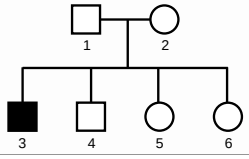
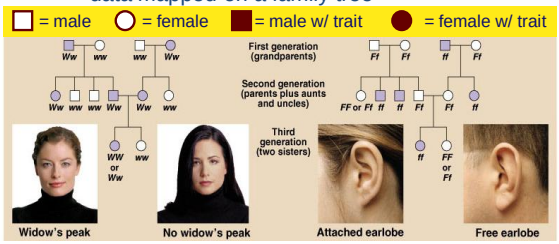
Human Genetic Diseases



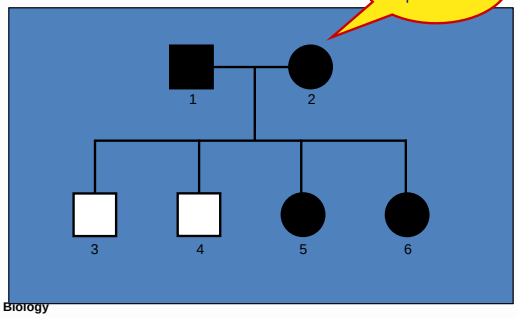
Pedigree analysis

- Pedigree analysis reveals Mendelian patterns in human inheritance
  - data mapped on a family tree



Simple pedigree ana

What's the likely inheritance pattern?



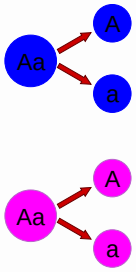
Heterozygote crosses

- Heterozygotes as carriers of recessive alleles

Aa x Aa

male / sperm

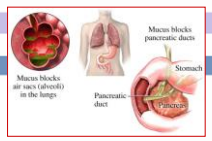
female / eggs	A	a
A	AA	Aa carrier
a	Aa carrier	aa disease

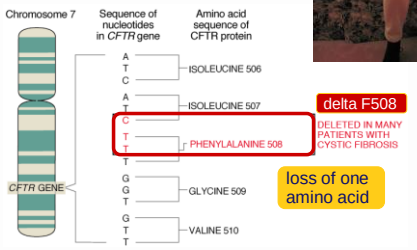


Cystic fibrosis (rece

normal lung tissue

- Primarily whites of European descent
  - strikes 1 in 2500 births
    - 1 in 25 whites is a carrier (Aa)
  - normal allele codes for a membrane protein that transports Cl^- across cell membrane
    - defective or absent channels limit transport of Cl^- & H_2O across cell membrane
    - thicker & stickier mucus coats around cells
    - mucus build-up in the pancreas, lungs, digestive tract & causes bacterial infections
  - without treatment children die before 5; with treatment can live past their late 20s





Tay-Sachs (recessive)

- Primarily Jews of eastern European (Ashkenazi) descent & Cajuns (Louisiana)
  - strikes 1 in 3600 births
    - 100 times greater than incidence among non-Jews
  - non-functional enzyme fails to breakdown lipids in brain cells
    - fats collect in cells destroying their function
    - symptoms begin few months after birth
    - seizures, blindness & degeneration of muscle & mental performance
    - child usually dies before 5yo

Sickle cell anemia (recessive)

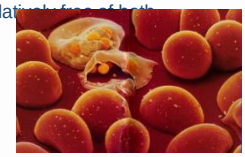
- Primarily Africans
  - strikes 1 out of 400 African Americans
    - high frequency
  - caused by substitution of a single amino acid in hemoglobin
  - when oxygen levels are low, sickle-cell hemoglobin crystallizes into long rods
    - deforms red blood cells into sickle shape
    - sickling creates pleiotropic effects = cascade of other symptoms

Sickle cell phenotype

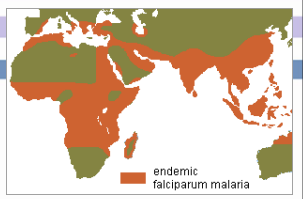
- 2 alleles are codominant
  - both normal & mutant hemoglobins are synthesized in heterozygote (Aa)
  - 50% cells sickle; 50% cells normal
  - carriers usually healthy
  - sickle-cell disease triggered under blood oxygen stress
    - exercise

Heterozygote advantag

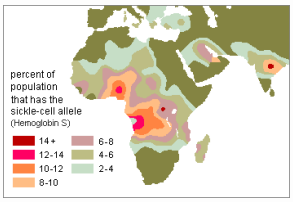
- Malaria
  - single-celled eukaryote parasite spends part of its life cycle in red blood cells
- In tropical Africa, where malaria is common:
  - homozygous dominant individuals die of malaria
  - homozygous recessive individuals die of sickle cell anemia
  - heterozygote carriers are relati
    - reproductive advantage
- High frequency of sickle cell allele in African Americans is vestige of African roots



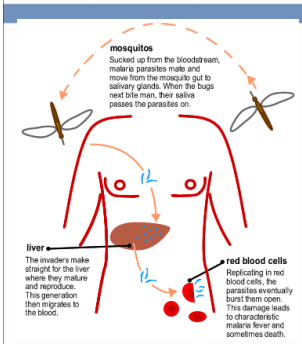
Prevalence of Malaria

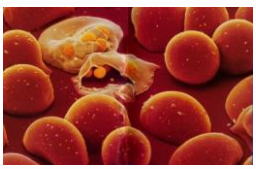


Prevalence of Sickle Cell Anemia



Malaria



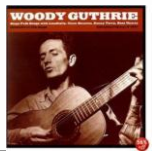


Huntington's chorea (dominant)

- Dominant inheritance
  - repeated mutation on end of chromosome 4
    - mutation = CAG repeats
    - glutamine amino acid repeats in protein
    - one of 1st genes to be identified

Testing… Would you want to know?

build up of "huntingtin" protein in brain causing cell death
- memory loss
- muscle tremors, jerky movements
  - "chorea"
- starts at age 30-50
- early death
  - 10-20 years after start



Genetics & culture

- Why do all cultures have a taboo against incest?
  - laws or cultural taboos forbidding marriages between close relatives are fairly universal
- Fairly unlikely that 2 unrelated carriers of same rare harmful recessive allele will meet & mate
  - but matings between close relatives increase risk
    - "consanguineous" (same blood) matings
  - individuals who share a recent common ancestor are more likely to carry same recessive alleles

A hidden disease reveals itself

AA x Aa

male / sperm: A A

female / eggs	A	A
A	AA	AA
a	Aa	Aa

Aa x Aa

male / sperm: A a

female / eggs	A	a
A	AA	Aa
a	Aa	aa

- increase carriers in population
- hidden disease is revealed