is our genetic information stored?

Chromosomes

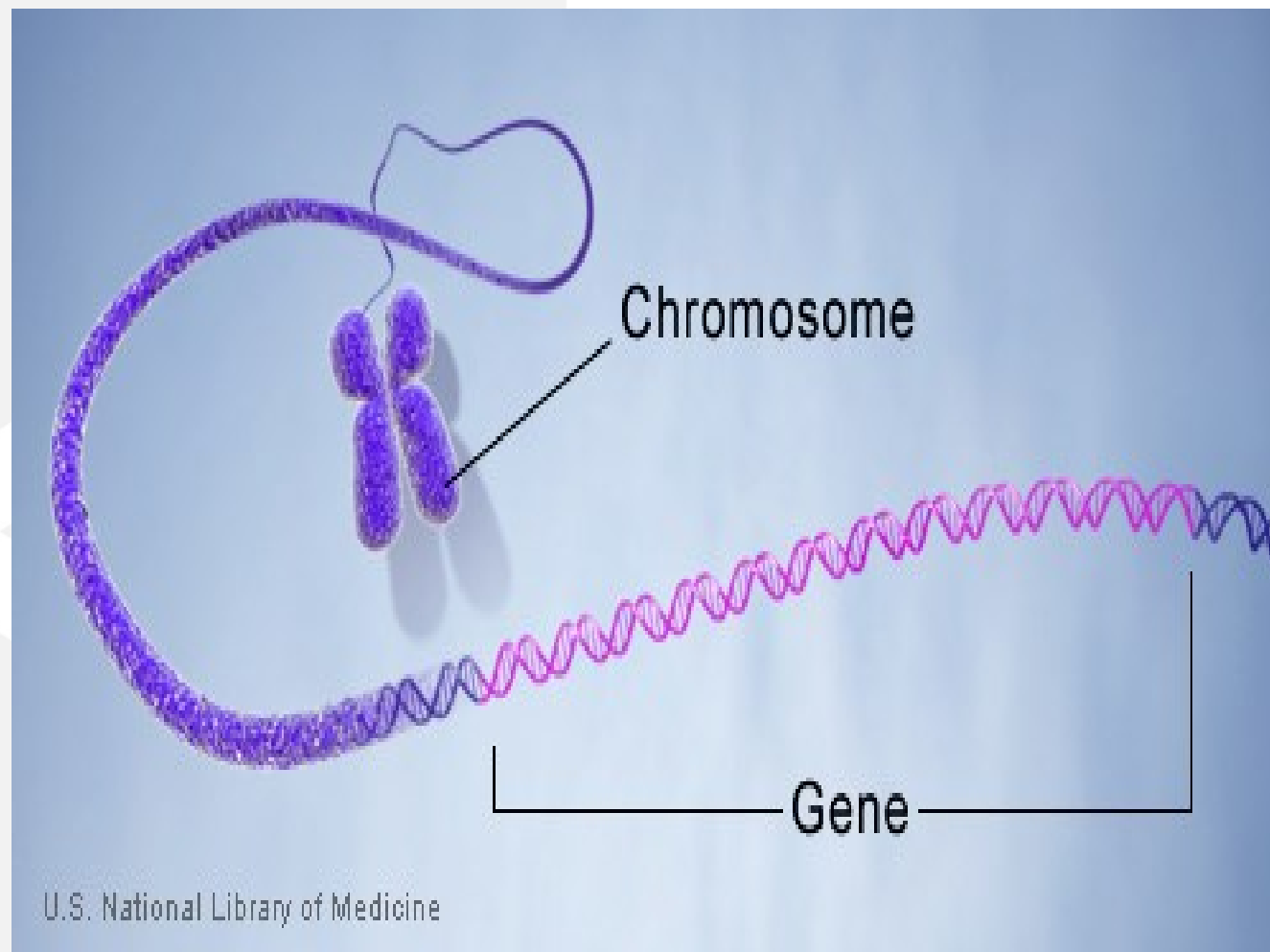
Cell

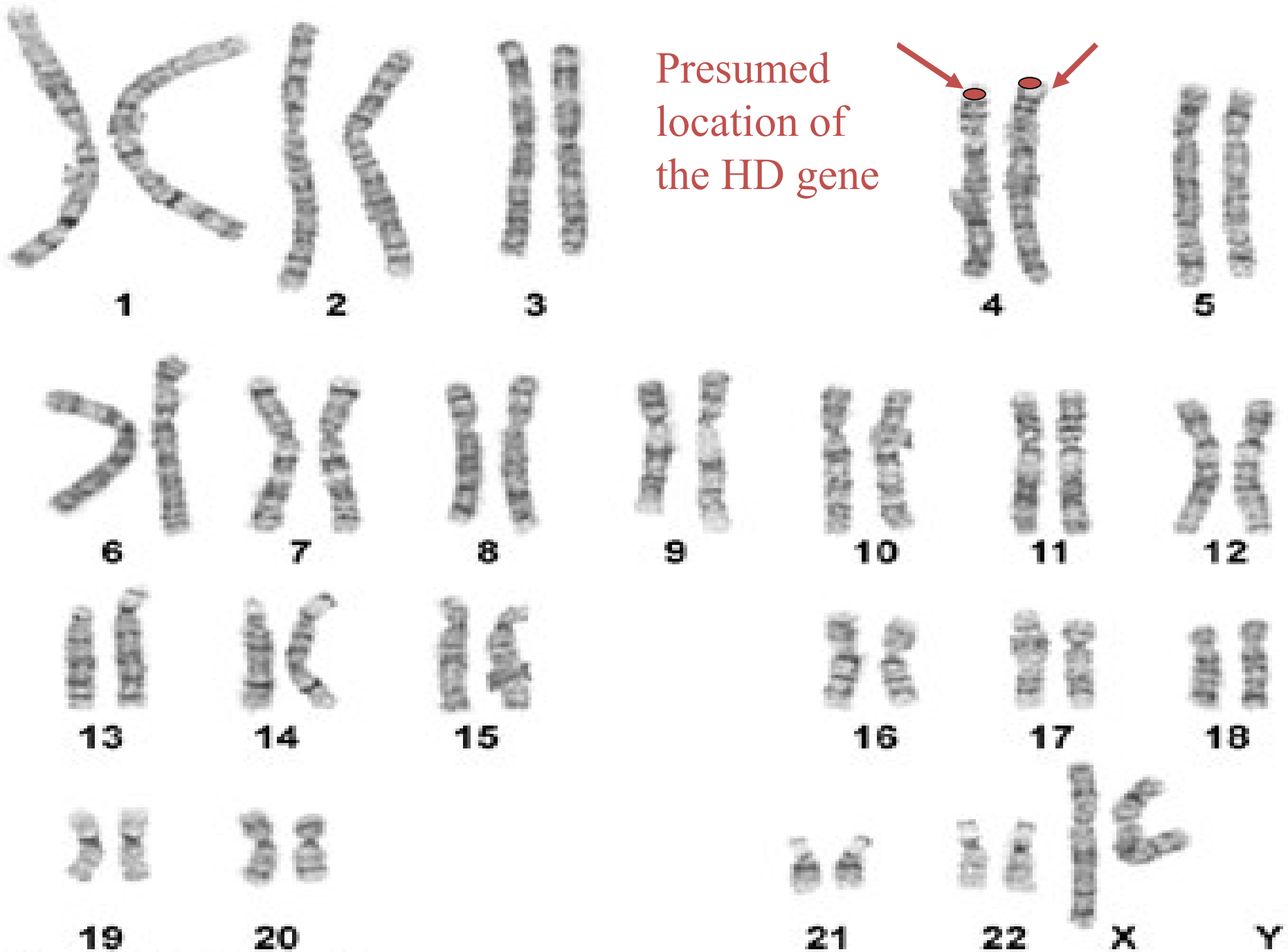
Nucleus

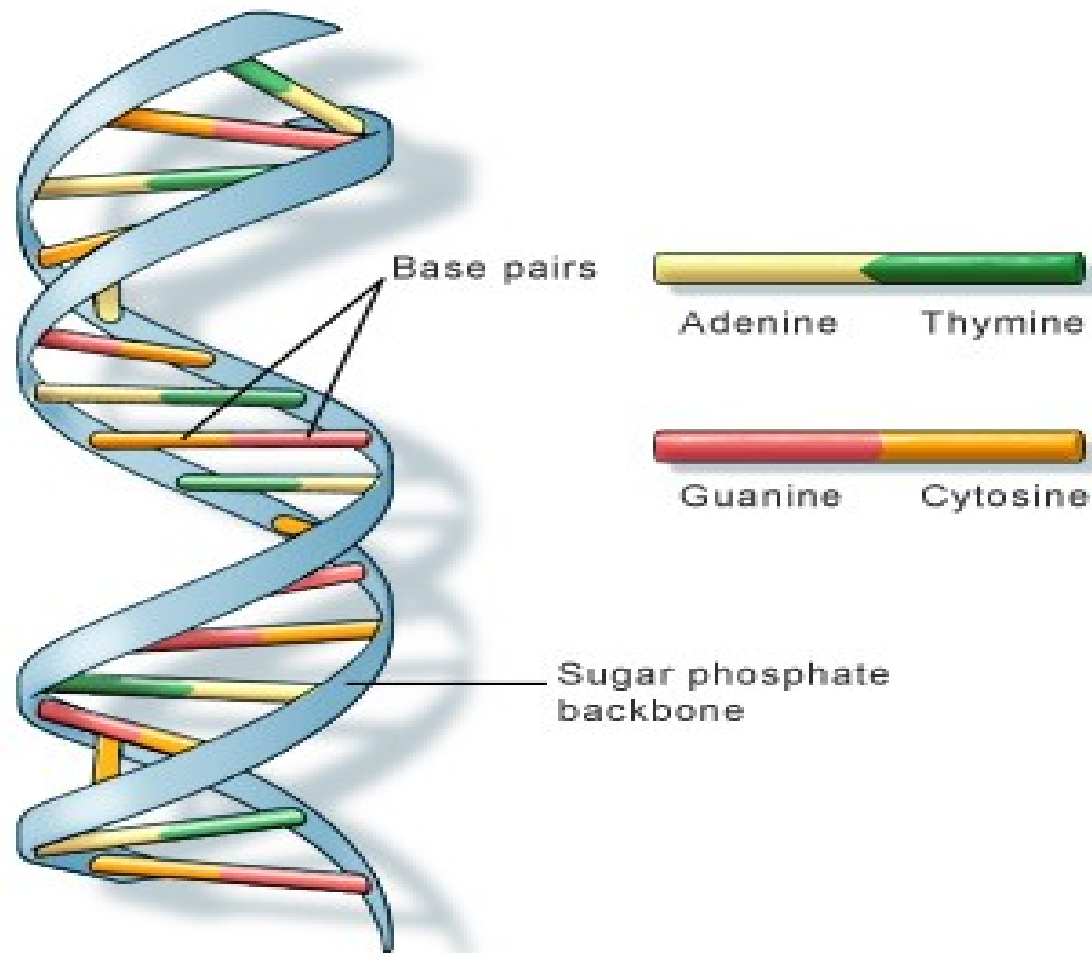






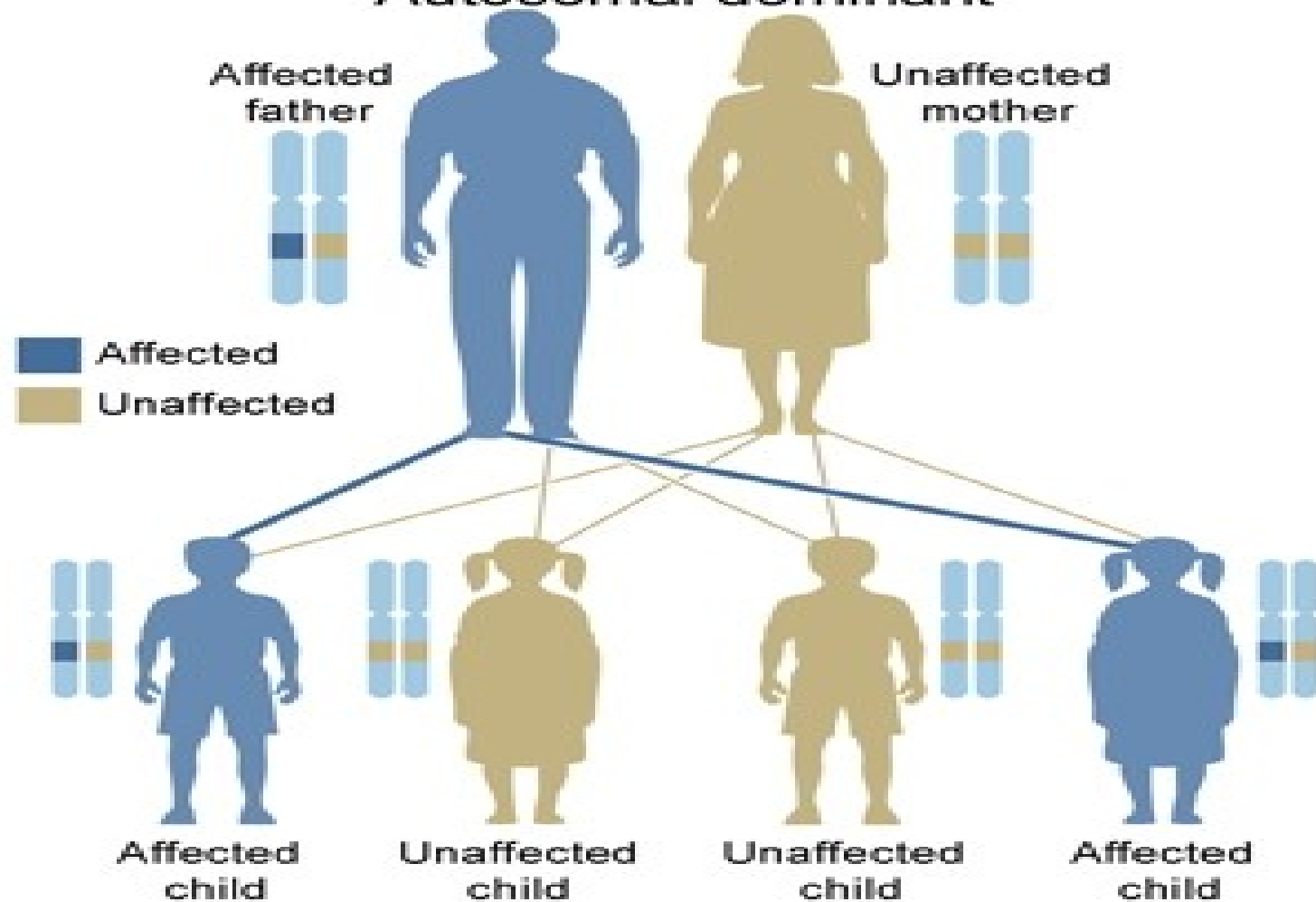






U.S. National Library of Medicine

# Autosomal dominant



U.S. National Library of Medicine

## Key points on autosomal dominant inheritance:

**Autosomal**- Both males and females can be affected with HD. Both males and females can pass HD to their children.

**Dominant**- If a person has Huntington disease, there is a 50% risk for each of their children.

If a person does not inherit HD from their parent, they cannot pass it to their children.

Each child of a person with HD has an independent 50% risk. (i.e. their risk is not changed by whether or not their brothers' or sisters' test results).

# The Huntington Gene

- 1993: Identification of the gene, **IT-15** Interesting transcript-15 on short arm of chromosome 4 encoding **huntingtin**
  - Expanded CAG repeat in exon 1 as causative mutation
    - Normal: <27
    - Intermediate: 27-35
    - Reduced penetrance: 36-39
    - Pathogenic:  $\geq 40$
  - Higher CAG repeat length correlates with earlier age of onset of disease
    - But CAG repeat length accounts for only 50-60% of onset age variability.
  - Belongs to family of expanded CAG repeat disorders

# Official repeat ranges for HD

- **9-26 repeats= Normal**

- No risk for HD and no known risk to children.

- **27-35 repeats=Intermediate**

- No risk for HD, but a small risk to children

- **36-39 repeats=Reduced penetrance**

- May develop HD and a 50% risk to children

- **40+ repeats=Full penetrance**

- Will develop HD and a 50% risk to children

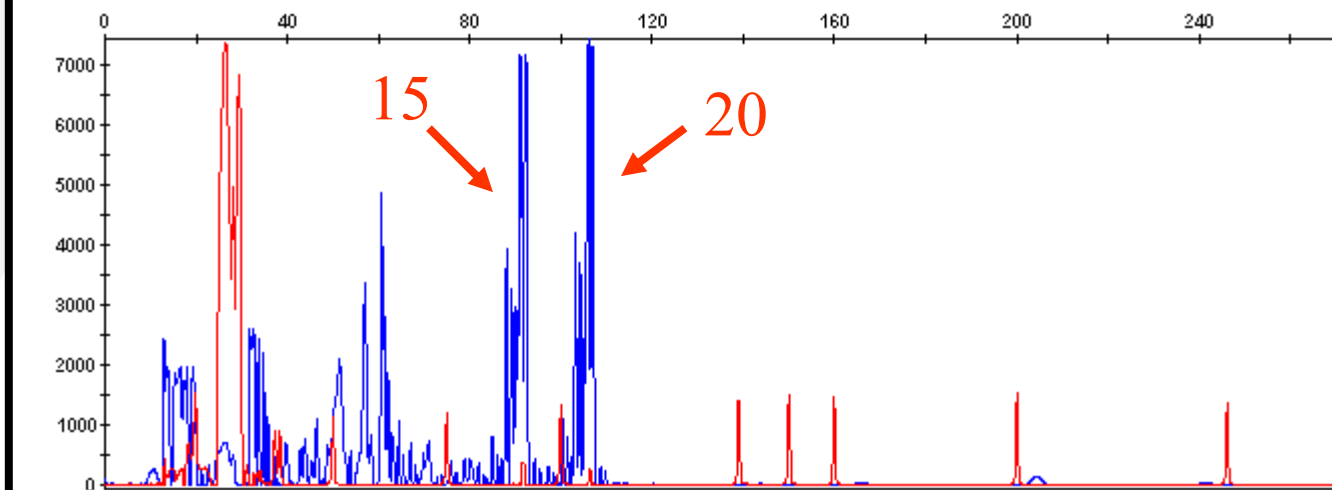
## Anticipation is due to expansion of CAG repeats

- CAG repeat numbers can expand when passed to offspring.
- Expansion occurs more often with male transmission.
- Expansion occurs more with larger repeat numbers.



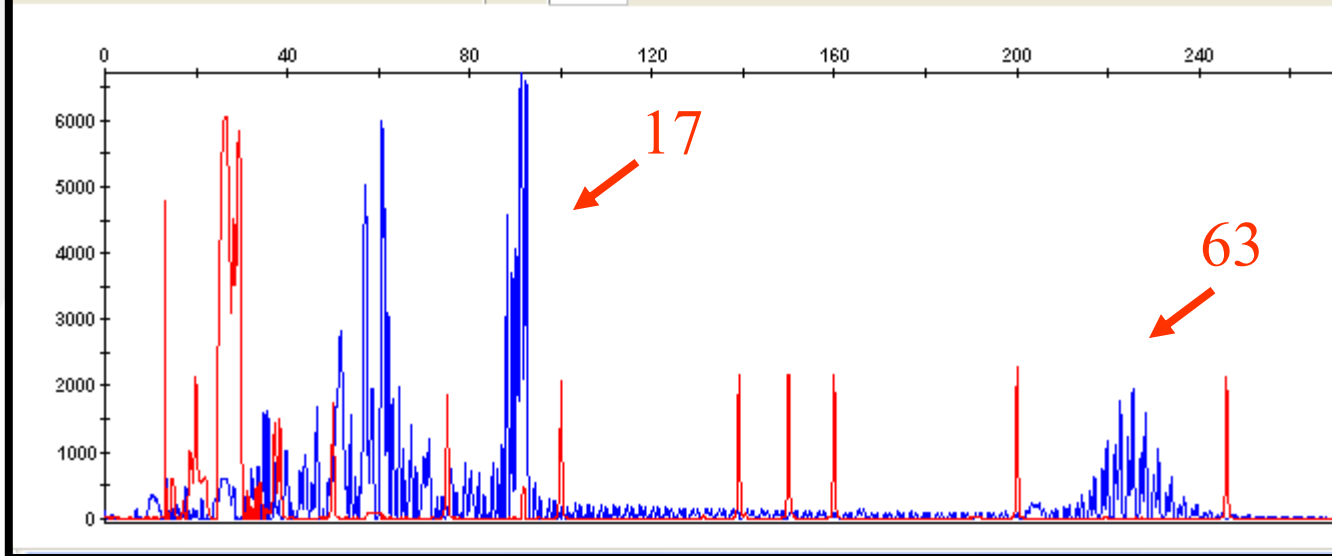
# Juvenile-onset HD

- Dystonia and parkinsonism predominate
- Seizures
- Typically paternal inheritance due to anticipation; expansion of CAG repeat
  - > 60 CAG repeats
- Faster progression (duration 5-15 years)



15 and 20 CAG  
repeats

5\_064611c\_HD13\_3130x11\_13-31-03\_2009-08-26\_0030



17 and 63 CAG  
repeats

# Genetic Counseling

- Genetic counseling is the process of helping people understand and adapt to the medical, psychological and familial explanations of hereditary disease.
- Informed decision making
- Shared decision making

# Pre-Conception Genetic Counseling

- Explore thoughts, feelings, values
- Partner disagreement
- When to start family
- Taking care of affected family member and children
- Experience with HD
- Weigh pros and cons of reproductive options

# Genetic Counseling

- Obtain family history/establish rapport
- Information about HD
- Genetics of HD
- CAG triplet repeats/ranges/age of onset
- Explanation of juvenile onset HD
- Discuss motivations for testing
- Experience with HD: living with HD vs new dx in family
- Timing of testing

# Genetic Counseling

- History of depression, suicidality, therapy
- Support system, family, community
- Coping strategies
- Concerns about current at risk status
- Issues of privacy, confidentiality
- Insurance concerns
- Predictive HD testing as model for genetic testing

# Reproductive Options

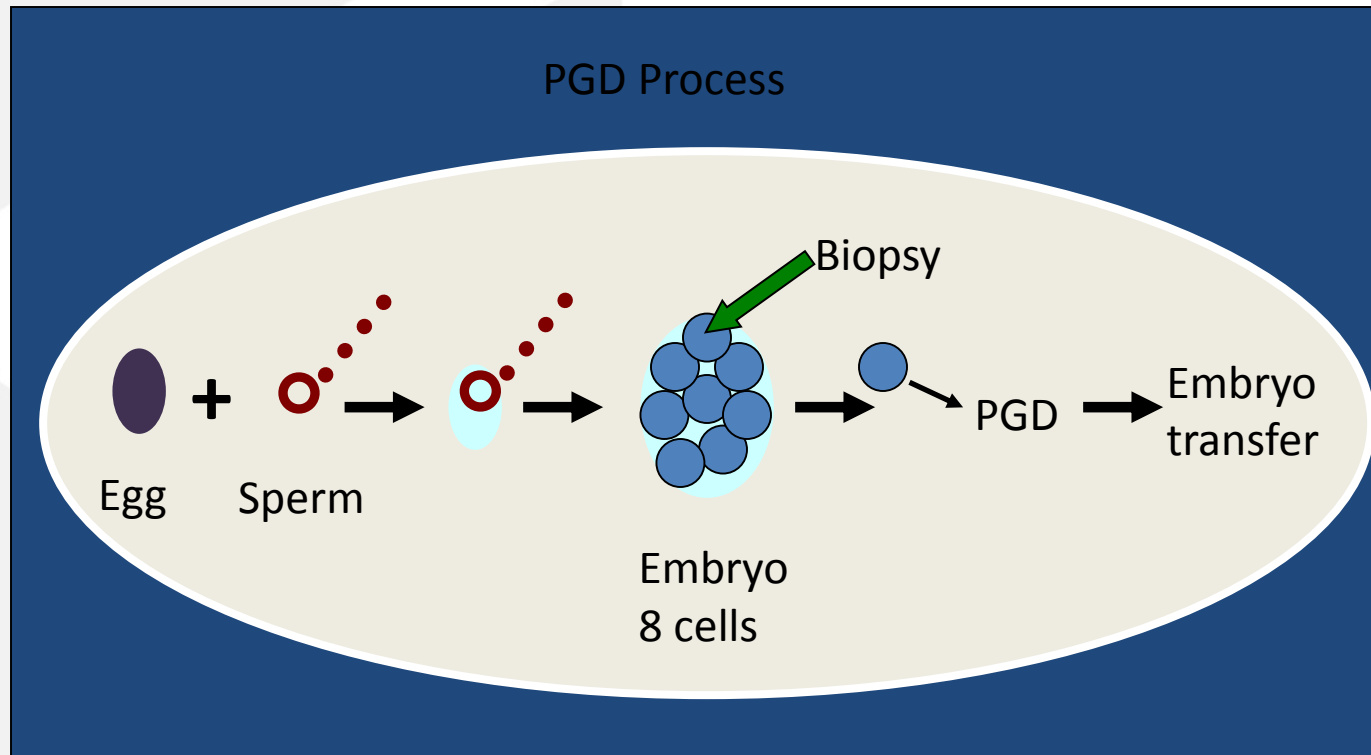
- Not knowing gene status
- Not monitoring pregnancy
- Preimplantation Genetic Diagnosis
- Prenatal diagnosis-CVS/Amniocentesis
- Sperm/Egg Donor
- Adoption

# Genetic Testing: Motivations

- 18-25 year old
  - Waiting for years to be tested
  - Education/career pathways
- 25-40 year old
  - Reproductive options
  - Financial planning
- Over 40 years
  - Want to know HD status for children
  - Financial planning



# Preimplantation Genetic Diagnosis: PGD



# Future of Prenatal Testing

- NIPT/Non invasive prenatal screening/testing
- Blood test during first trimester of pregnancy
- Cell free fetal DNA
- Determine CAG repeats
- Confirm with diagnostic test

# Family Stories

## Genetic Counseling Issues

# Prenatal HD Testing

- 25 year old pregnant woman seeks genetic counseling because partner is at risk for HD  
Wants prenatal diagnosis
- Partner is 27 years old and has not been tested; does not want to know HD status
- Issues: Couple disagrees, family pressures, who is the patient?

# Prenatal HD Testing

- 17 year old, unplanned pregnancy wants HD testing and prenatal diagnosis for HD
- Moratorium for testing minors
- Issues: who makes the decisions?

# Not knowing

- 35 year old woman with long history of infertility in early pregnancy
- Tested positive for HD gene at the age of 30
- Does not want to take small chance to miscarry with invasive diagnostic procedure
- Issues: cure/effective treatment in the future

# Adoption

- Couple at risk for HD (husband has tested positive)
- Facing the future with HD

# Unplanned Pregnancy

- 22 year old, gene positive, determined to end legacy of HD in her family
- Decides on CVS and facing 50/50 risk to fetus
- What to do?



# Asymptomatic parent

- 28 year old wants to know gene status for family planning purposes
- 45 year old mother does not want to know gene status
- What to do?

# PGD

- 30 year old at risk for HD, wants PGD but not to know her own HD status
- IVF costs, ?pregnancy rate
- IVF Center to implant only embryos without HD  
CAG expansion

# Reproductive Decision Making

- Complex issues
- Preconception genetic counseling
- Preconception psychological counseling
- Seeking help from qualified professionals
- Identifying support system

# Take Home Message

- You are not alone
- HDSA Centers of Excellence
- HDSA Predictive Testing Centers
- National Society of Genetic Counselors