PKU: GENETICS AND INHERITANCE

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OUTLINE

- How genetics work
- Genetics of PKU
- Inheritance of PKU
- Genetic testing

PKU AND GENETICS

- "PKU is a **genetic** condition"
  - Caused by changes in **genes**, not by the environment
  - Passed down through generations in a **recessive** inheritance pattern

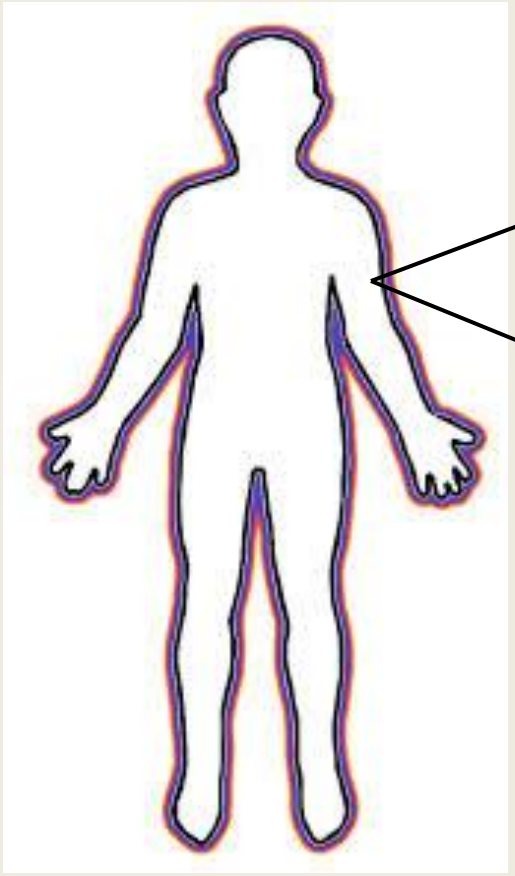
EFFECTS OF GENETICS

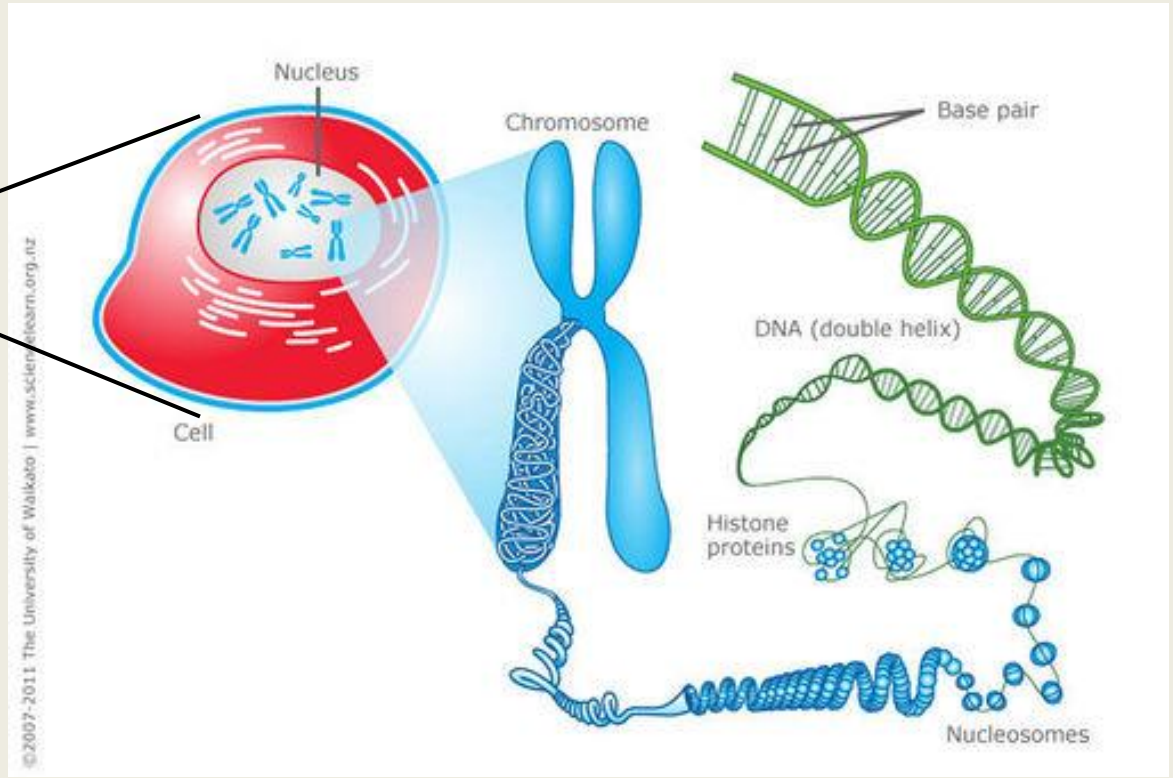
- Traits and variation between people
  - Hair color
  - Height
  - Skin color
  - Taste preferences
  - Ear lobe shape

- Impact of genetics on health
  - Genetic disorders
    - Examples: PKU, cystic fibrosis, Down syndrome
  - Genetic + environmental disorders
    - Examples: Diabetes type II, coronary heart disease, cancer

HOW DO GENETICS WORK?

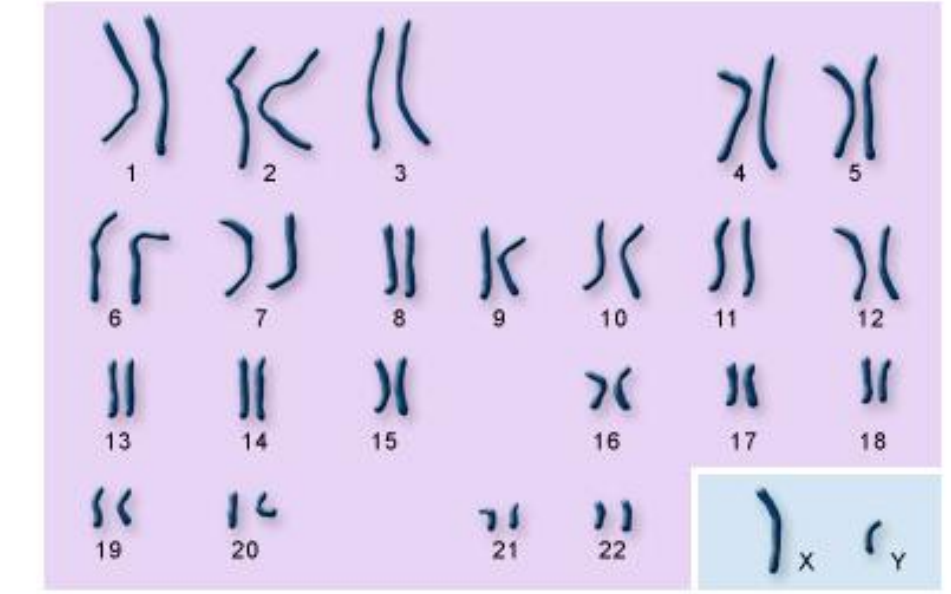
Human → Cell → Chromosomes → DNA





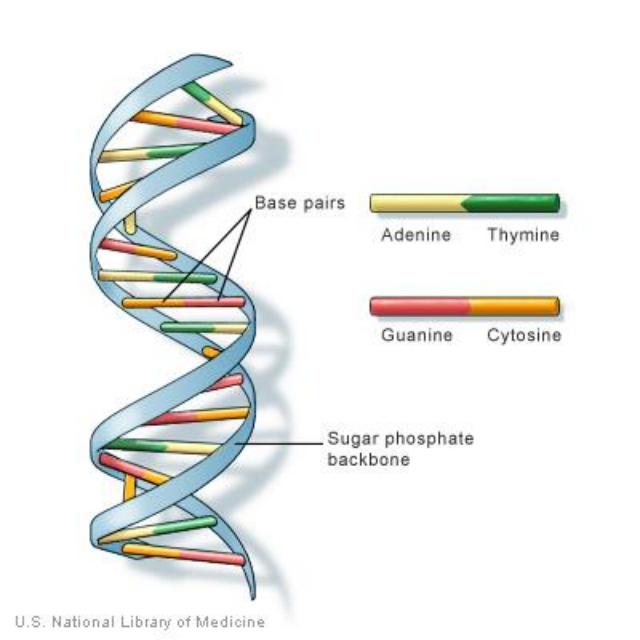
CHROMOSOMES

- Thread-like structures that hold all of our DNA
- 46 chromosomes inside every cell in the body
  - 2 copies of 22 autosomes, plus XY for males, XX for females
    - 1 copy is from mom, and 1 copy is from dad



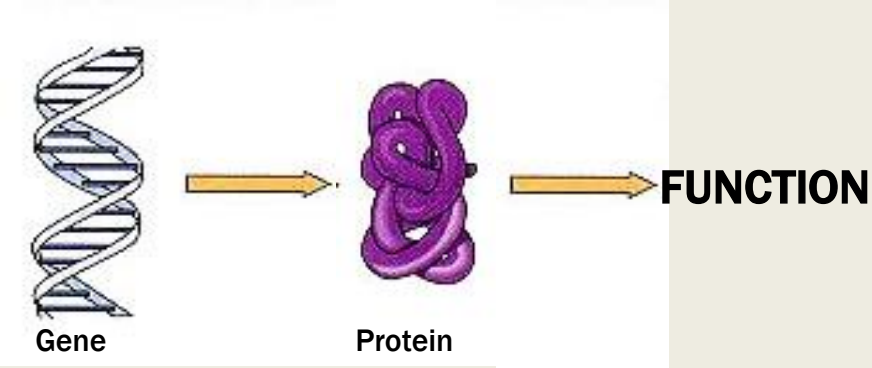
DNA

- Hereditary material in humans
- String of letters (base pairs) that make a code
- Code gives instructions for body to grow and develop



GENE

- Segment of DNA that produces a protein with a specific function
  - 1 gene = 1 protein
  - Each protein has at least one distinct role in the body



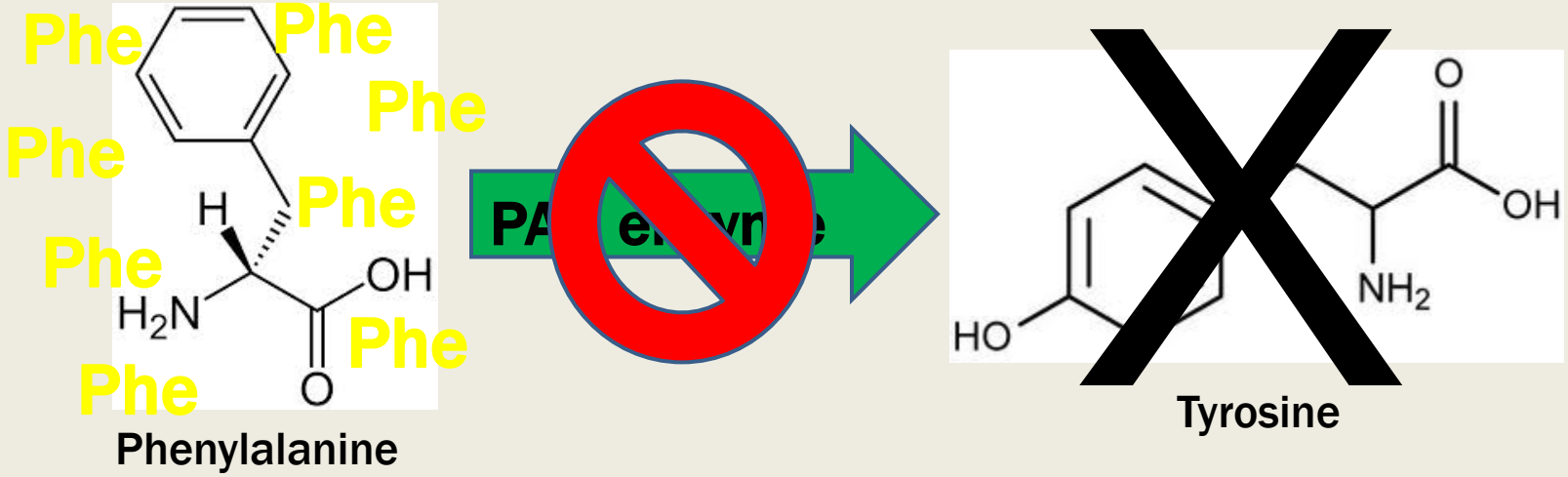
- Humans have 20,000-25,000 genes
  - 2 copies of each- one from mom, one from dad
- Can be anywhere from ~300 to ~2million letters long

GENETIC MUTATIONS

- Mutation- a change in a gene, different from the typical letter sequence
  - Types:
    - Example:
      - Typical sequence: AATGCGG
      - Mutation: AACGCGG
- We all have mutations that cause us to be different from one another
  - Most mutations do not cause disease = “variants”
- Some mutations result in a change in the function of the protein, or cause the protein not to be made at all
  - These mutations are “disease-causing”

GENETICS OF PKU

- PKU is caused by mutations in the gene *PAH*
- This gene codes for an enzyme (type of protein) called phenylalanine hydroxylase (PAH)
  - PAH breaks down phenylalanine to make tyrosine



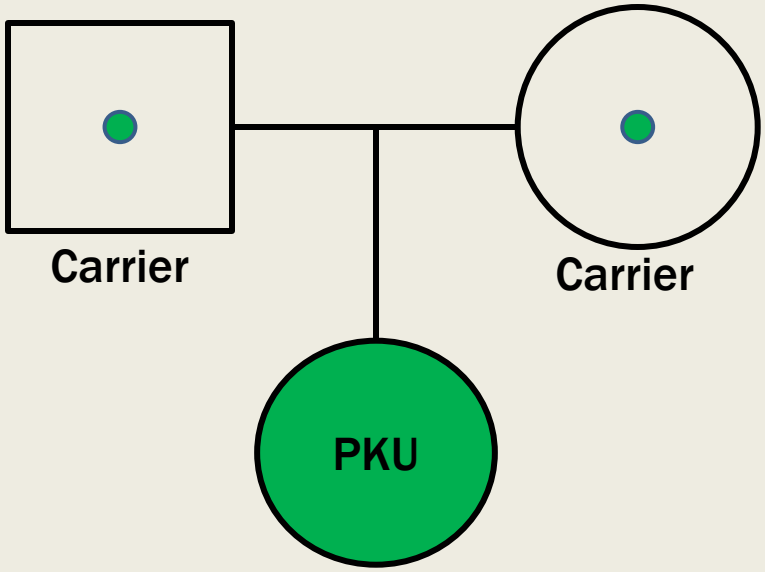
Phenylalanine

Tyrosine

- Severity of PKU is determined by the amount of enzyme activity- we call this "residual activity"

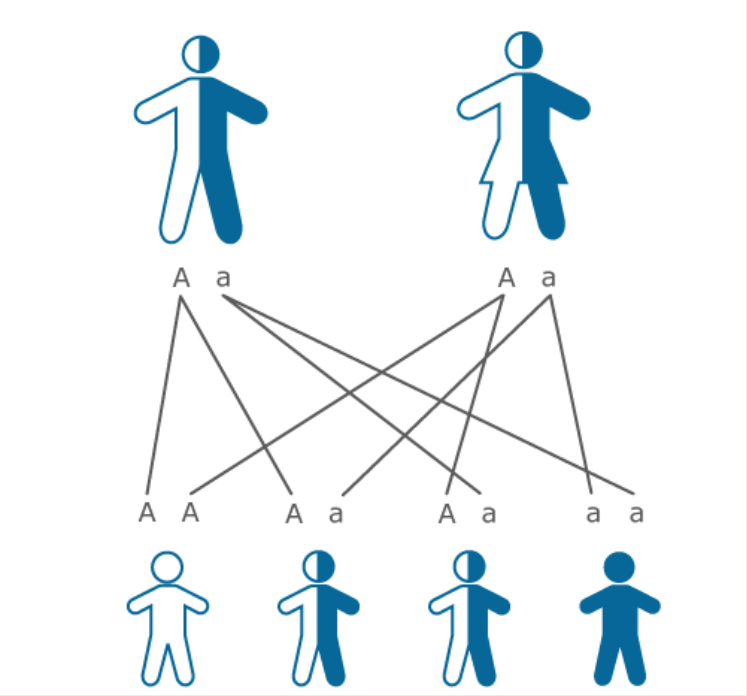
INHERITANCE OF PKU

- Autosomal recessive pattern
  - A person must have a mutation on BOTH of his/her two copies of the *PAH* gene in order to have PKU
  - This only occurs if both parents are **carriers** for PKU



FOR 2 CARRIERS…

- There is a 1 in 4 (25%) chance to have a child with PKU, in each pregnancy



FOR A PERSON WITH PKU…

- All children will inherit a mutation and will be (at least) a carrier
- The chance for a child to have PKU depends on the partner
  - 2% (1 in 50) of the population is a carrier for PKU
  - If unknown whether the partner is a carrier, the chance to have a child with PKU is 1 in 100 (1%)
    - **Carrier testing is available for partners**
  - If the partner is a carrier, the chance to have a child with PKU is 1 in 2 (50%)
  - If partner has PKU, all children will have PKU too

GENETIC TESTING

- Genetic testing can be performed to identify the two PAH gene mutations
  - Not done standardly, but can be for interested families
  - Would not tell us which one came from which parent
- If mutations are known…
  - Carrier screening for family members can be performed
  - Prenatal screening for siblings can be performed

- **All children born in hospitals in the USA are screened for PKU at birth**

THANK YOU ☺