the FOUNDATION for PERIPHERAL NEUROPATHY®

Welcome!

FPN Webinar:

Hereditary Neuropathy and Genetic Testing
with Sami L. Khella, MD
and Shawna Feely, MS, LGC

Thursday, October 6, 2022

Sponsored by: Alnylam® PHARMACEUTICALS

We will begin our presentation shortly.

the FOUNDATION for PERIPHERAL NEUROPATHY®

Moderator:

Lindsay Colbert
Executive Director
the Foundation *for* Peripheral Neuropathy

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Before We Begin

This presentation is being recorded. The recording link will be emailed to you so you can view it again later.

Submit your questions anytime via the Questions Box. We will try to answer them during this webinar.

If you are having trouble with the audio using your computer, you can dial in by phone (check your email for dial-in instructions).

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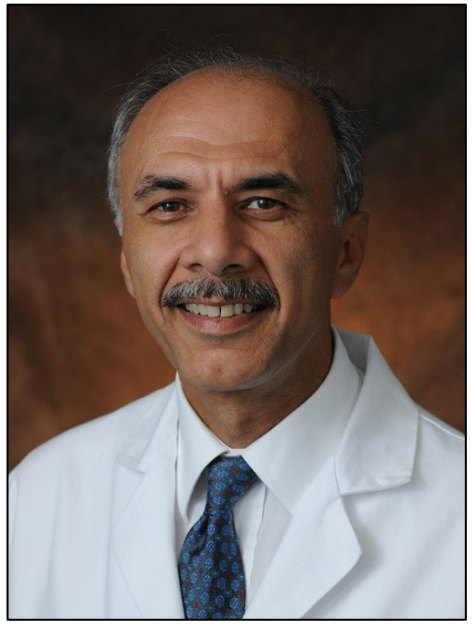
Presenters:



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Hereditary Neuropathies

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Certified Genetic Counselor
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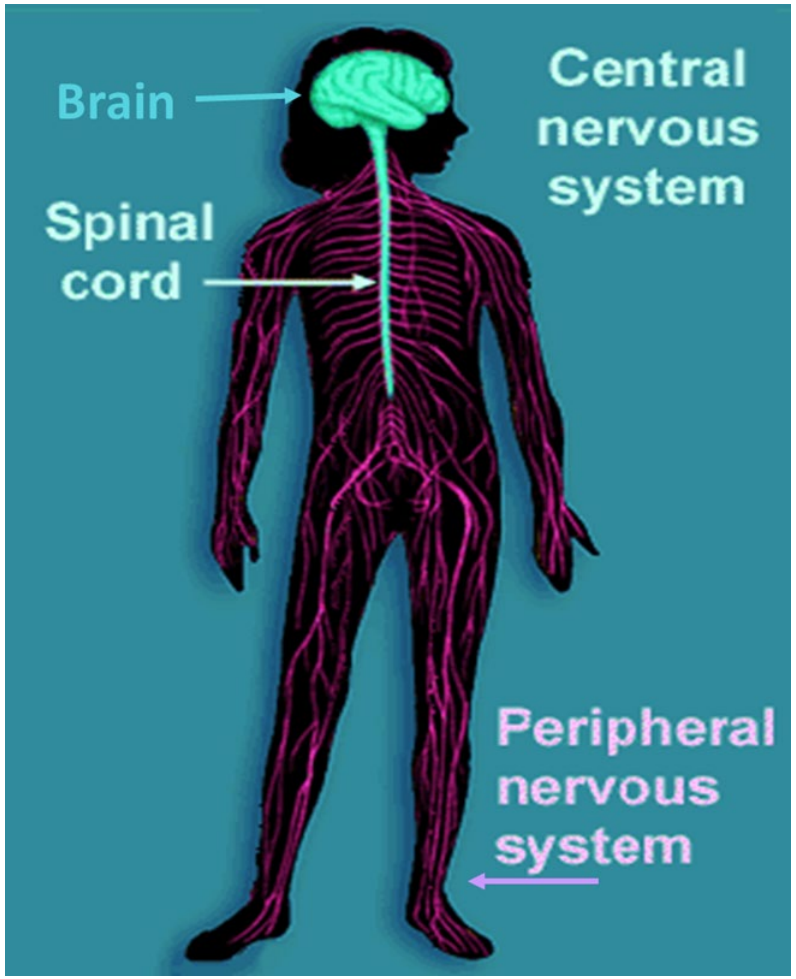
Overview

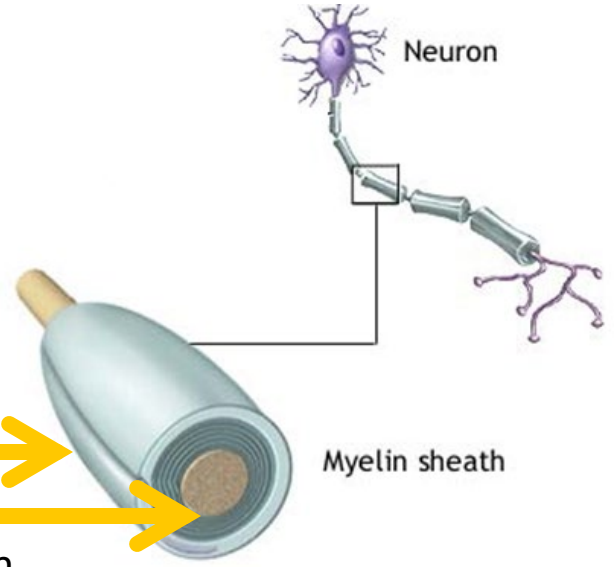
- What is Hereditary Peripheral Neuropathy?
- Different forms of Hereditary Neuropathy
- What is genetic testing?
- Why do people get genetic testing?
- What is genetic counseling?

What Hereditary Peripheral Neuropathy?



Types of Hereditary Neuropathy

- Neuropathies: Primary diseases of nerve
- Peripheral Nerves
  - Demyelinating Neuropathy
  - Axonal Neuropathy
- Clinical Hallmarks
  - Distal muscle weakness and atrophy
  - Loss of proprioception and abnormal sensation
  - Classical steppage gait, pes plannus or pes cavus
  - Fatigue and depression can often accompany disease
- Genetic heterogeneity
  - Hundreds of known genetic causes



General subtypes of Hereditary Neuropathies

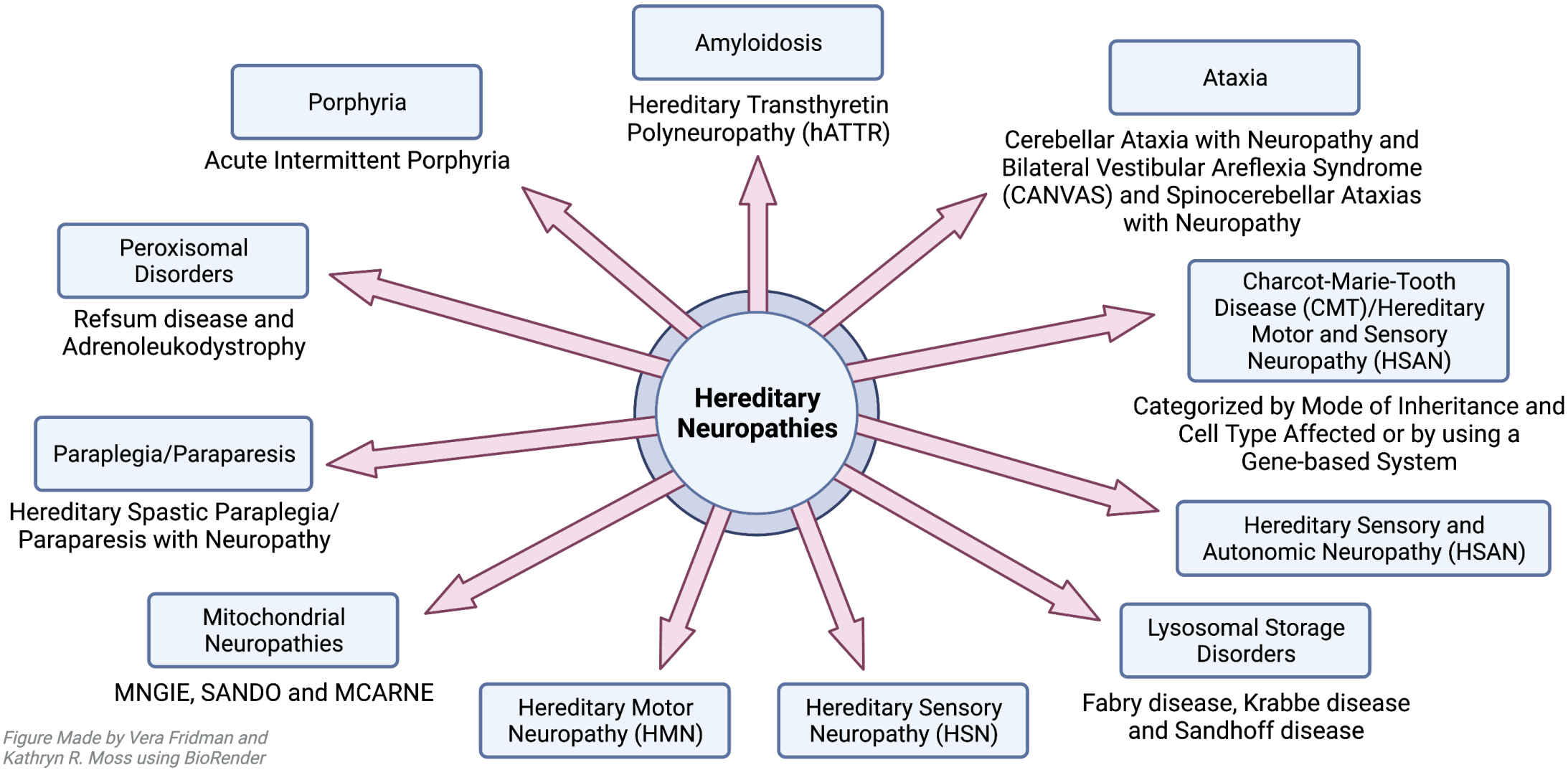
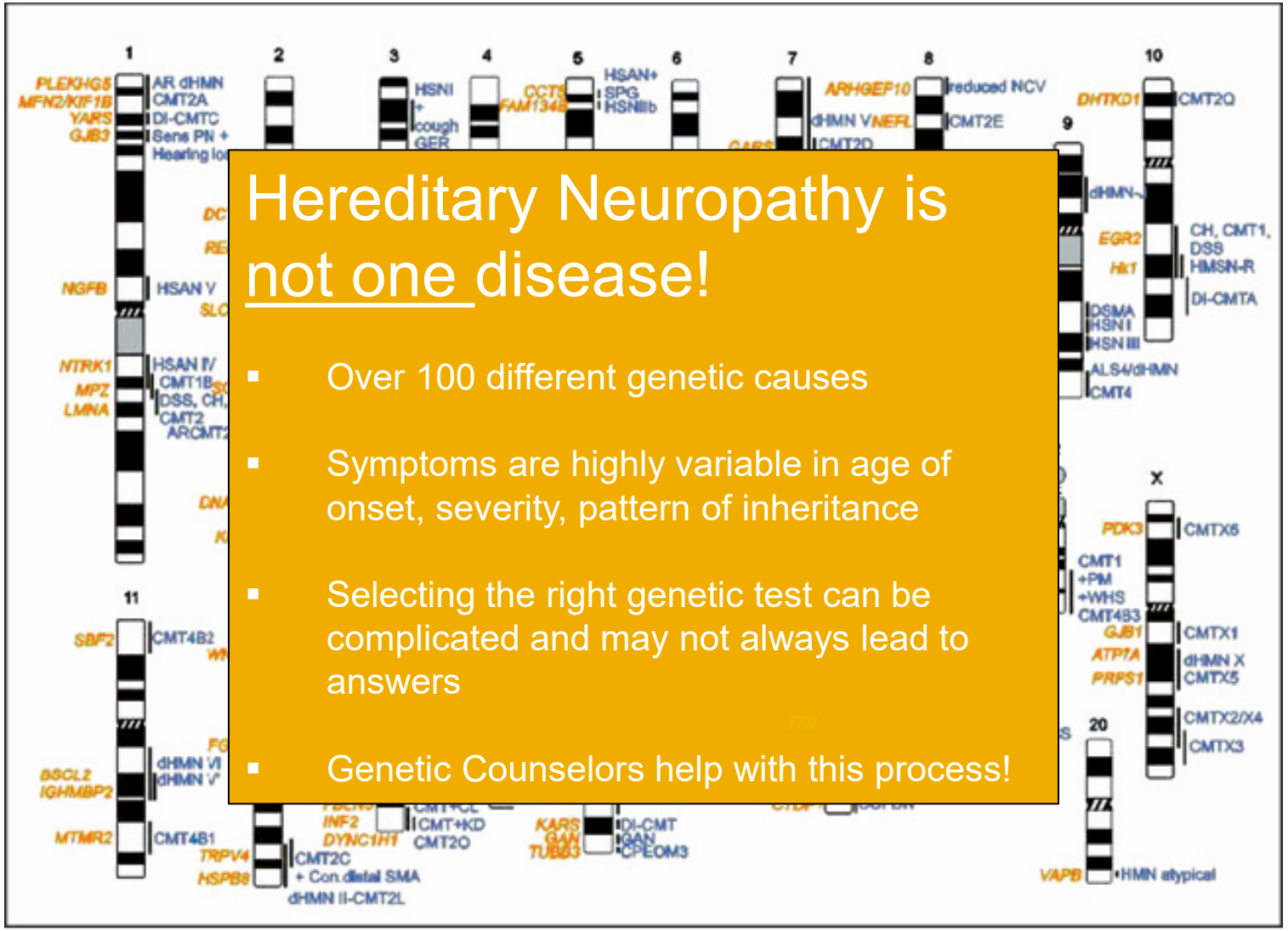


Figure Made by Vera Fridman and Kathryn R. Moss using BioRender

What is genetic testing?

- Typically, medical genetic testing involves a blood test to look for changes in genes associated with a certain medical condition.
- This type of specialty testing often goes through a specialty lab and has to be ordered by a physician or provider.
- Genetic testing can be complex , many genes, many labs, and different costs can lead to confusion.



Hereditary Neuropathy is not one disease!

- Over 100 different genetic causes
- Symptoms are highly variable in age of onset, severity, pattern of inheritance
- Selecting the right genetic test can be complicated and may not always lead to answers
- Genetic Counselors help with this process!

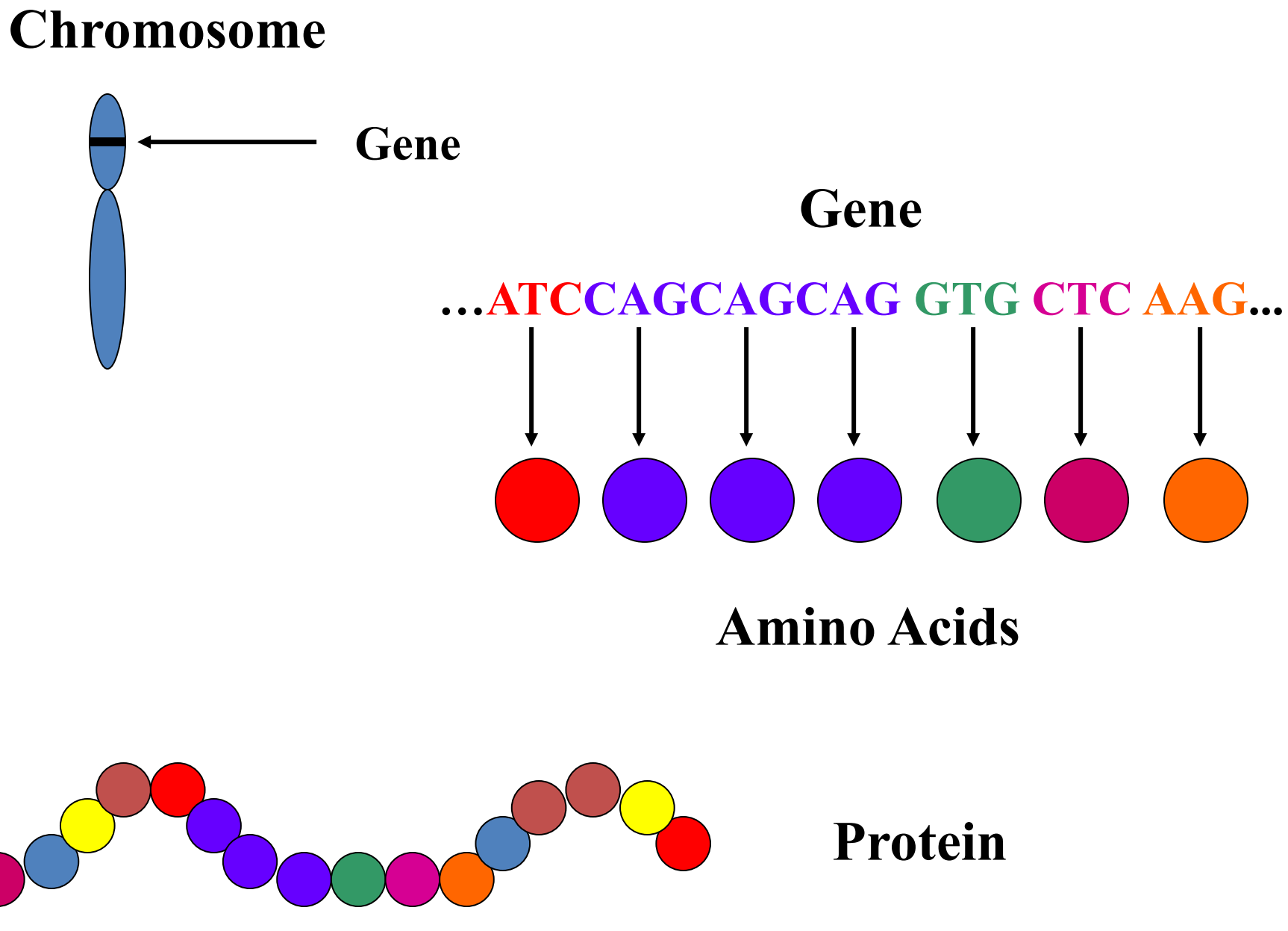
Figure-2: Genes and loci for Charcot-Marie-Tooth (CMT) and related inheritedperipheral neuropathies.

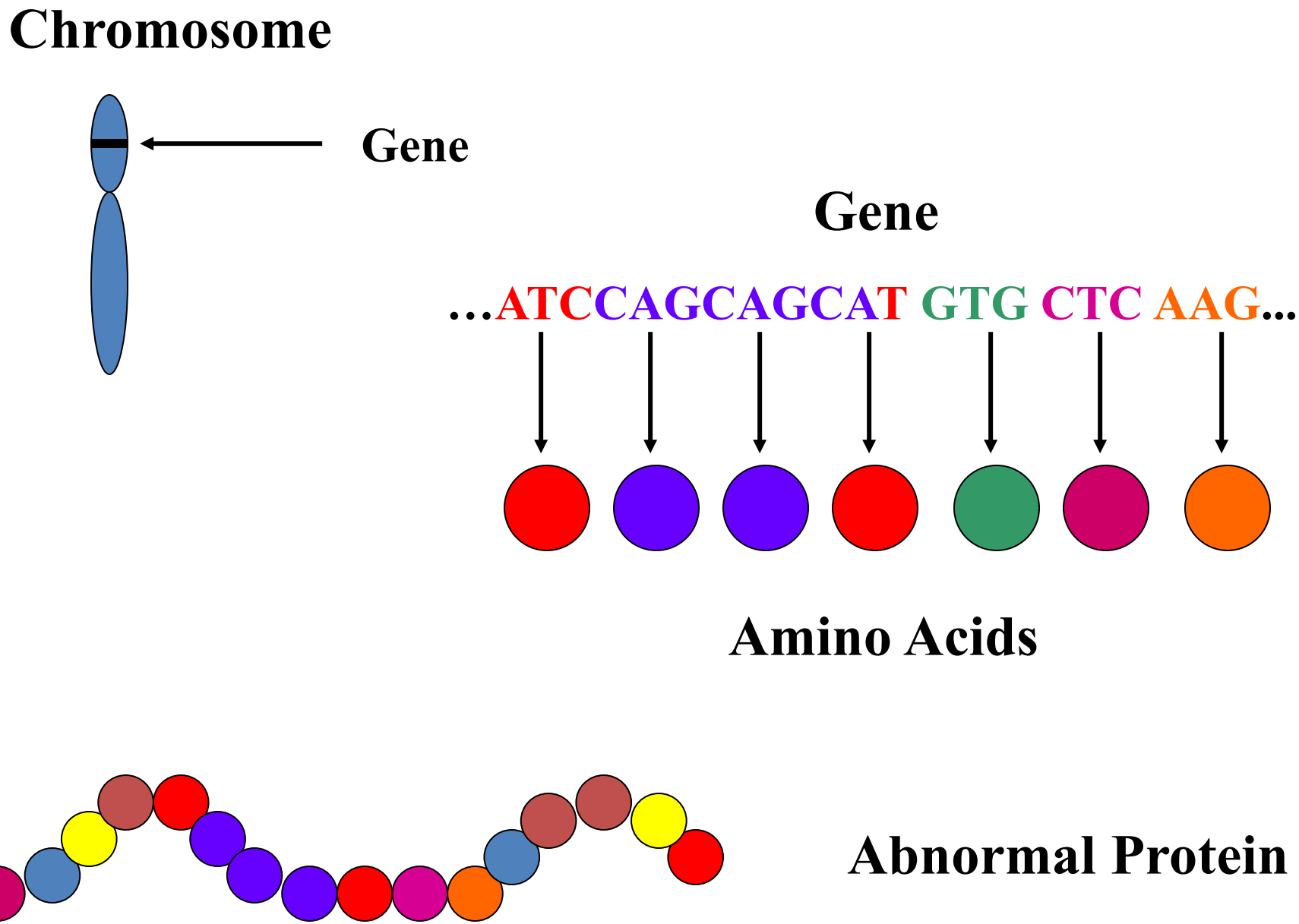
Perveen et al 2015, JPMA

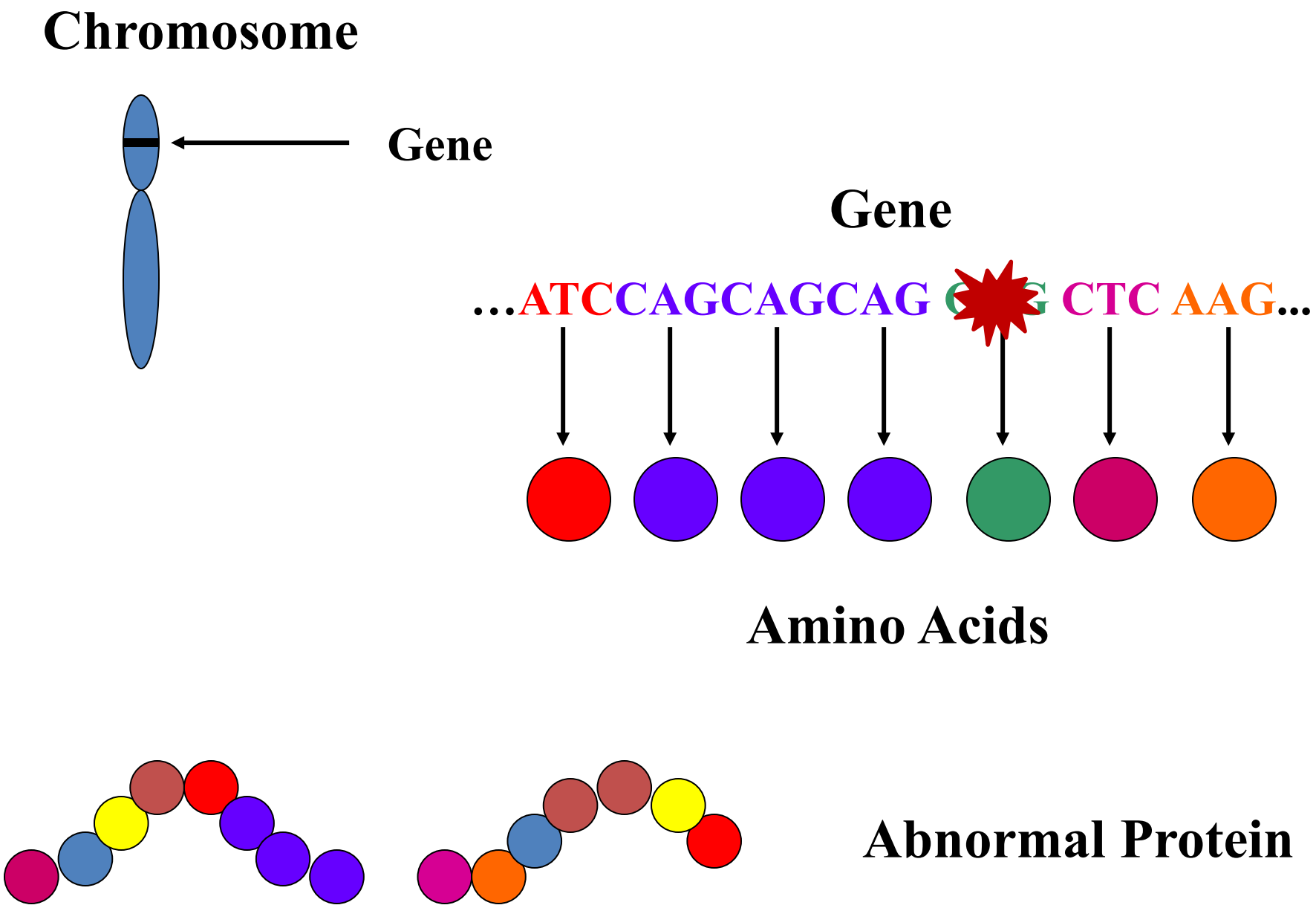
Many labs do genetic testing for Neuropathy

Not all genetic testing is the same!

- Labs differ in cost, what insurance is accepted for coverage, genes that are included in their testing, and the number of genes that are tested
- Panels change from year to year for all these things
- Genetic Counselors help people living with genetic disease to navigate this process!


Chromosome
Gene
Gene
…ATCCAGCAGCAG GTG CTC AAG…
Amino Acids
Protein


Chromosome
Gene
Gene
…ATCCAGCAGCAT GTG CTC AAG…
Amino Acids
Abnormal Protein


Chromosome
Gene
Gene
…ATCCAGCAGCAG CTC AAG…
Amino Acids
Abnormal Protein

Genetic Counselors role

- Process of helping people understand and adapt to the medical, psychological, and familial implications of genetic contributions to disease (NSGC.org)
- Help to guide through the testing process
- Facilitate the most cost-effective approach to testing
- Identify the most likely way to get a positive result
- Review the pros and cons of testing for patients to make an informed choice
- Interpret genetic information and inform / educate patients

Genetic Testing: Pros

- To determine if other family members are at risk
- Family planning

Family Planning Options

BIOLOGICAL CHILDREN

- **During Pregnancy:**
  - Chorionic Villus Sampling (CVS)
    - As early as 10 weeks
  - Amniocentesis
    - Typically past 15 weeks
  - Maternal fetal cell analysis
    - Not yet available for CMT
- **Before Pregnancy:**
  - Preimplantation Genetic Testing (PGT)
  - Costs ~$20,000 - $25,000

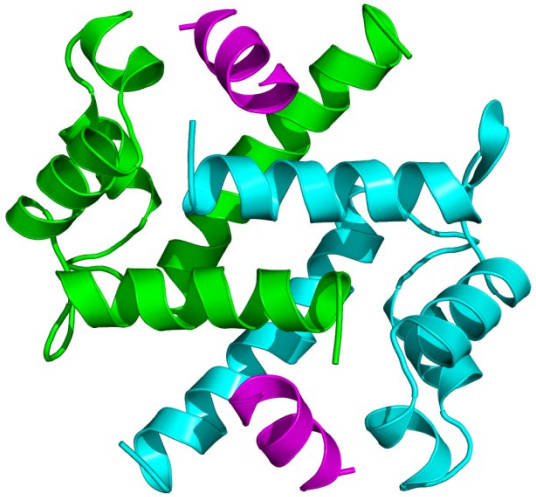
DONATION/ADOPTION

- **Donor options**
  - Sperm donation (banks)
    - Costs ~$1,000
  - Egg donation
    - Costs ~$15,000 - $50,000
- **Embryo Adoption**
  - Costs ~$10,000 - $15,000
- **Traditional Adoption**
  - Costs ~$10,00 - $40,000

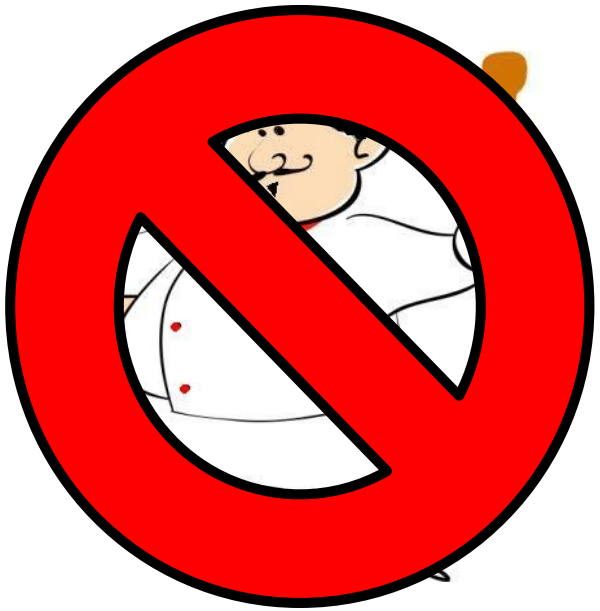
Genetic Testing: Pros

- To determine if other family members are at risk
- Family planning
- Having a definitive diagnosis
- Possible access to treatments or clinical trials (example is gene therapy, gene silencing)

Our Genetic Recipe



Our Genetic Recipe



Genetic Testing: Cons

- May have inconclusive results – what then?
- Emotional impact on the family system of positive *or* negative results
- May not have a genetic test available – research-based testing
- Genetic Discrimination – GINA & YOU / HIPPA
- Cost
- Other issues like testing children / non-paternity

Summary

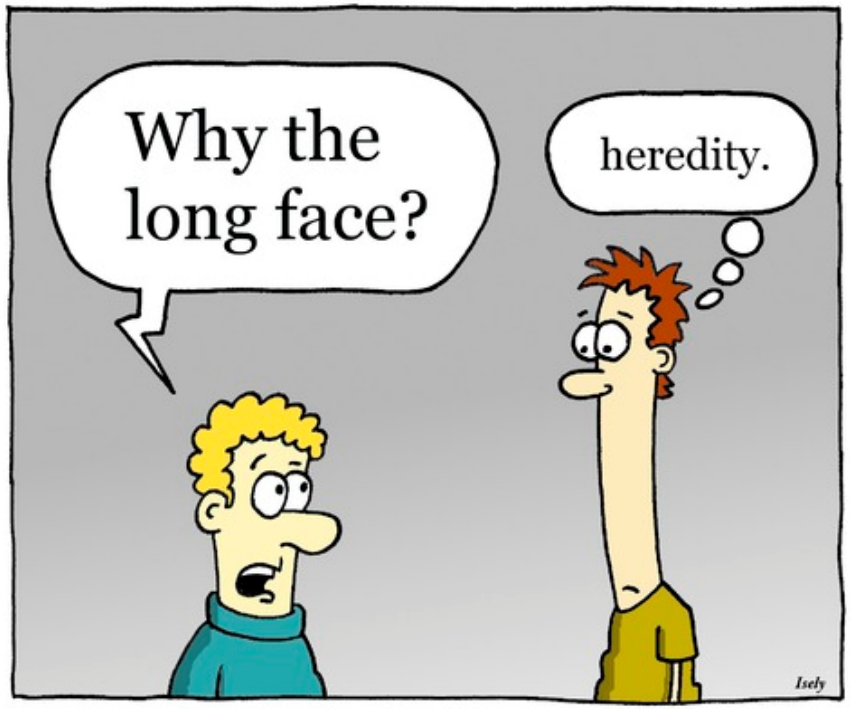
- There are many types of Hereditary Neuropathy or CMT
- Genetic testing may be informative for you/your family
- Genetic testing may lead, in some cases, to treatment or to a clinical trial
- Genetic counselors can help people navigate the genetic testing process https://findageneticcounselor.nsgc.org/

Additional Slides

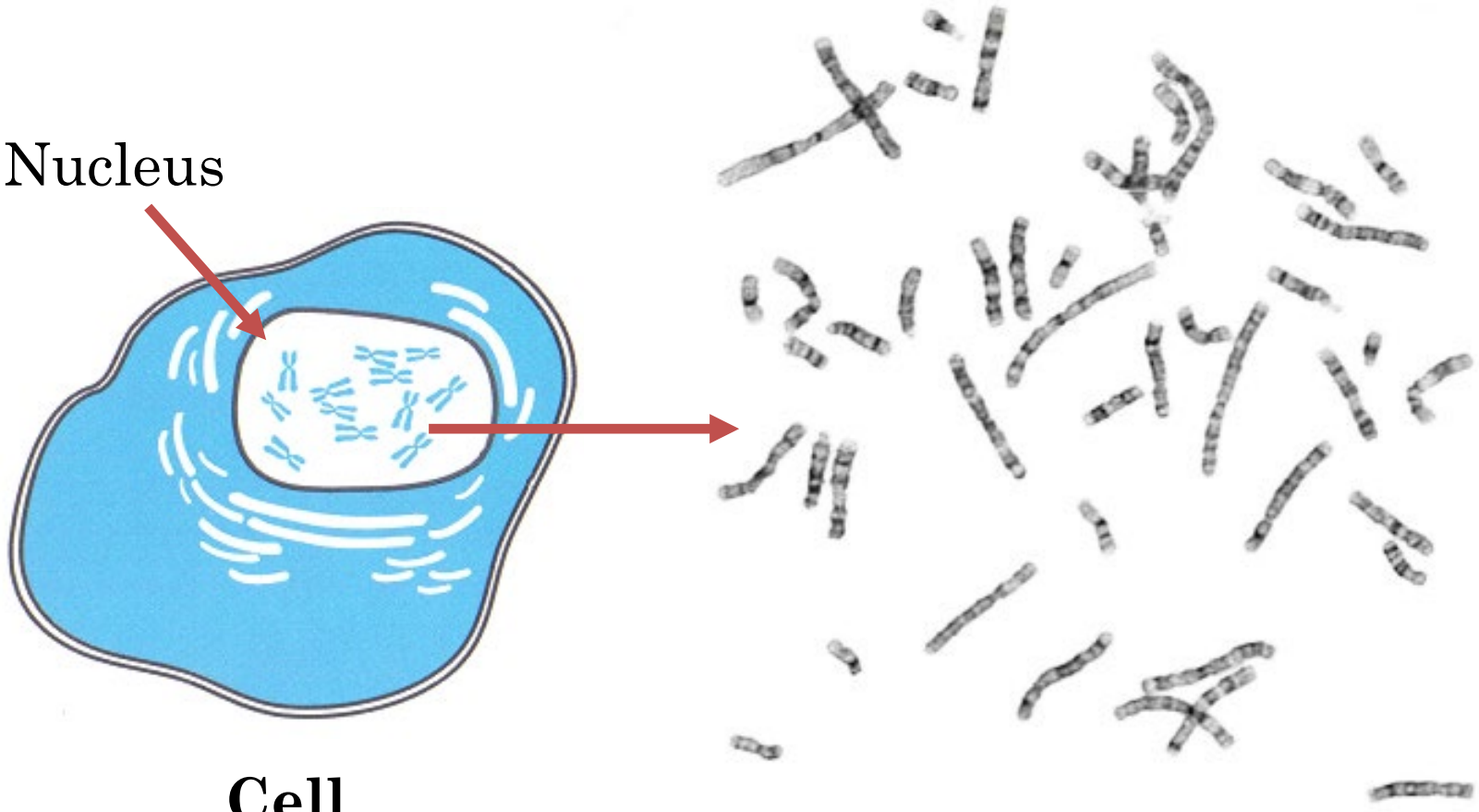
Family History:
Modes of Inheritance

- Three main methods of inheritance:
  - Autosomal Dominant
  - Autosomal Recessive
  - X-linked

- The method of inheritance does not change within a family

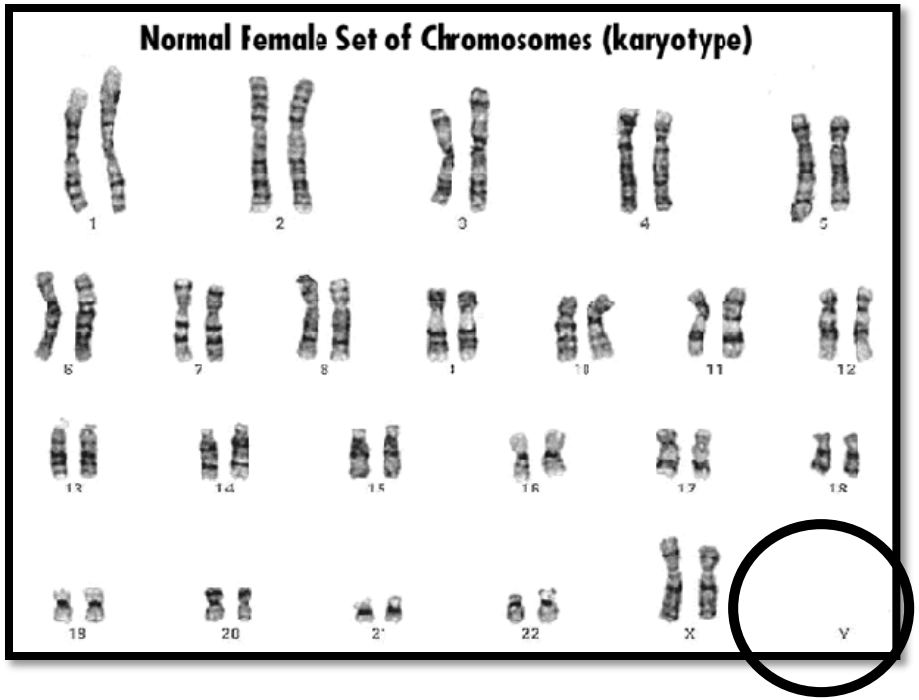


Chromosomes Are Found In Each Cell

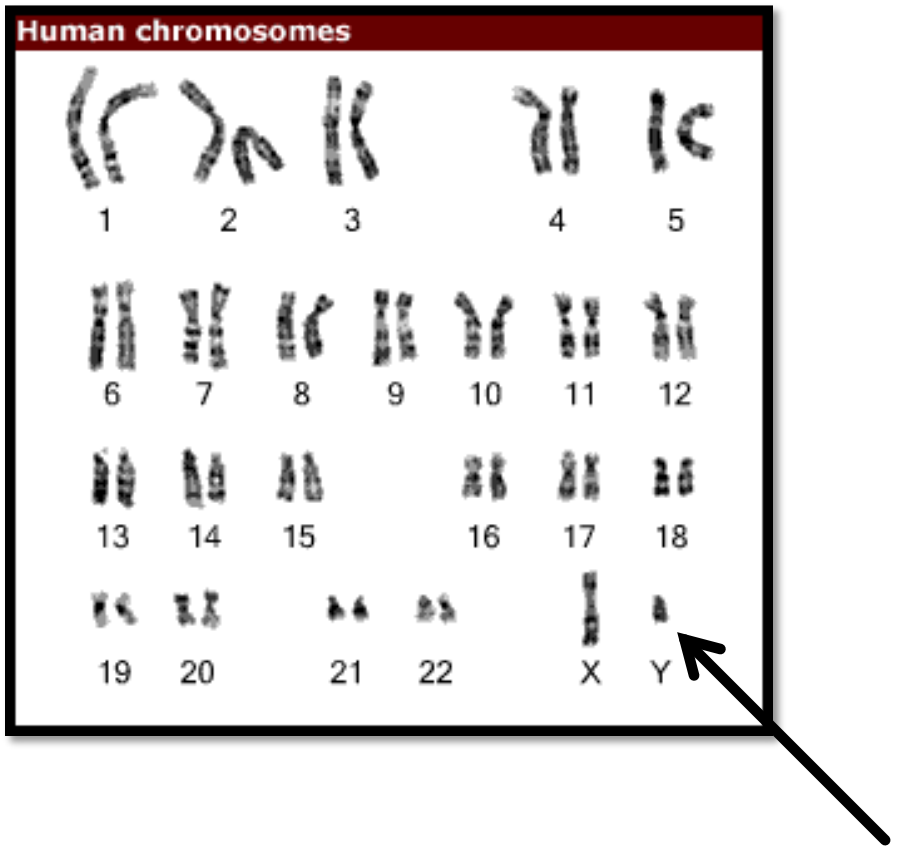


Chromosomes

Female Chromosomes



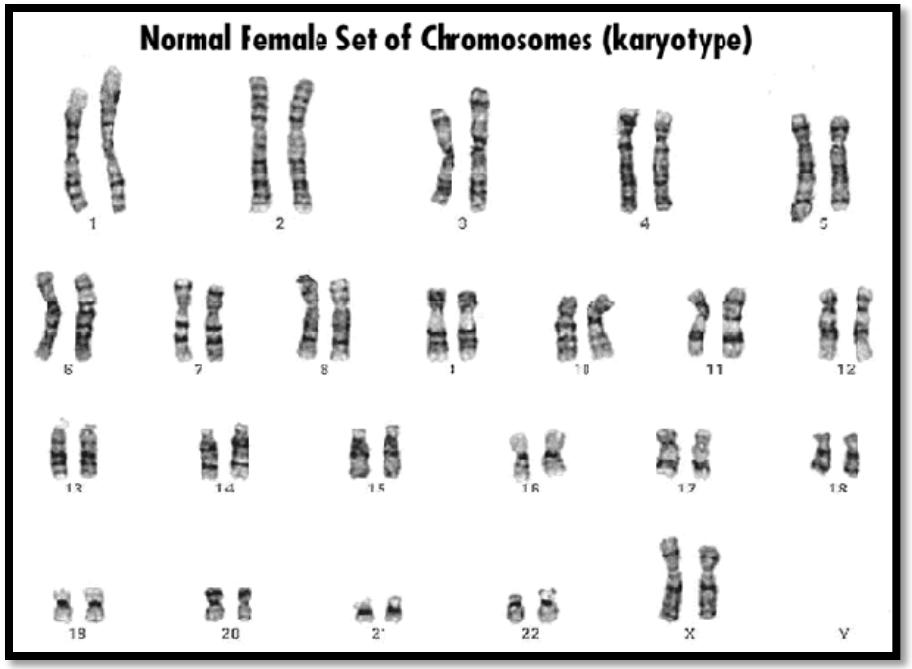
Male Chromosomes



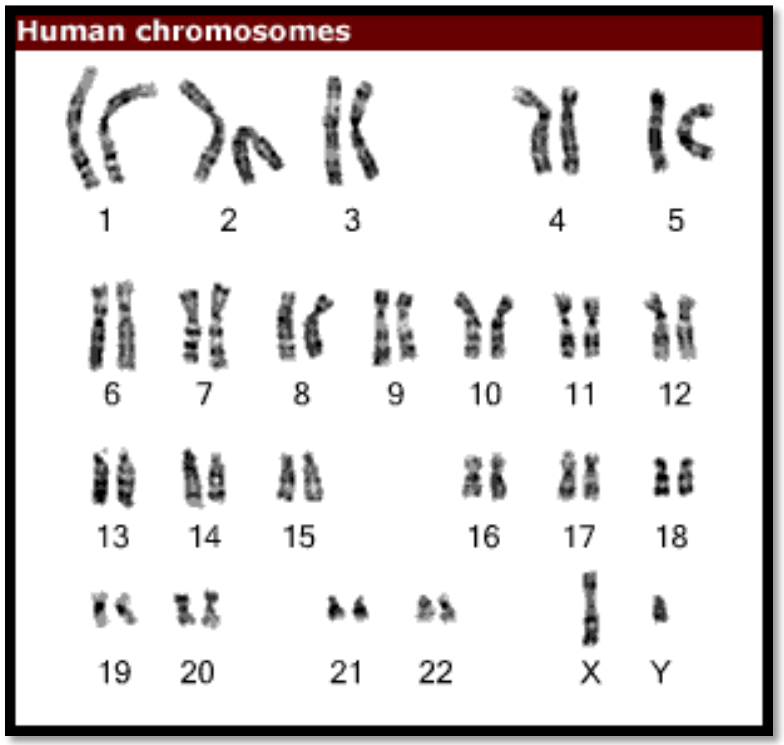
Chromosomes

Autosomes: Chromosomes that are the same between men and women (#1-22)

Female Chromosomes

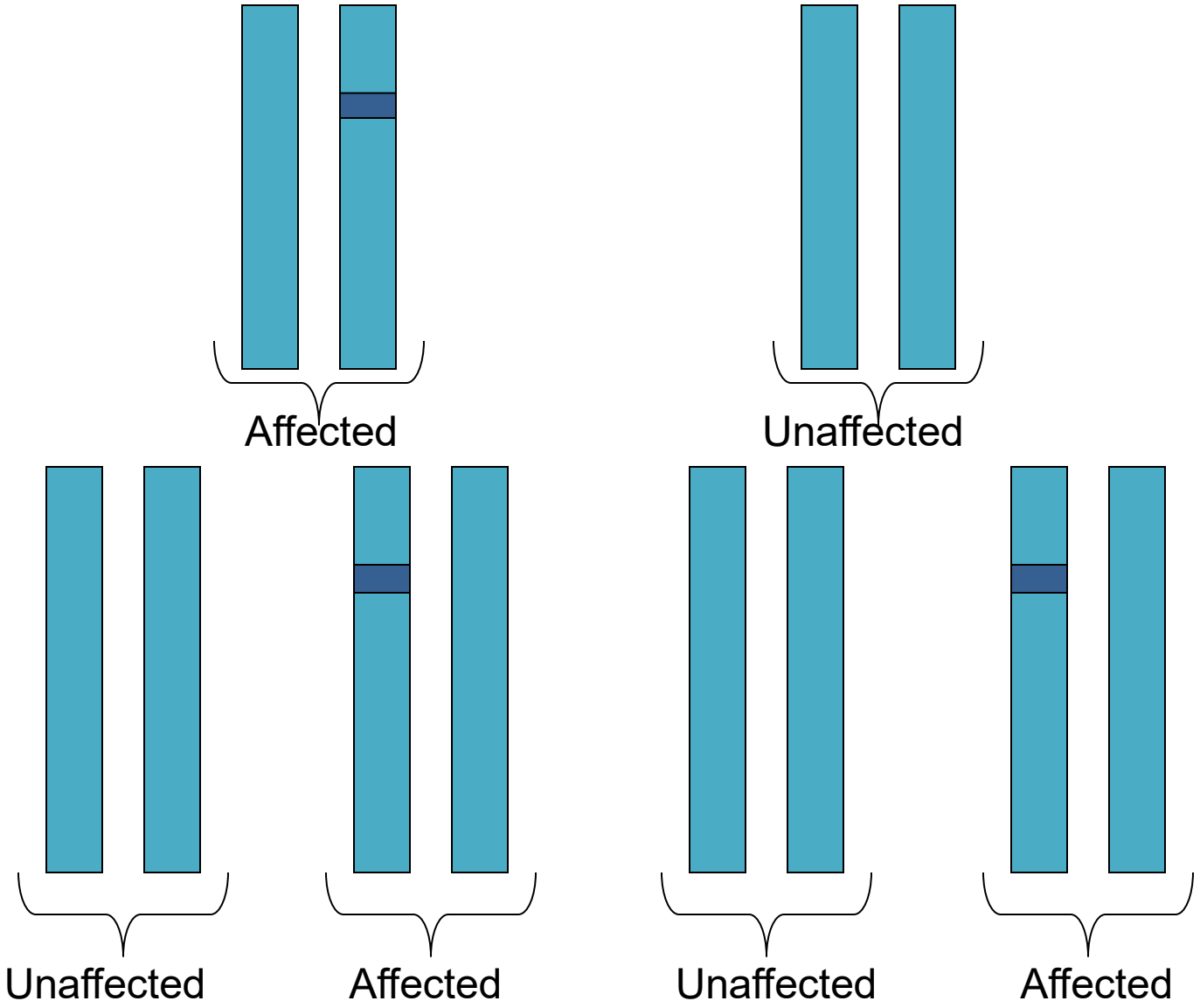


Male Chromosomes

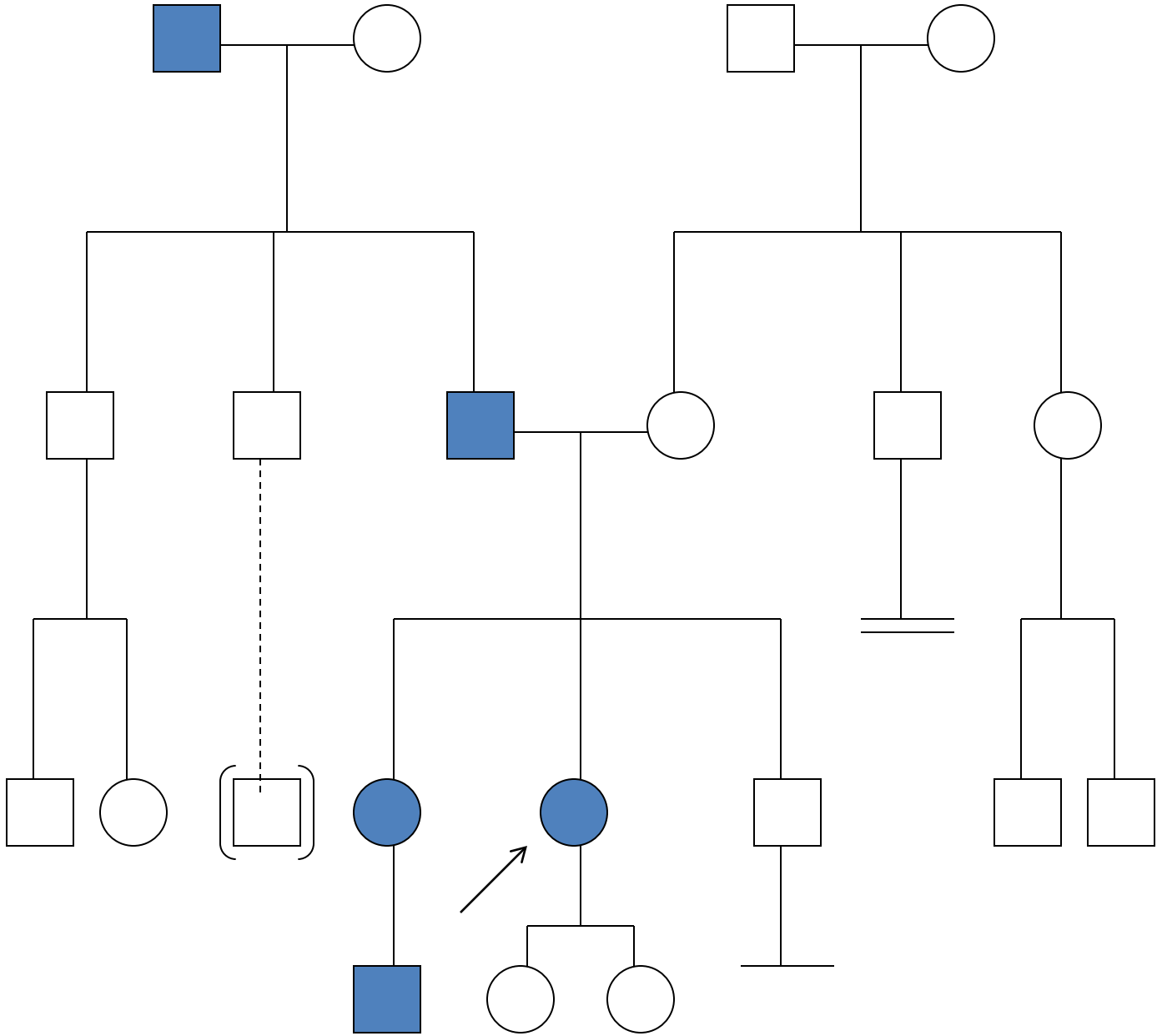


Dominant vs Recessive: A gene that requires only **1** mutation vs a gene that requires **2**

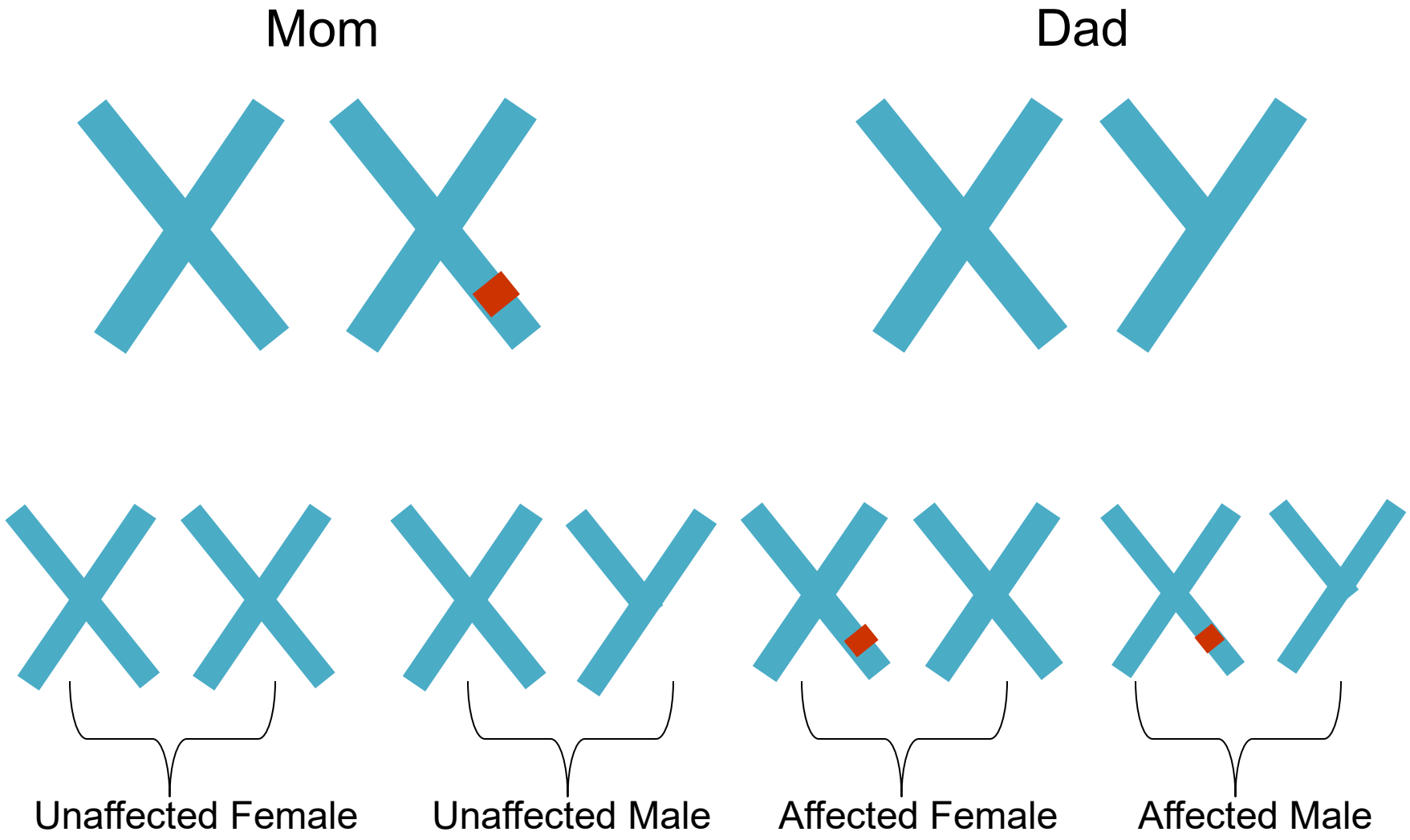
Autosomal Dominant Inheritance



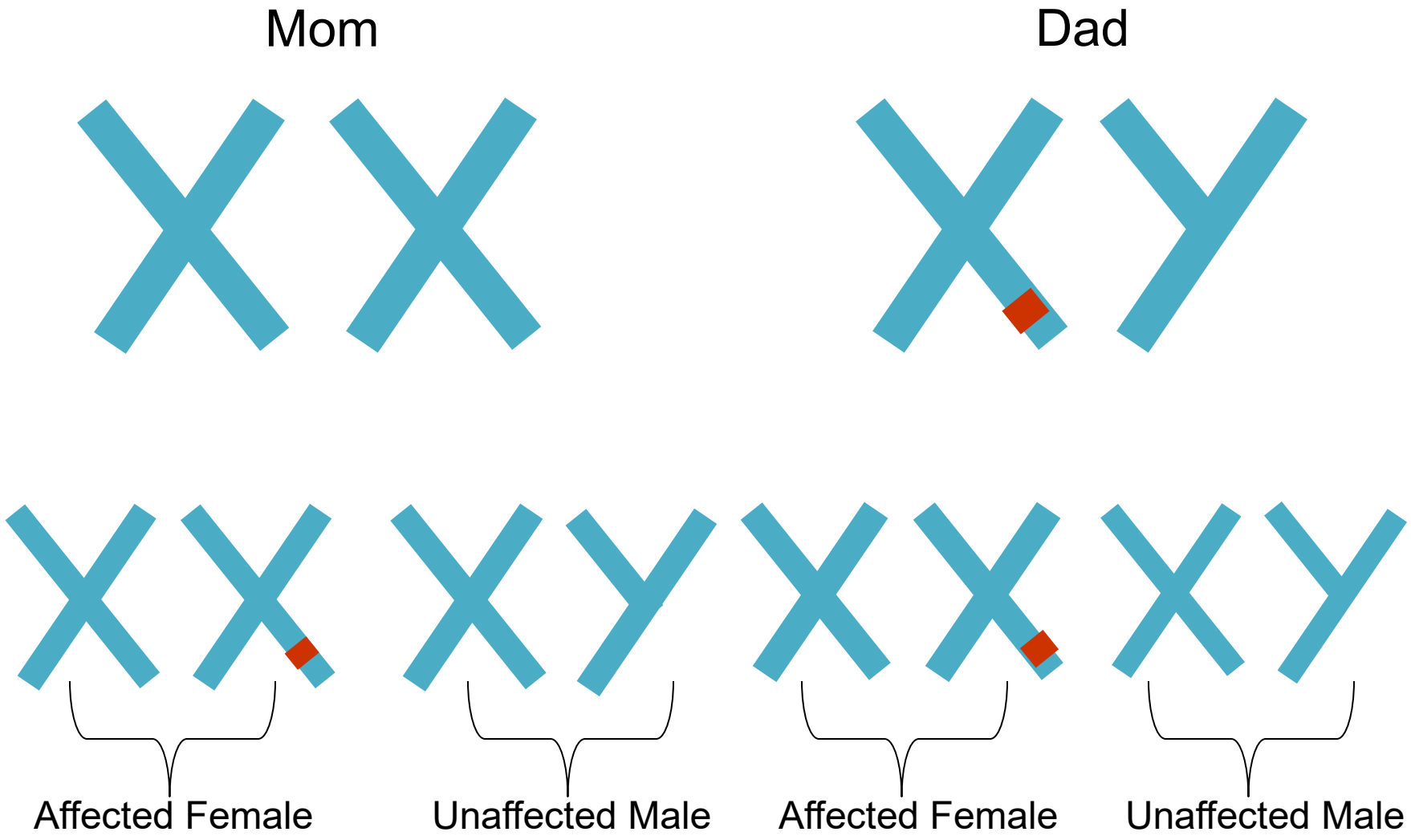
Autosomal Dominant Inheritance



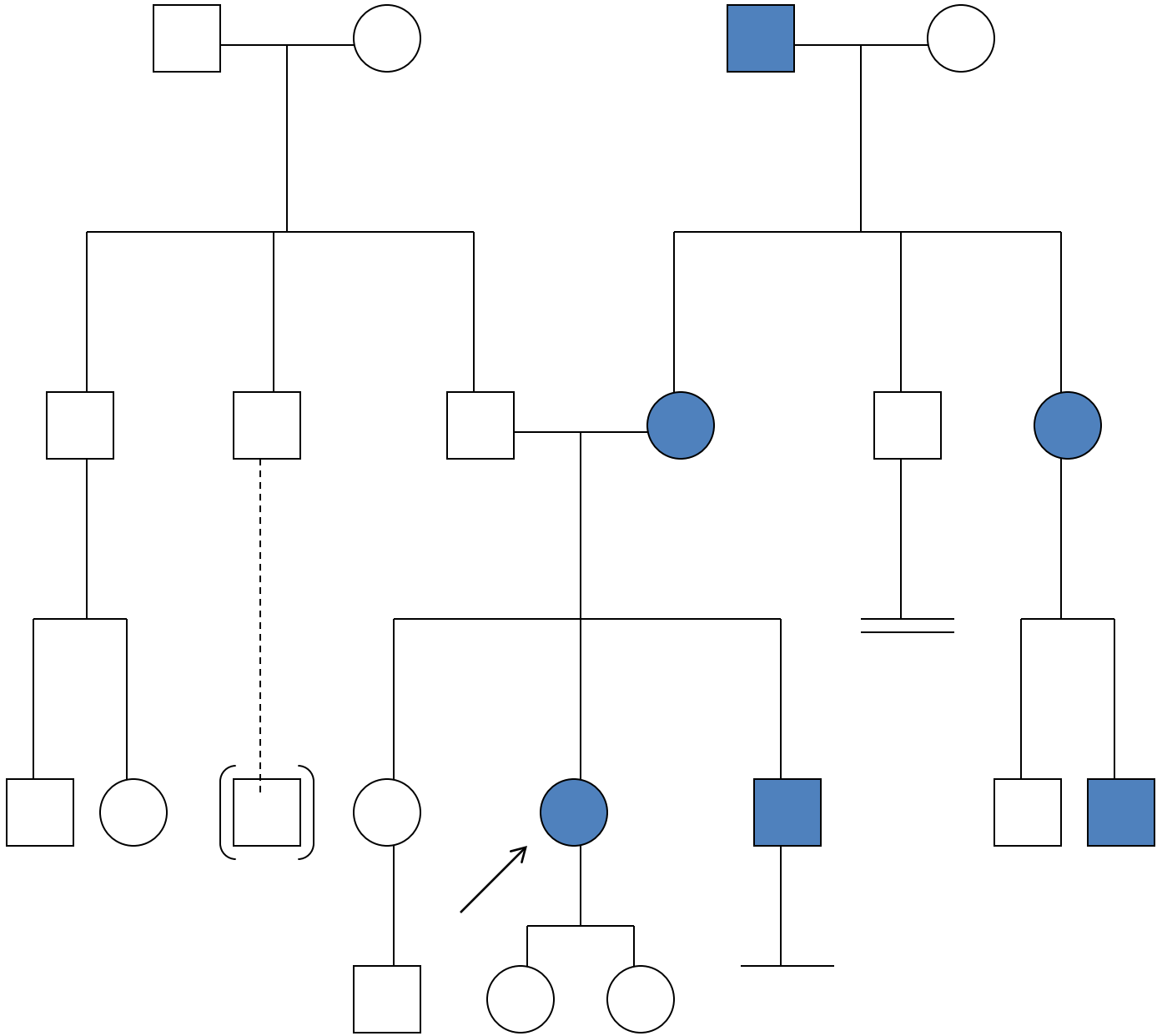
X-Linked


Mom
Dad
Unaffected Female
Unaffected Male
Affected Female
Affected Male

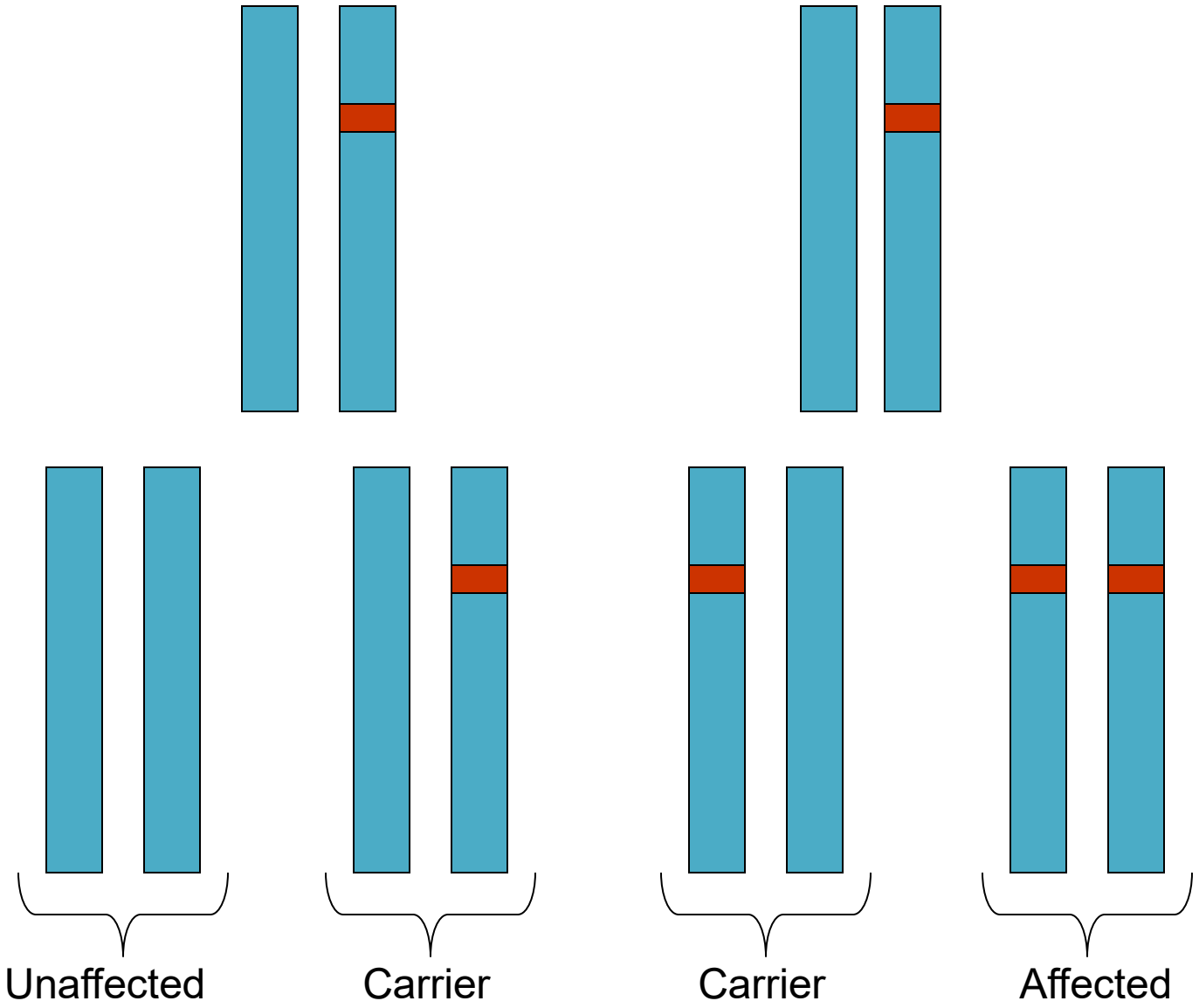
X-Linked


Mom
Dad
Affected Female
Unaffected Male
Affected Female
Unaffected Male

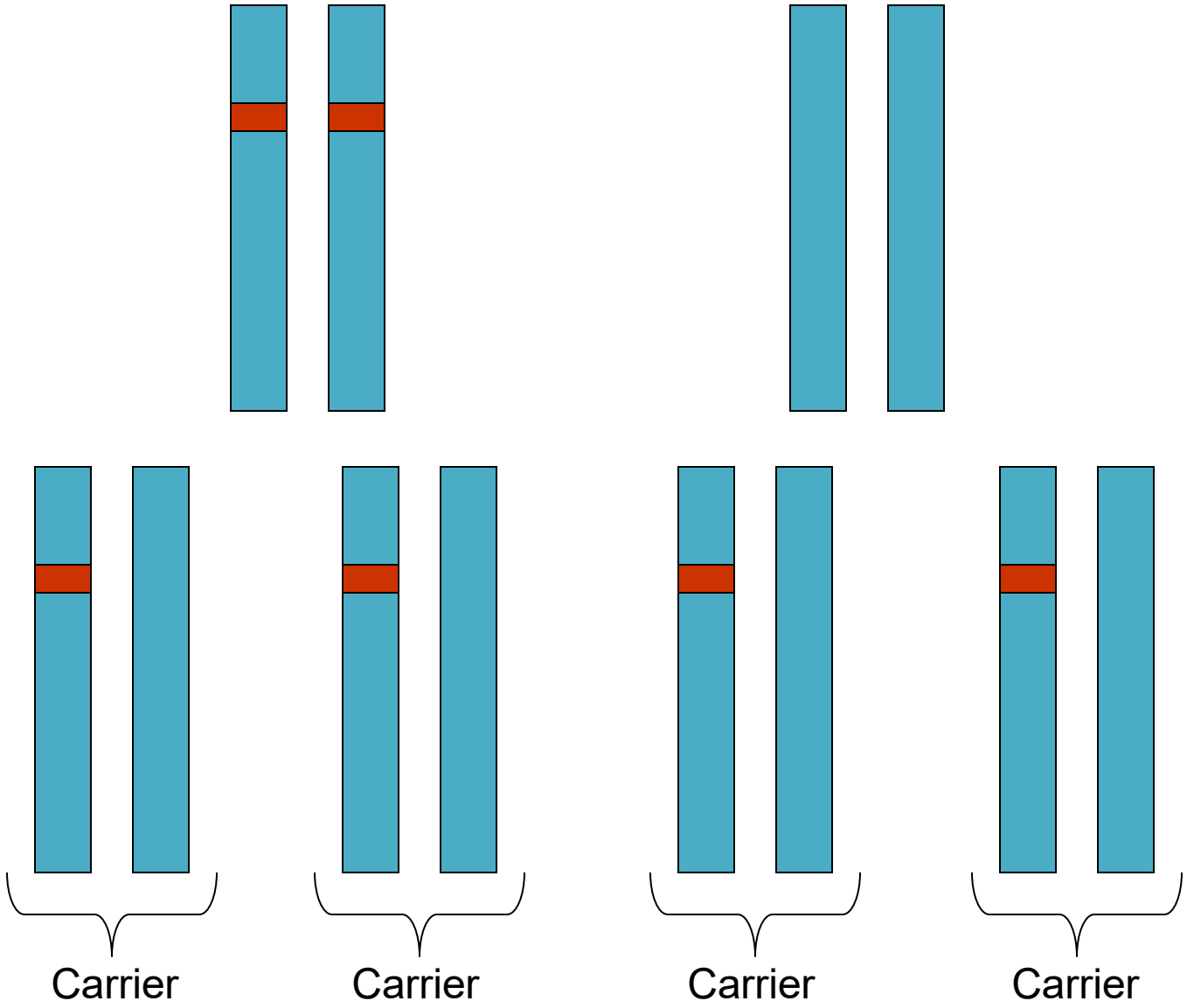
X-Linked Inheritance



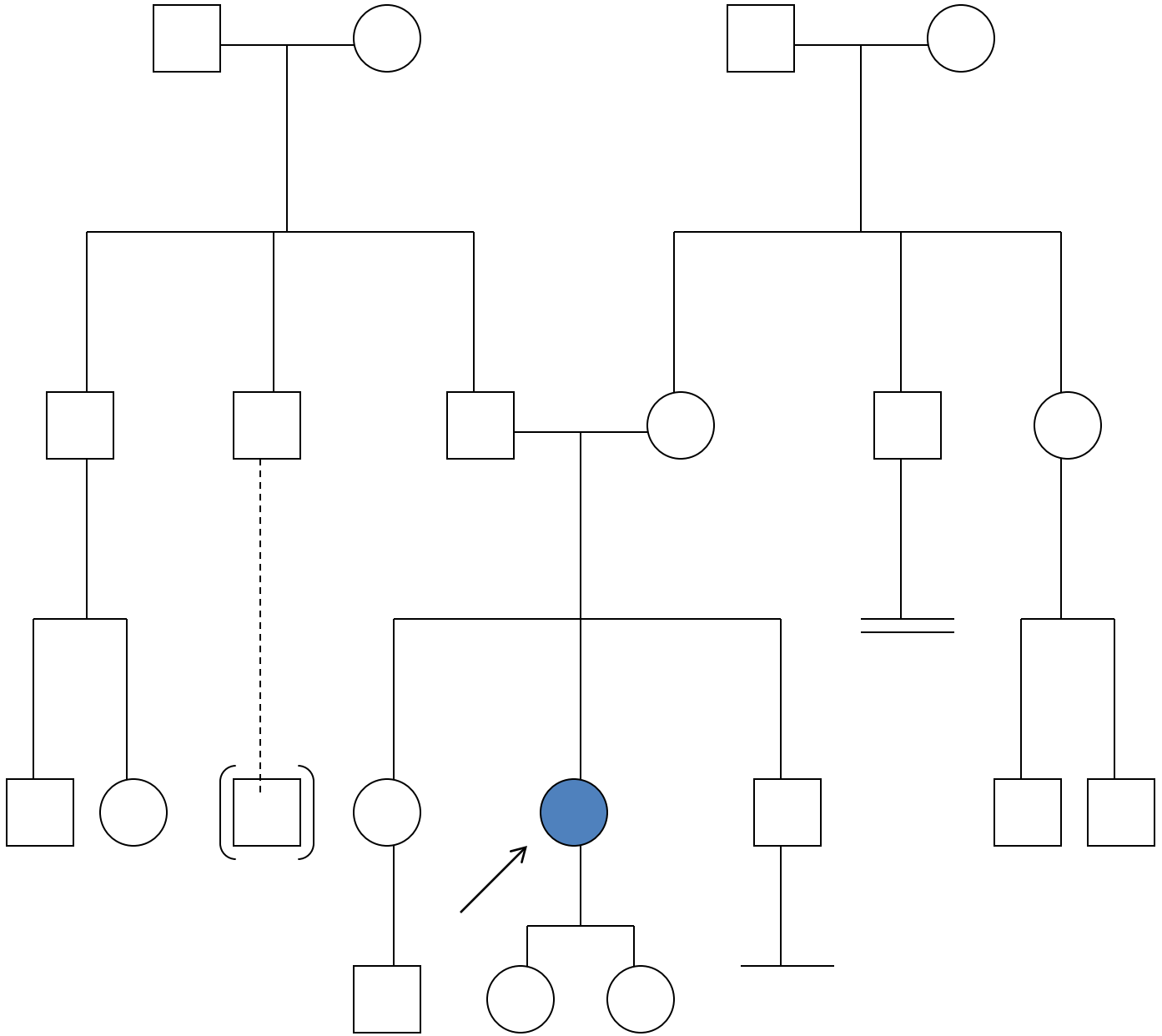
Recessive Inheritance



Recessive Inheritance



Autosomal Recessive Inheritance



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