Huntington's Disease Society of America

Family Planning and Huntington's Disease

Lisa Kinsley, MS, CGC
Senior Genetic Counselor
Northwestern University
Feinberg School of Medicine
Department of Neurology

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Presenter Disclosures

Lisa Kinsley, MS, CGC

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

No relationships to disclose
or list

Genetic Counseling

What is it?
Who am I?
What do I do?

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Who are Genetic Counselors?

- Health professionals with specialized graduate degrees and experience working in the areas of medical genetics and counseling
- Work as members of a health care team
- Provide information and support to families who have members with birth defects or genetic disorders and to families who may be at risk for a variety of inherited conditions
- Act as resources for other health care professionals and for general public
- Many engage in research activities related to field of medical genetics and/or genetic counseling

Genetic Counseling is…

- the process of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease

- this process integrates:
  - **interpretation** of family and medical histories to assess the chance of disease occurrence or recurrence
  - **education** about inheritance, testing, management, prevention, resources, and research
  - **counseling** to promote informed choices and adaptation to the risk or condition

Genetic Counseling Training

- Master's degree in Genetic Counseling
- 2-3 year program
- Training in medical genetics and psychosocial counseling
  - guide and support patients seeking more information about how inherited diseases and conditions might affect them or their families
  - interpret test results

Genetic Counseling Session

- Session components
  - Obtain family history
  - Give information about HD
  - Explain genetics of HD
  - Discuss motivations for testing
  - Explore person's experience with HD
  - Discuss timing of testing
  - Testing process logistics
    - Insurance coverage? Blood vs. saliva?
  - Review protections for employment, insurance discrimination
  - Results disclosure

Genetics Refresher

genes
chromosomes
proteins

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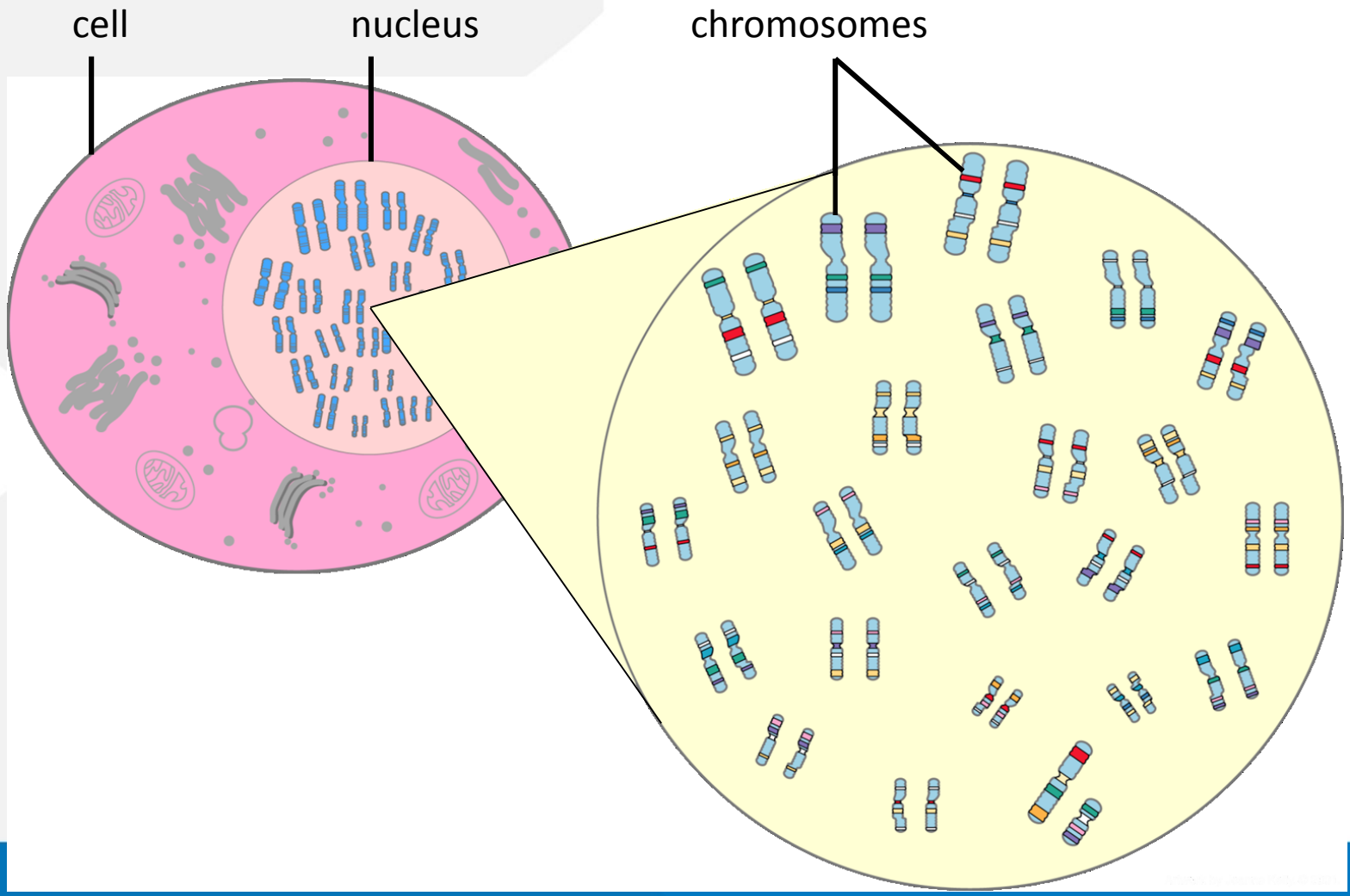
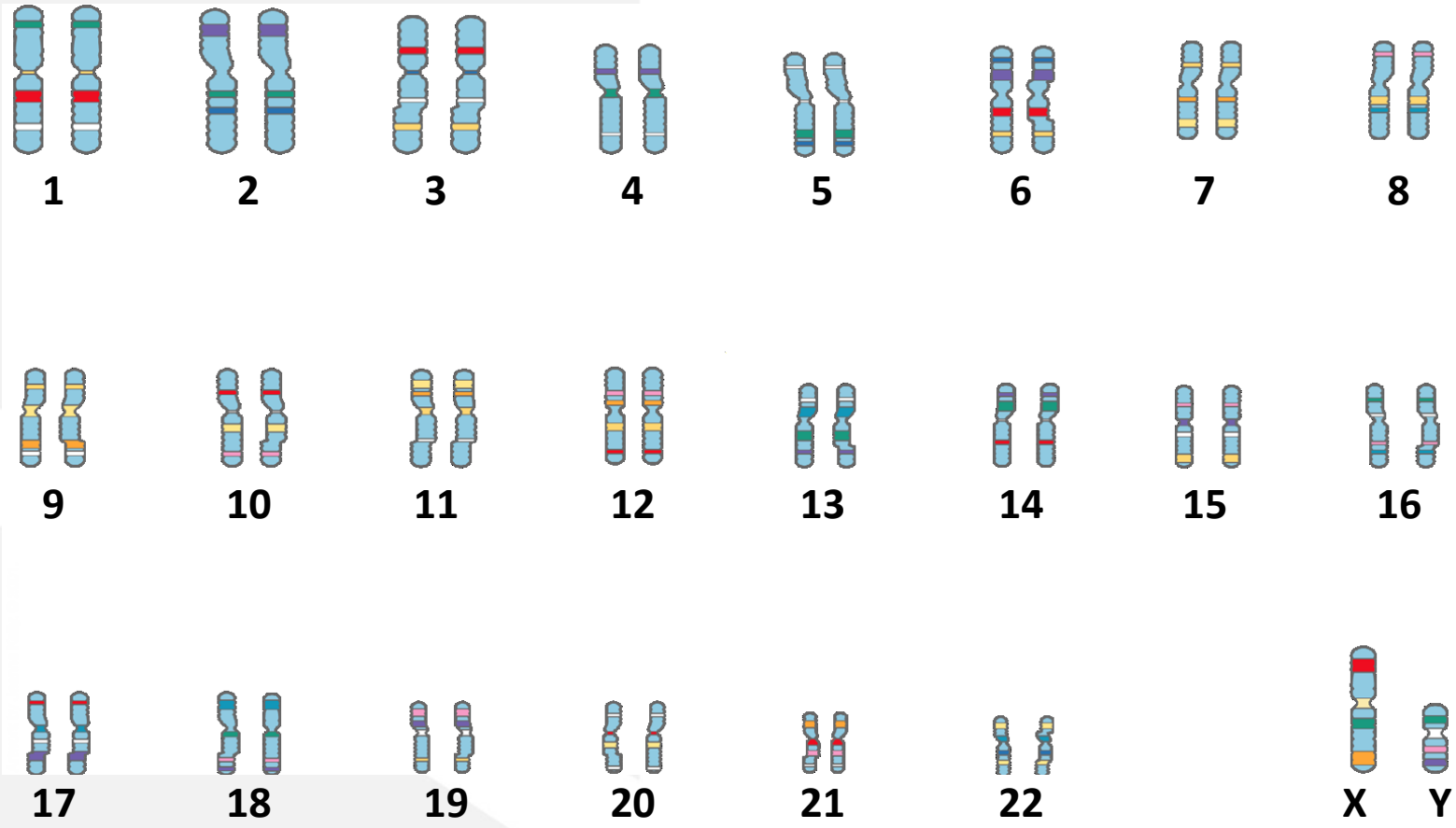
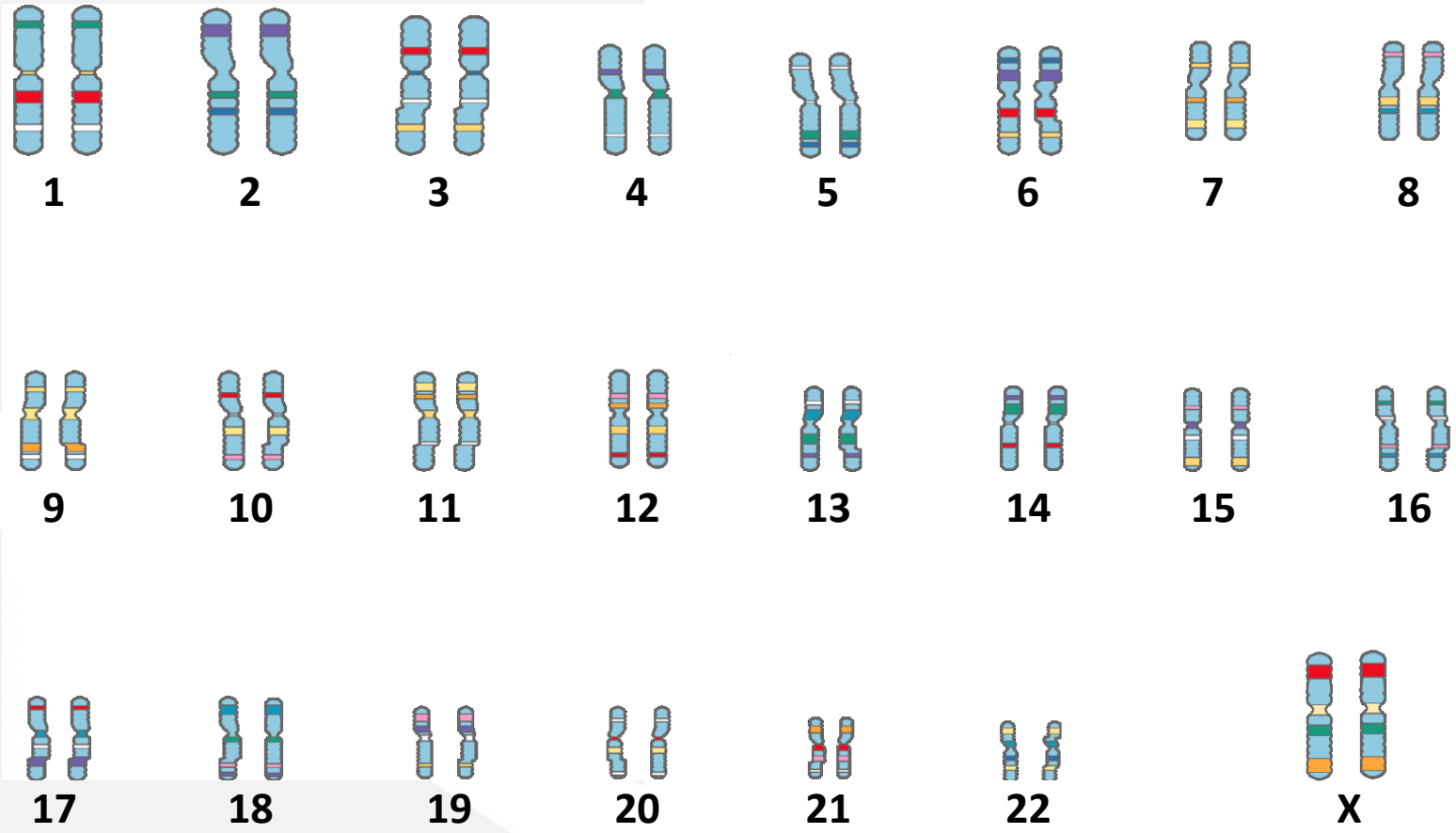
The basics



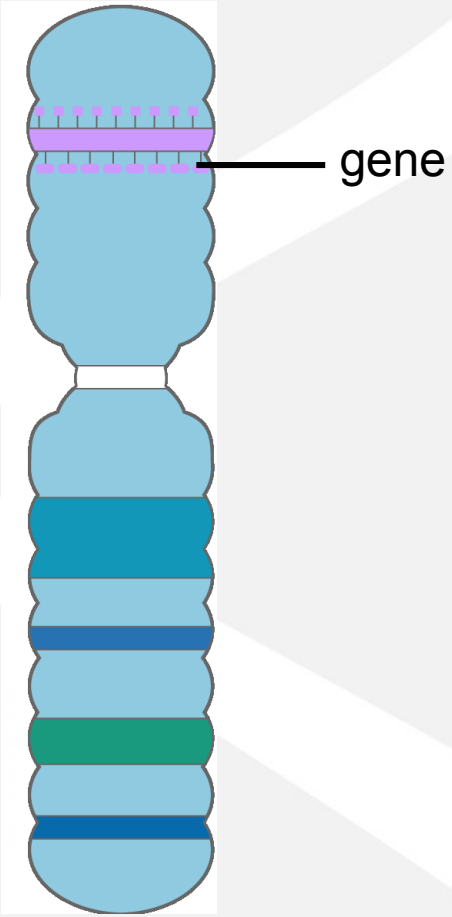
Male chromosomes

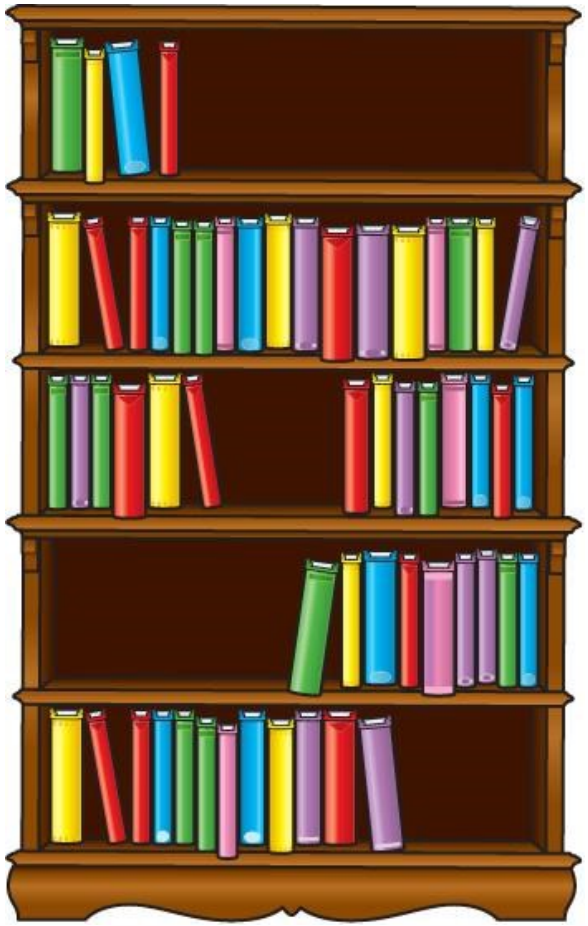


Female chromosomes

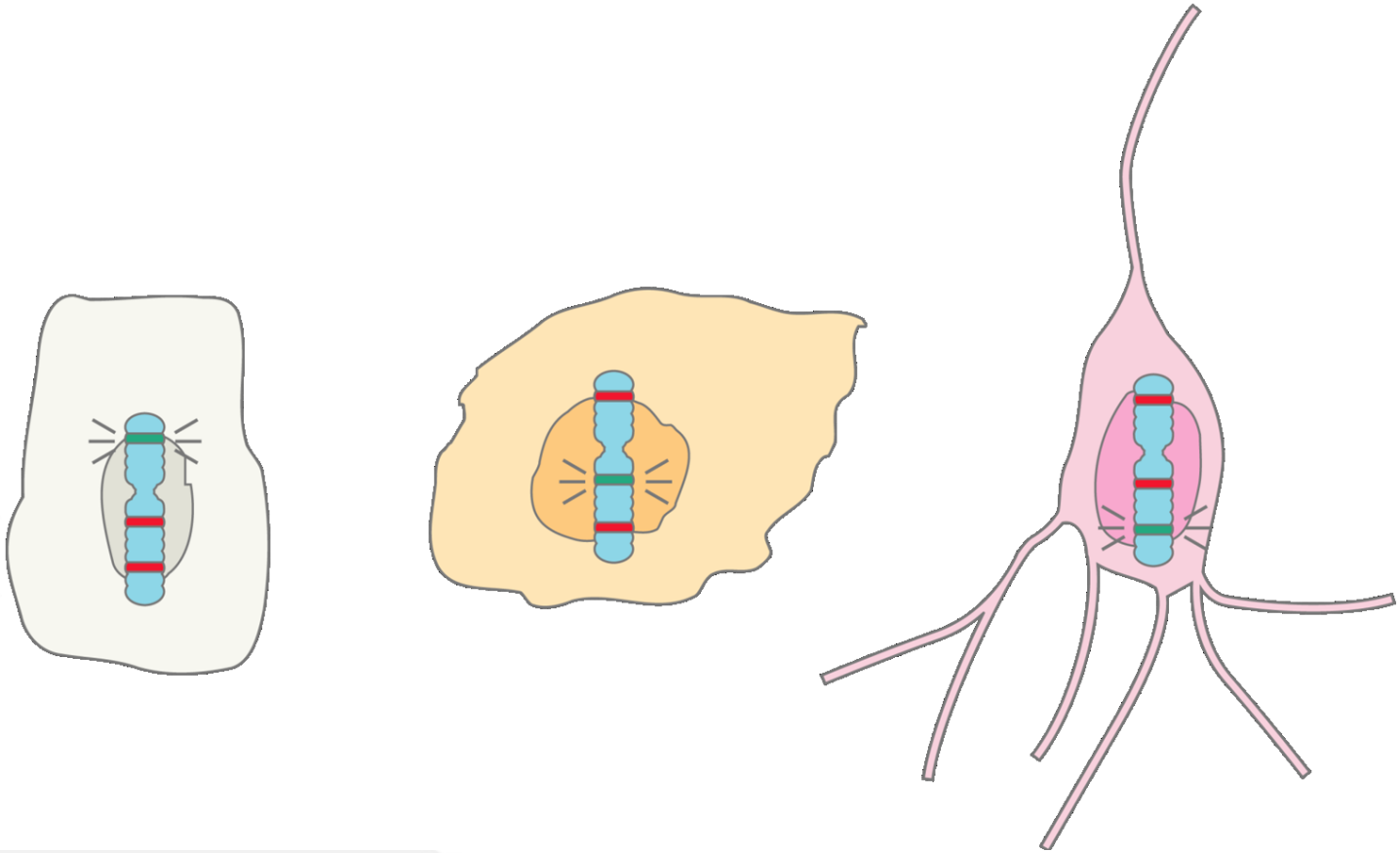


Chromosome structure





Different genes, different cells

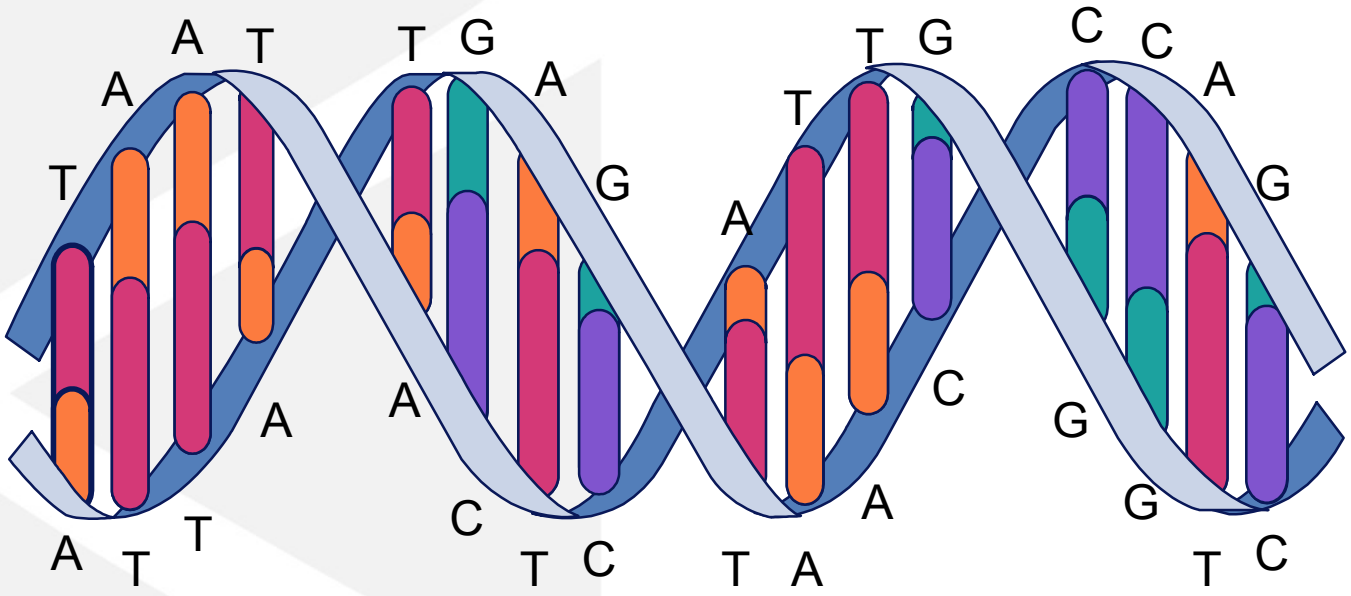


bone cell

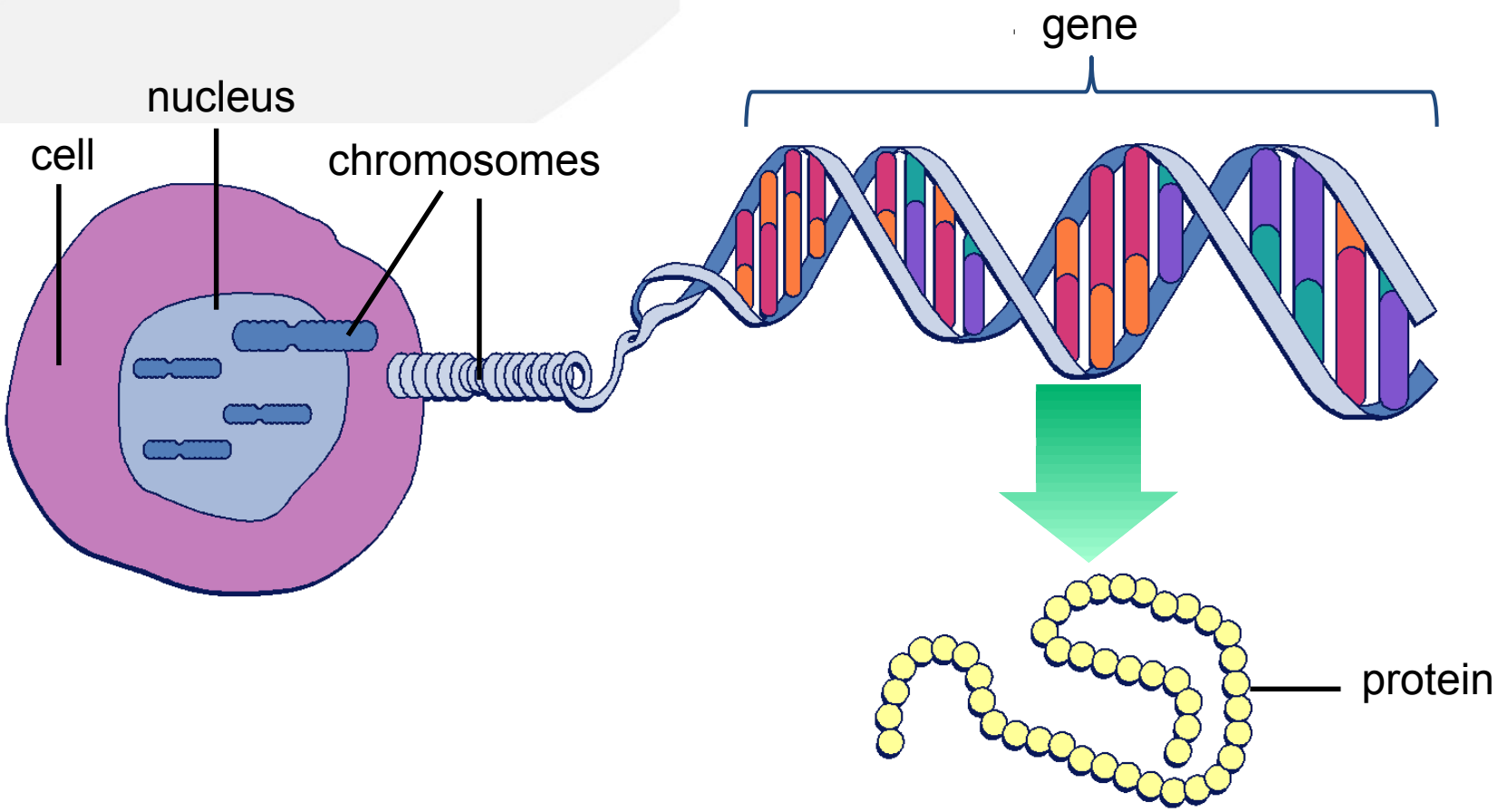
pancreas cell

brain cell

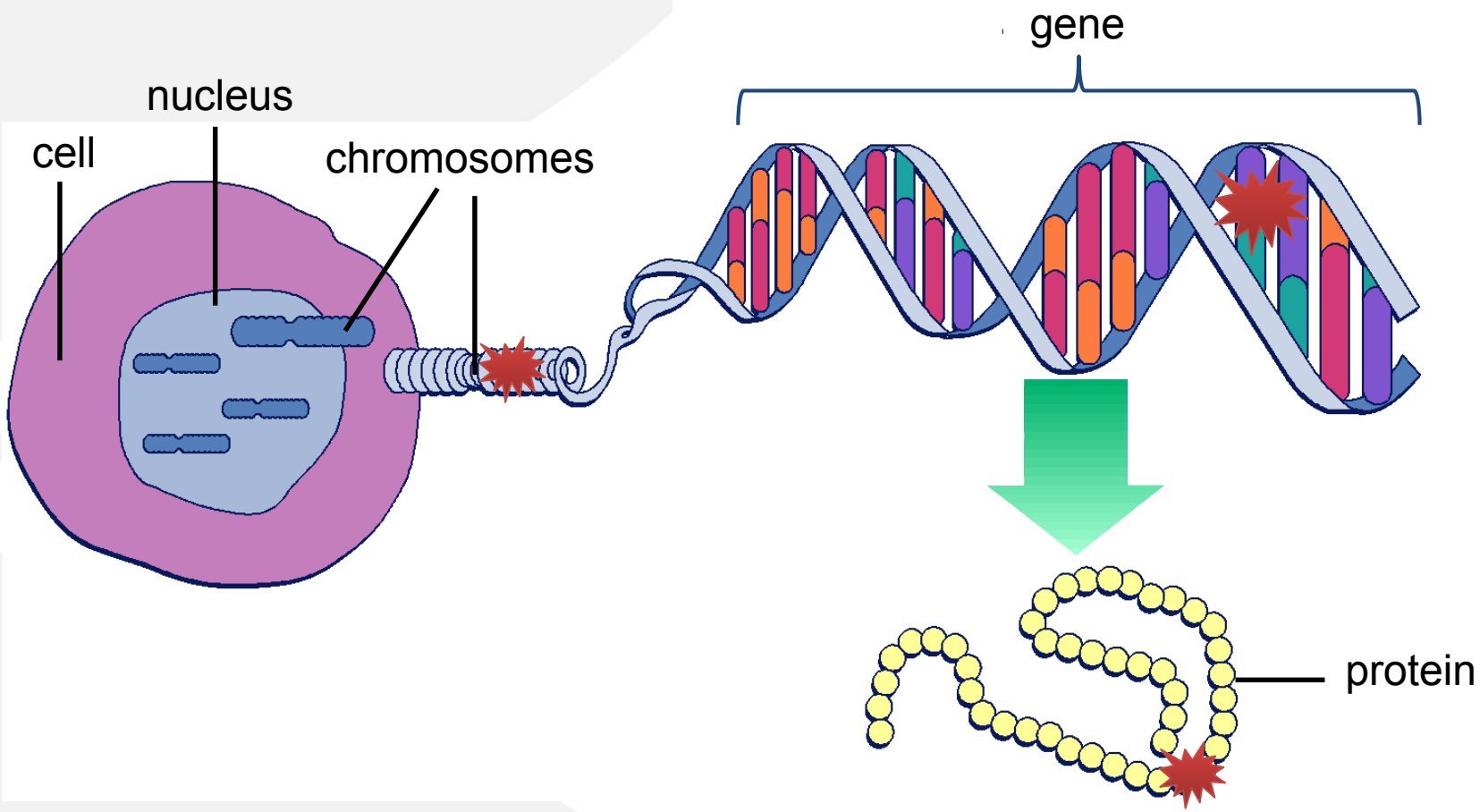
DNA



DNA to proteins



Mutated DNA leads to altered proteins



Inheritance

autosomal dominant
50% risk

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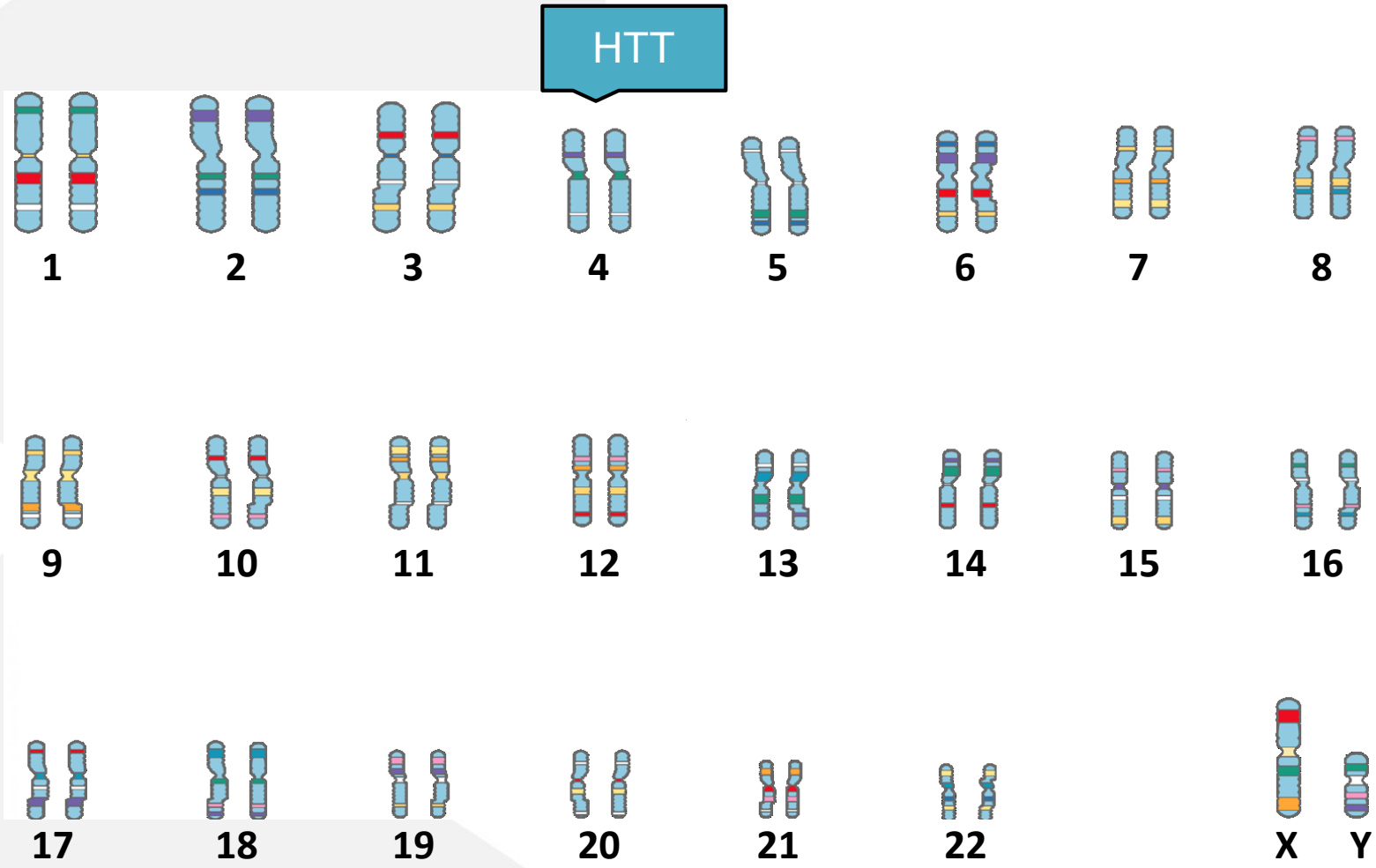
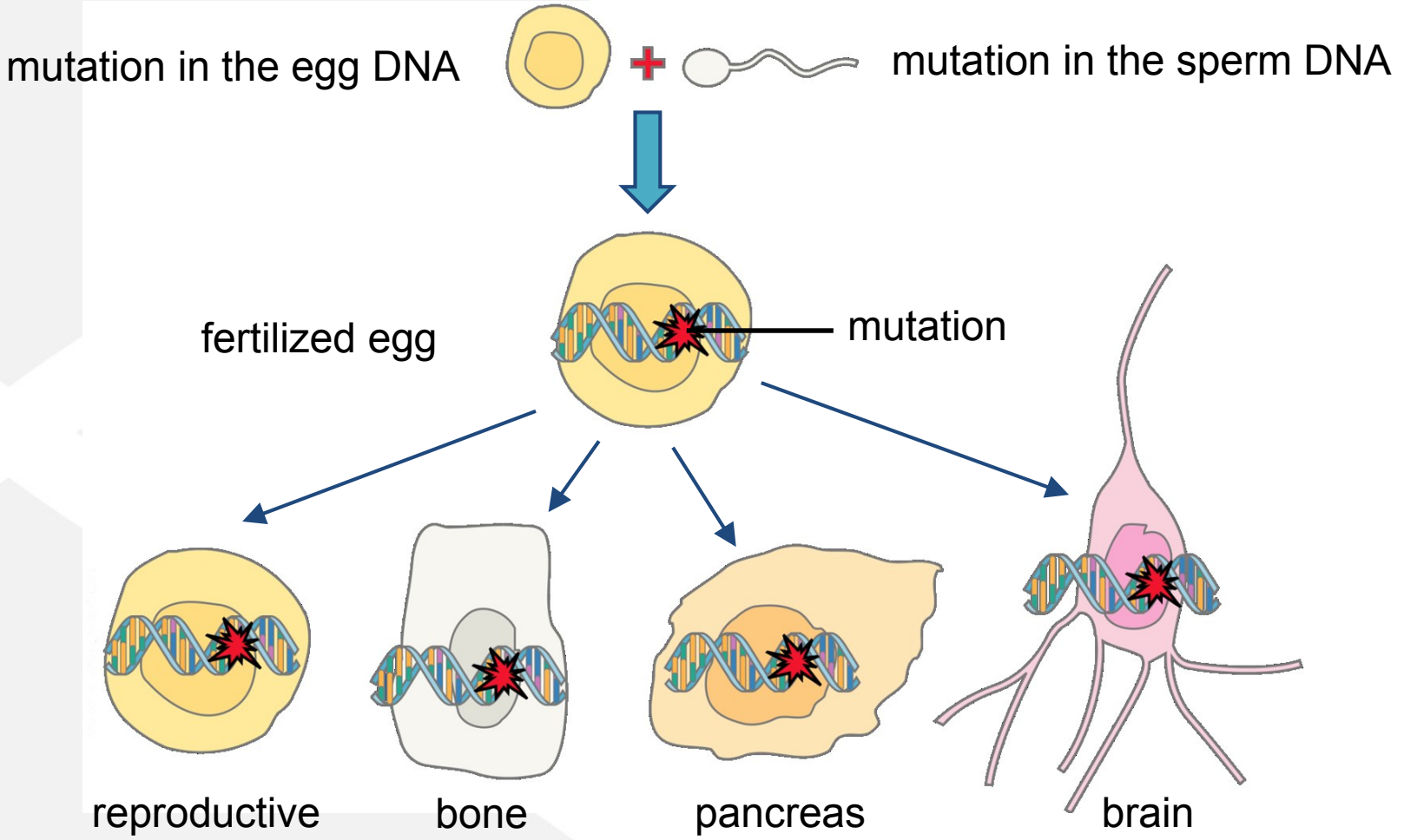
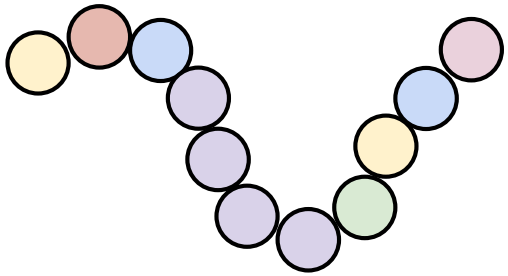
Gene location

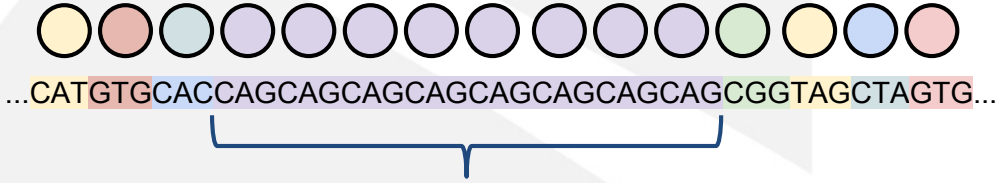


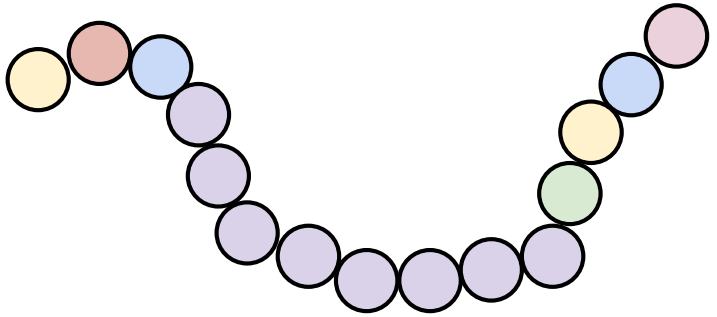
Mutation inheritance



DNA expansions







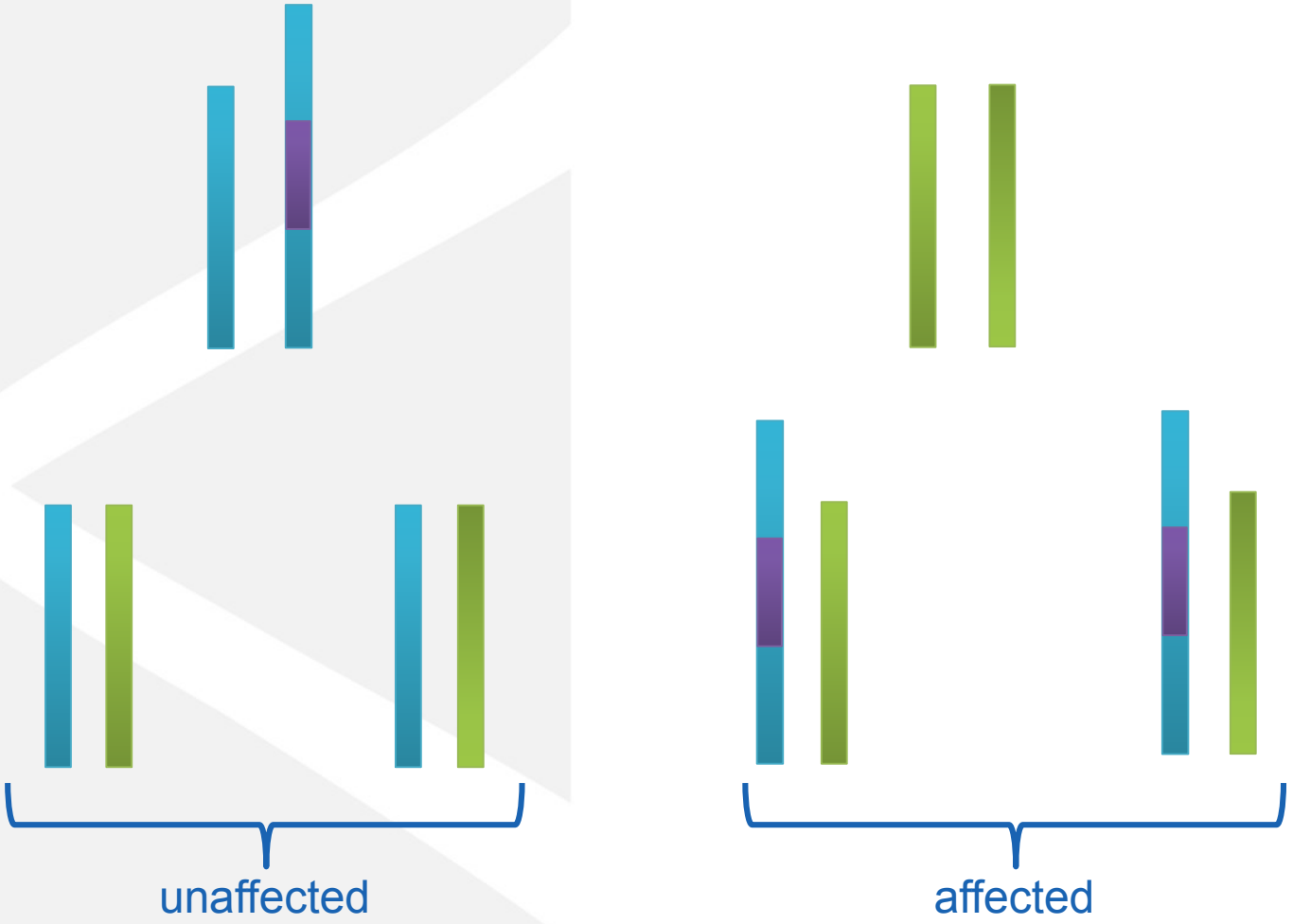
Autosomal dominant inheritance

- **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 HD, there is a 50% risk to each child

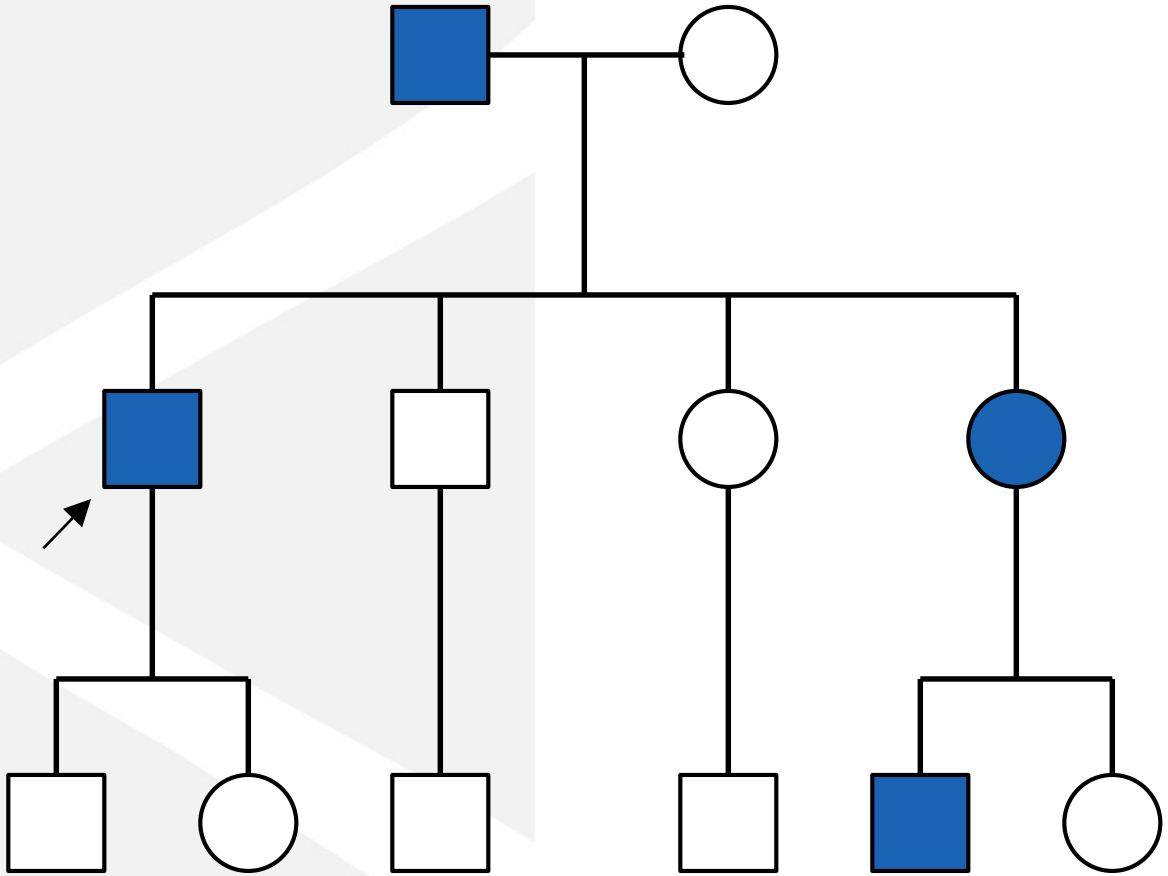
- If a person does not inherit HD from their parent, they cannot pass it to their children

- Each child of a person with HD has an **independent** 50% risk
  - Their risk is not changed by their siblings' status

Autosomal dominant inheritance



Example pedigree



HD Overview

- Onset can range from 1 year to 90 years of age
- ~6% present before the age of 20 years (juvenile HD)
- Prevalence is 7-10 per 100,000
  - Likely an underestimate
- 15-20 year duration

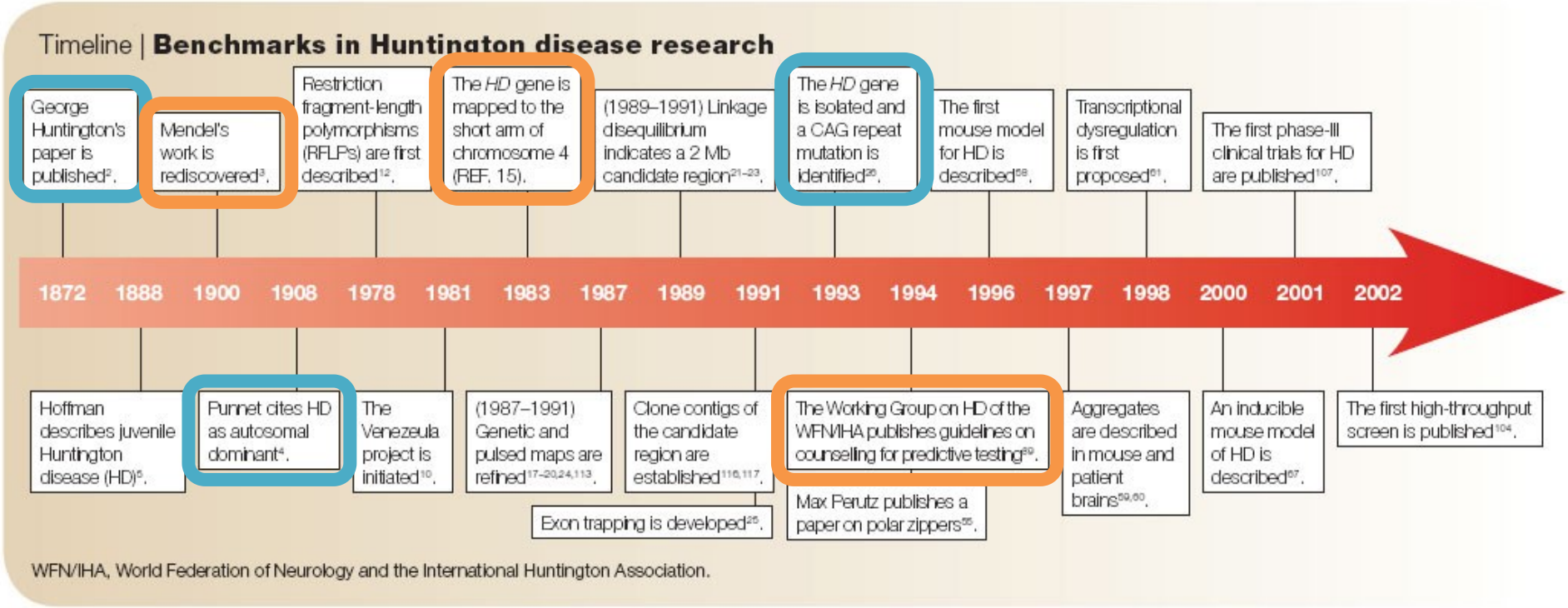
HD Anticipation

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

Genetic Testing

gene identification
diagnostic vs presymptomatic
results

History of HTT



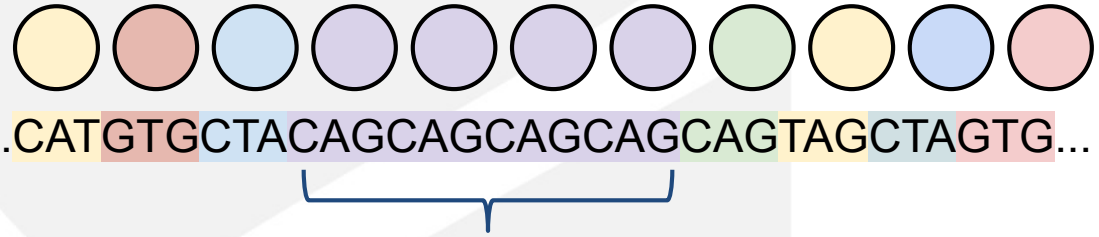
Diagnostic testing process

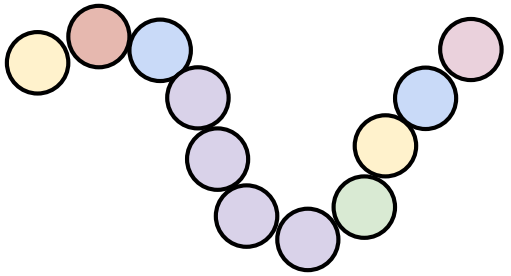
- Test is done on a blood sample
- Must be ordered by a physician
- Genetic counseling is involved in the process
- Laboratory extracts DNA from white blood cells
- Test ‘counts’ the number of repeats in each gene copy
- Final result report gives two numbers

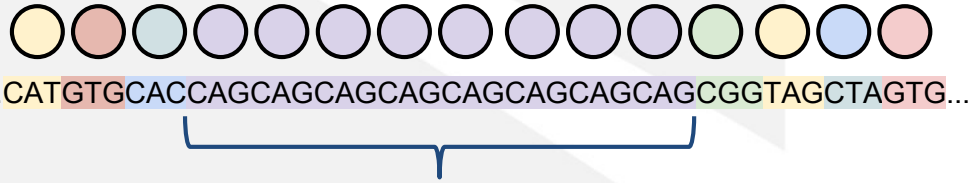
Diagnostic vs presymptomatic testing

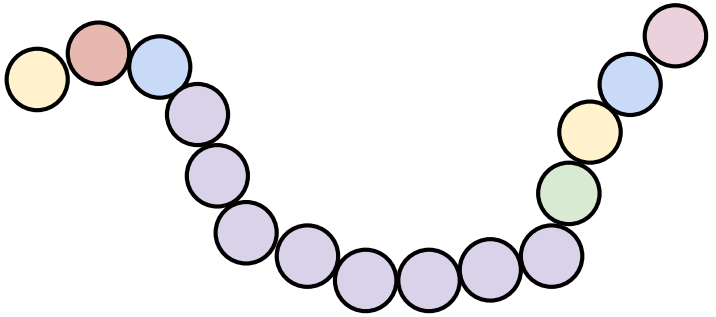
- diagnostic testing is for individuals who have symptoms
  - fairly straightforward
  - can have psychosocial implications
- presymptomatic testing is for individuals who are risk of developing symptoms
  - need family information for this to be an option
  - very likely to have psychosocial implications
  - Huntington's disease testing protocol
    - » meet with genetic counselor and neurologist
    - » pre-test counseling, exam, results disclosure, post-test followup
- cannot prevent or predict for many adult onset conditions
  - onset of symptoms, age of onset, or disease progression

DNA expansions









Expansion sizes

Normal alleles	26 or fewer CAG repeats	unaffected
Intermediate alleles Mutable normal alleles Gray zone alleles	27-35 CAG repeats	not at risk of developing symptoms of HD, but because of instability, may be at risk of having a child with an allele in the HD-causing range.
Reduced-penetrance alleles	36-39 CAG repeats	at risk for HD but may not develop symptoms. In rare cases, elderly asymptomatic individuals with CAG repeats in this range have been identified
HD-causing alleles Affected alleles Full-penetrance alleles	40 or more CAG repeats	Huntington Disease

Size of expansion is inversely correlated with age of onset but do not provide an exact age.

Reproductive Options

testing a pregnancy
adoption
donor egg or sperm
IVF with PGD

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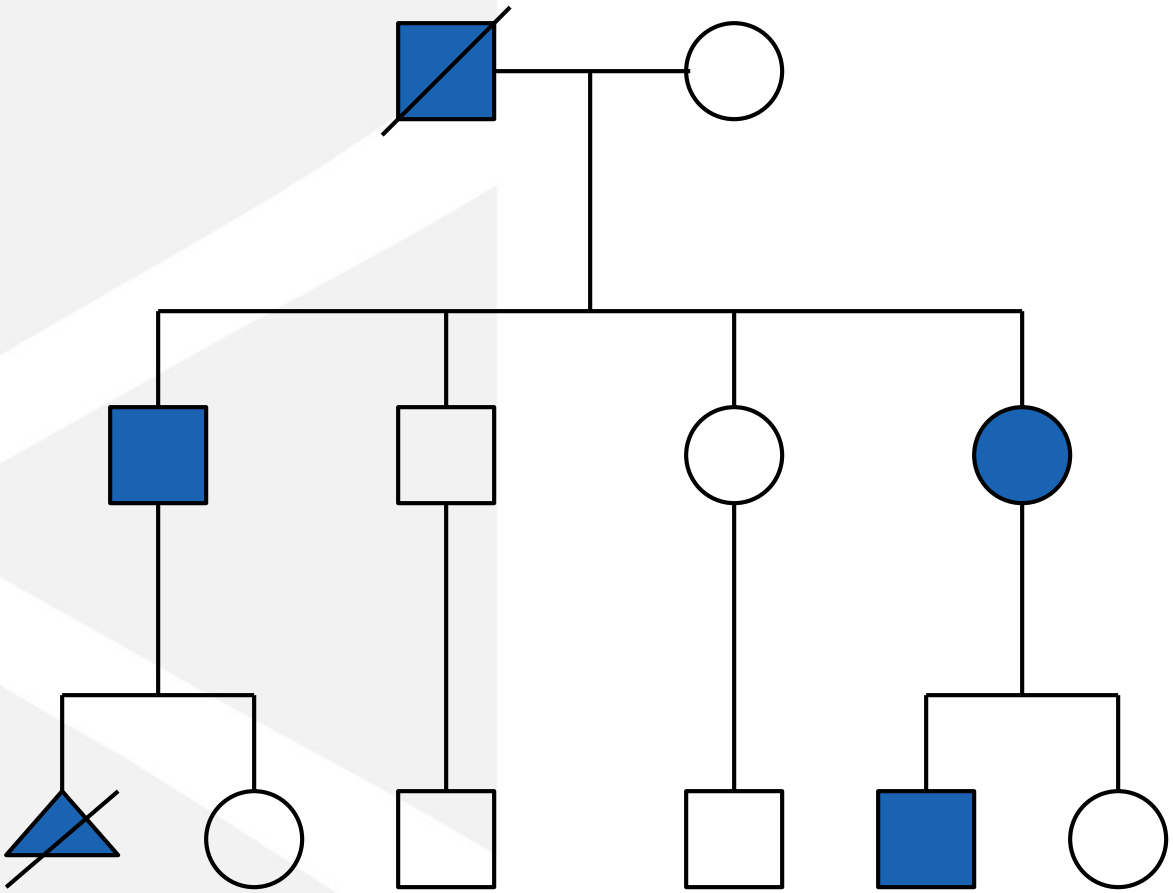
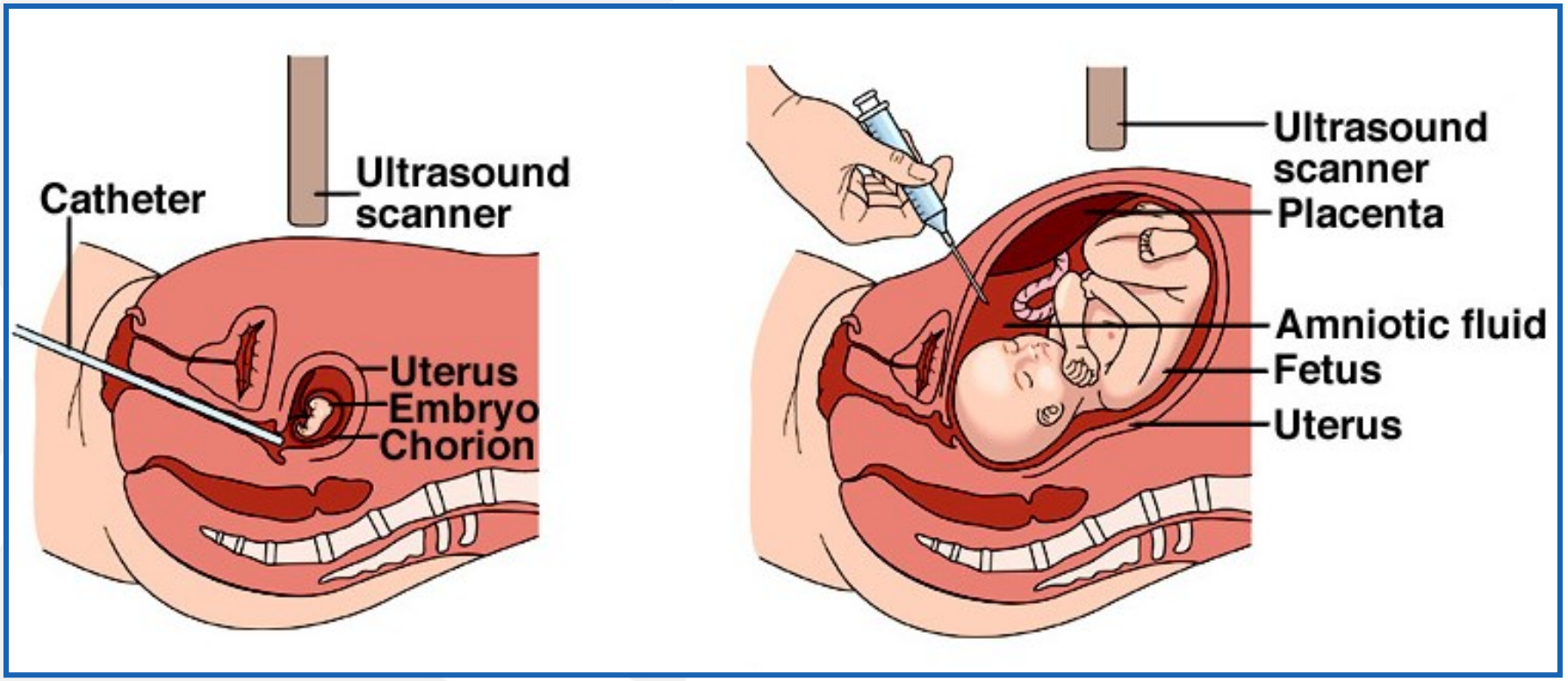
Prenatal testing



Testing a pregnancy



Chorionic villus sampling
10 – 12 weeks

Amniocentesis
15 – 20 weeks

Testing a Pregnancy

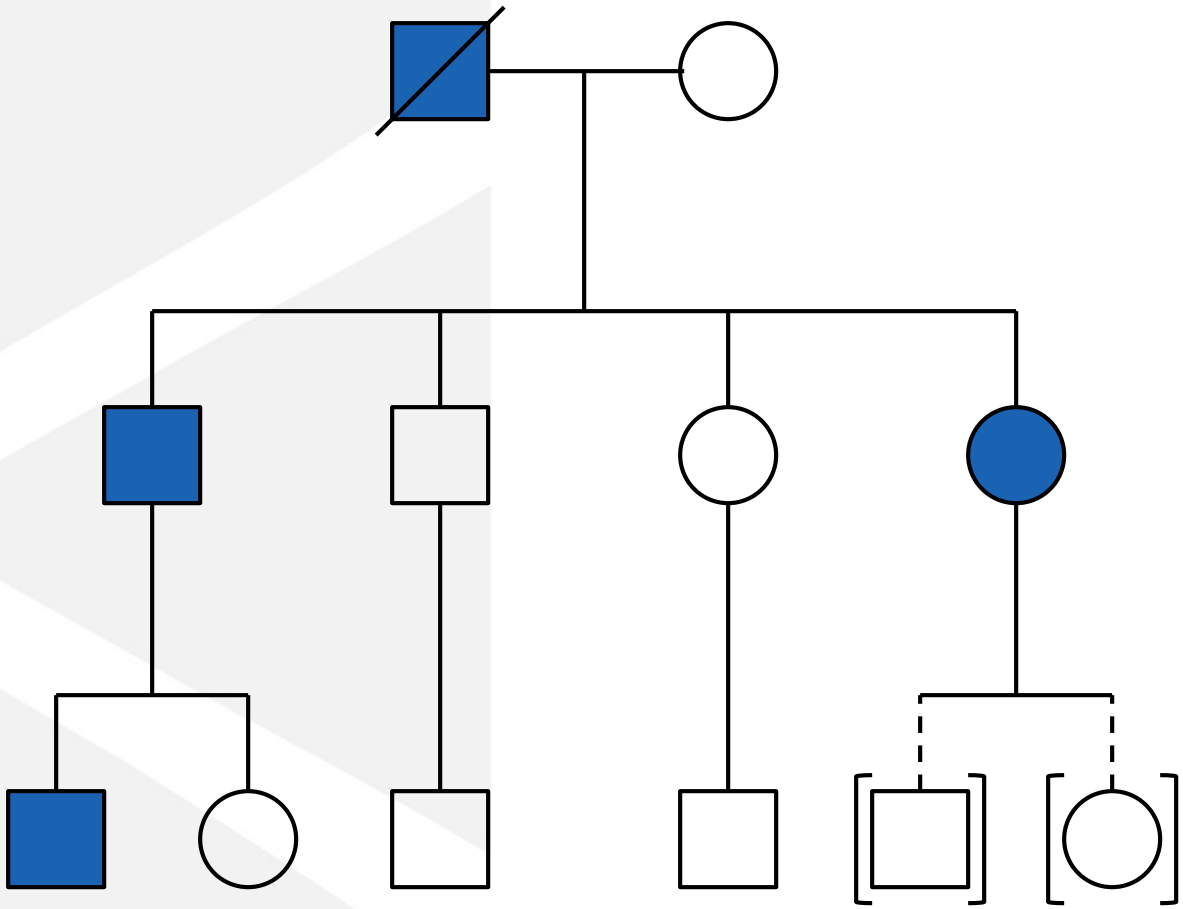
Pros

- Greatly reduces risk of passing on disease
- “Natural pregnancy”
- Biological relationship with offspring

Cons

- May have ethical considerations with decision to terminate pregnancy
- Costs will vary
- Procedure carries small risk of miscarriage
- Could reveal untested parent’s status

Adoption



Adoption

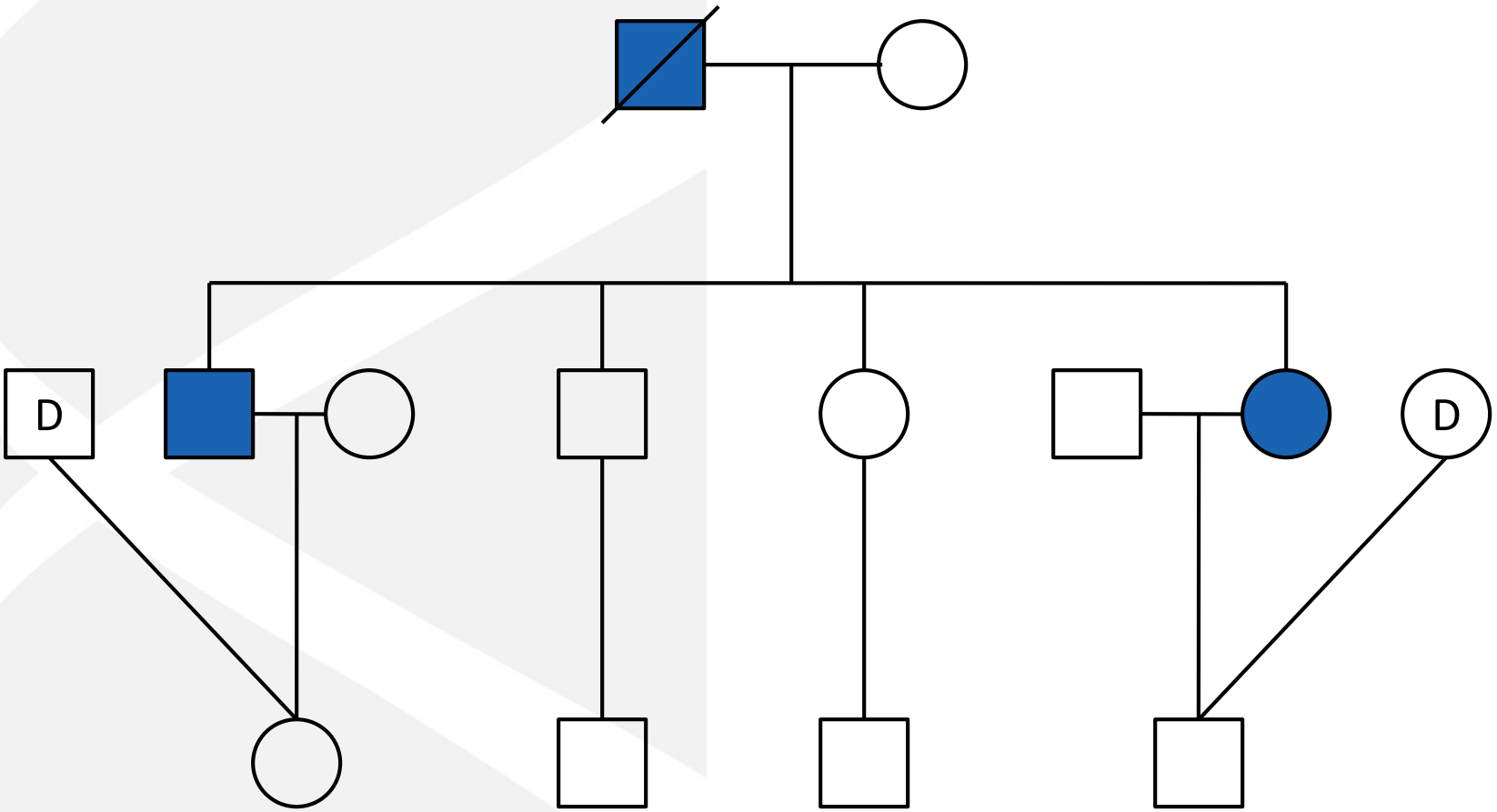
Pros

- Eliminates risk of passing on disease
- Helping a child, family, or woman in need

Cons

- Expensive process
  - ~$20,000
- Long process
- No biological relationship
- Possible long-term sequelae of adoption

Donor egg or sperm



Donor gametes

Pros

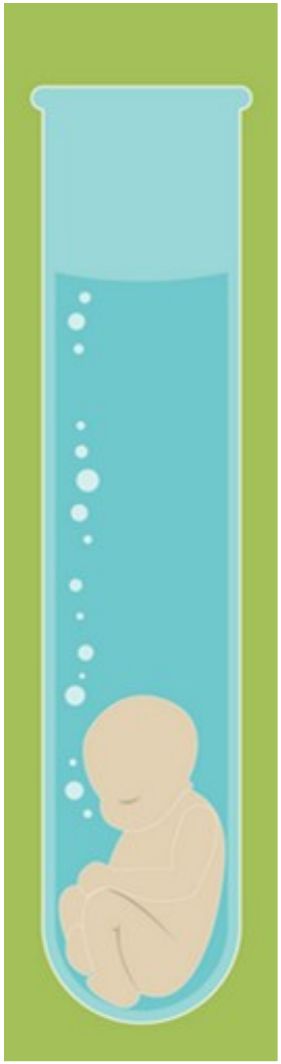
- Eliminates risk of passing on disease

Cons

- May involve several processes
  - *In-vitro* fertilization (IVF)
  - Artificial insemination
  - Egg donor/surrogacy
- Costs vary
  - $8,500 for donor eggs
  - $500 for donor sperm
- No biological relationship

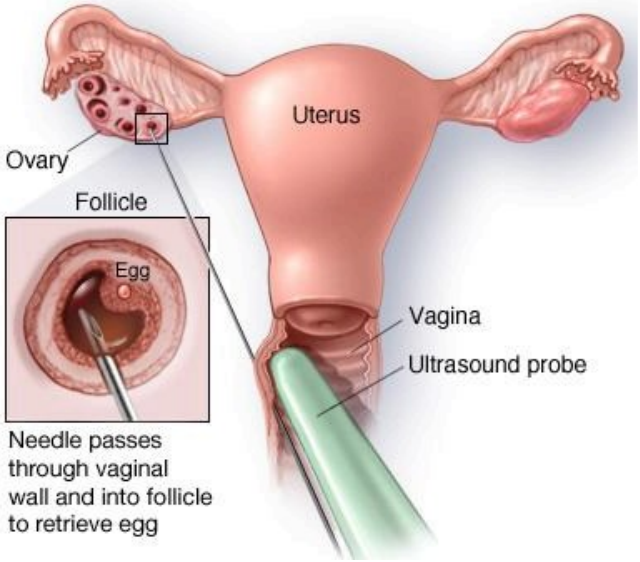
Preimplantation genetic diagnosis

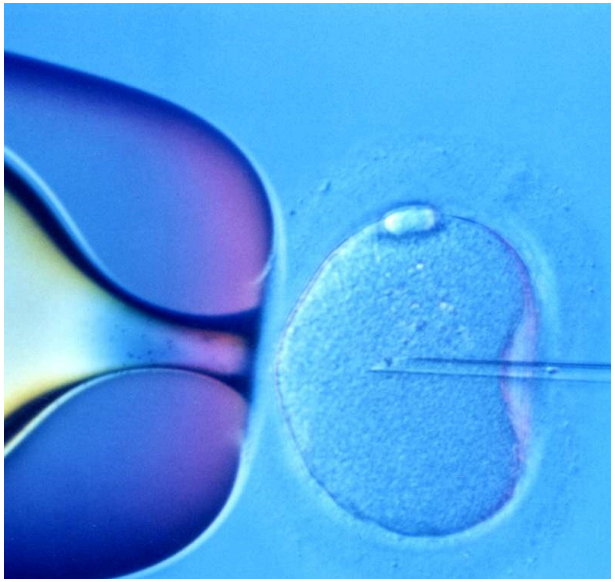
- aka PGD
- Method of screening embryos for a known genetic condition
- Must be performed in conjunction with IVF
  - Literally means ‘fertilization in glass’
  - Historically referred to as ‘test tube babies’

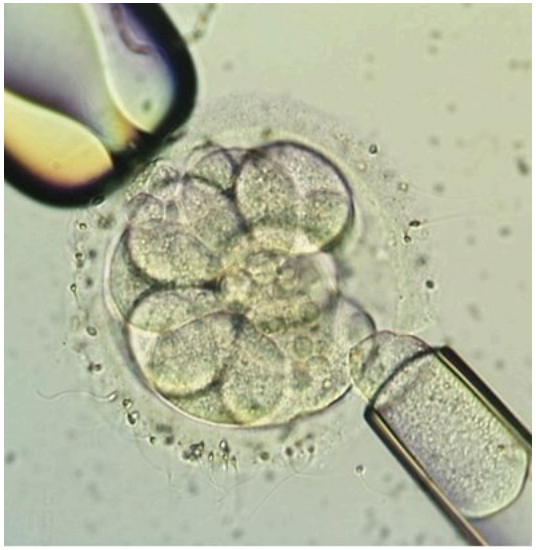


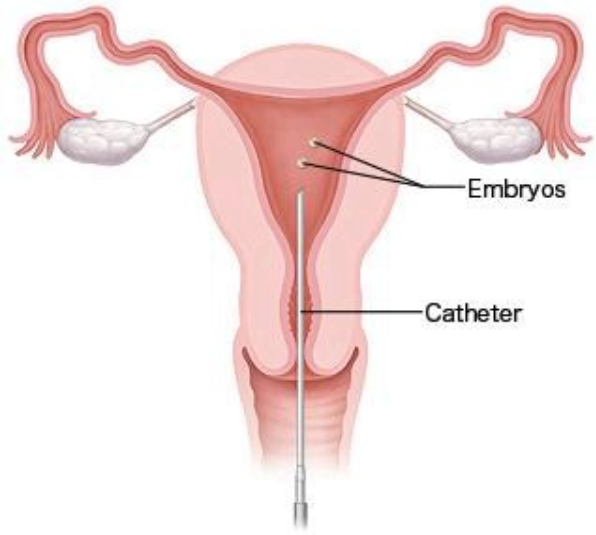
IVF with PGD


BD Vacutainer
Lithium Heparin
68 USP units
REF 367884
BD Vacutainer
SST™
REF 367986


Uterus
Ovary
Follicle
Egg
Vagina
Ultrasound probe
Needle passes through vaginal wall and into follicle to retrieve egg






Embryos
Catheter


pregnant
not pregnant

IVF with PGD

Pros

- Significantly reduces risk of passing on disease
- Non-disclosure testing available
- Reduced guilt
- No increased risk of birth defects
- Biological relationship
- Acceptable option for at-risk couples that would not consider terminating an affected pregnancy

Cons

- 'Experimental'
  - Maximum accuracy is 98%
  - DNA contamination
  - Testing process can fail
- Emotional and ethical considerations
  - Discarding embryos that could lead healthy, productive lives
- 'Take-home Baby' rate
- Can't predict future
- Risk of prenatal testing, multiple births
- May involve several processes
- Expensive process

IVF with PGD - financial

- IVF cycles
  - $16,000 - $18,000
    - Drugs are $3,000 - $5,000
  - Donor eggs ~$8,500
  - Donor sperm $500
- PGD testing per cycle
  - Additional $2,500 - $6,000
- More than one cycle is usually necessary
- Can be an economic barrier
- 15 of 50 states have laws requiring coverage
  - Eight states mandate coverage of IVF

Use of preimplantation genetic diagnosis for serious adult onset conditions: a committee opinion

Ethics Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Birmingham, Alabama

"PGD for adult-onset conditions is ethically justified when the condition is serious and no safe, effective interventions are available. It is ethically allowed for conditions of lesser severity or penetrance. The Committee strongly recommends that an experienced genetic counselor play a major role in counseling patients considering such procedures."

Family Stories

Genetic counseling issues
Things to consider

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Prenatal Testing

- 25 year old pregnant woman seeking genetic counseling because her partner is at risk for HD.
- She wants prenatal diagnosis.
- Partner is 27 years old and has not been tested. He does not want to know his HD status.

- Issues
  - Couple's disagreement
  - Family pressures from both sides
  - Who is the patient?

Adoption

- Couple at risk for HD – husband has tested positive
- Still want to start a family
- Considering adoption

- Issues
  - Facing future with HD
  - No guarantee of any child having two healthy parents
  - Will adoption agency ask about health?

Asymptomatic Parent

- 28-year-old wants to know her gene status for family planning purposes
- Her 45-year-old mother does not want to know her genetic status

- Issues
  - Testing daughter could reveal mom's status
  - Disagreement
  - Right to information
  - Keeping health information from family members
  - How to proceed?

Things to consider

- Must have a confirmed familial mutation!
- PGD can have implications for family members' risks
- Can undergo IVF with PGD without learning one's own status
- None are risk free, but reproductive options do exist for HD families

- Complex issues involved
- Seek help from qualified professionals
- Identify your support system

Take Home Messages

- HD is an autosomal dominantly inherited condition
- Family planning options exist for individuals who want to reduce the risk of passing the condition on to their children
  - Each method has pros and cons
- Affected and at-risk individuals can benefit from genetic counseling
- Genetic counseling can answer questions and address options for testing, family planning, and research participation

Any questions?

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