PKU: GENETICS AND INHERITANCE
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
- 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 ~2 million letters long
**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”
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

**Severity of PKU is determined by the amount of enzyme activity- we call this “residual activity”**
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

INHERITANCE OF PKU
There is a 1 in 4 (25%) chance to have a child with PKU, in each pregnancy.
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 😊