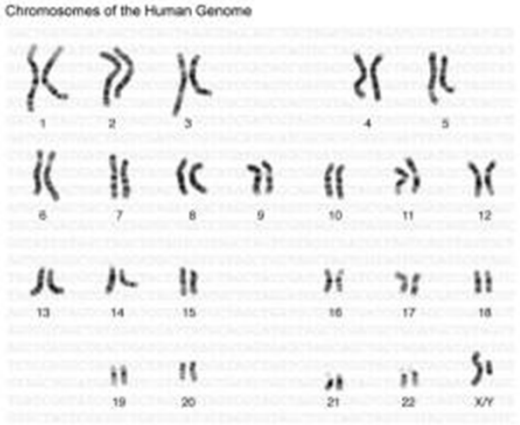
Introduction to genetic mapping

What is “genetic mapping”?

- Using associations between alleles at multiple spots (loci) in the genome to:
  - Determine where a gene is relative to other genes
  - Localize a gene causing a phenotype
    - Disease genes!

Mapping genetic diseases

- A primary goal of the Human Genome project was to develop new and better tools to find human disease genes faster
  - Identified virtually all of the ~20,000 human genes
  - Assembled **~3 billion bases of DNA**, sorted along 23 pairs of chromosomes



BUT, how go from DNA sequence to “disease-causing gene”?

- We can get some ideas of normal functions of genes from sequence, but can only guess what sequences may cause problems

- ATGGCGAGCTAGCGCGACGTTTCAGCTAAATAG

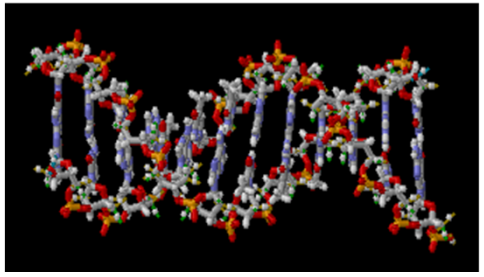
Genetic mapping is a first approach, very much like Drosophila examples!

- Identify location of “disease mutation” relative to other spots in the genome

- BUT, to do this, we need **reference points**
  - “Genetic markers” mentioned last time

How do we get genetic markers?

- Multiple people used for original human genome sequence, and more people since
- Several nucleotide sites found to be variable
  - AACAGTCGAGCTATTTTAGCGTAGCGTAT
  - AACAGTTGAGCTATTTTAGCGTAGCGTGT
- Can genotype blood or tissue for these SNP (single nucleotide polymorphism) sites and use as genetic markers!



Resources Available

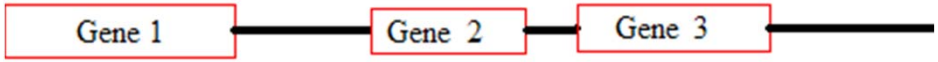
- We now have the genome sequence mostly put together from end to end on each chromosome
  - 23 long sequences corresponding to the chromosomes of humans
- We have computer predictions of what parts are likely "genes" encoding for proteins
- We also have data showing some bases that differ between a lot of humans ("HapMap")

Resources Available

- Genome sequence(s)

  AGCGAGCGAGCGACATGGTTTAGATGAGTAGTAG…

- Predicted genes



- HapMap SNP (single nucleotide polymorphism) data: **genetic markers!**
  - Within Gene 1

    ATGCATGGA – in many individuals (“B”)

    ATGCACGGA – in many other individuals (“b”)

Essence of all genetic mapping

- Ultimately comes down to **seeing an association between GENOTYPE and PHENOTYPE**
  - Genotype at markers
    - AA vs. Aa vs. aa
  - Phenotype may be disease or other trait
    - Healthy vs. diseased

Extreme example

- A and B are “SNP markers”
- Offspring of AB/ab carrier & ab/ab diseased
  - AB/ab (AaBb) — All OK
  - Ab/ab (Aabb) — All diseased
  - aB/ab (aaBb) — All OK
  - ab/ab (aabb) — All diseased

- What would you conclude about whether A or B marker is closer to the disease mutation?

Extreme example

- A and B are “SNP markers”
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  - aB/ab (aaBb) All OK
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