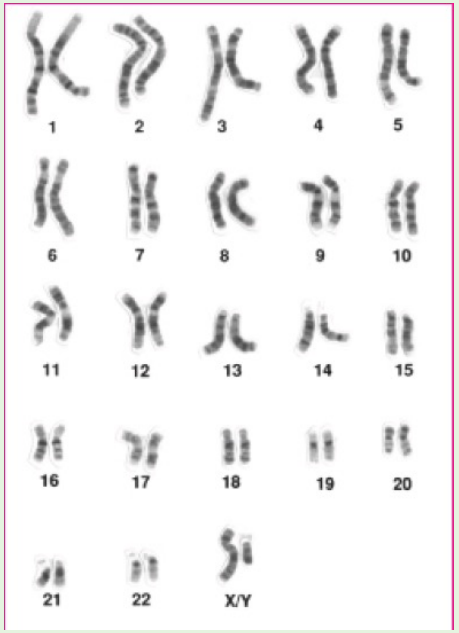
HUMAN CHROMOSOMES AND THE GENETIC MAPS



Human Genome Project

❖The human genome project is a major world-wide scientific undertaking to identify the location of all human genes.
❖In order to do this there has to be a way to find the specific location of genes on each individual chromosome.

❖There are three ways in which chromosomes are mapped. One way is to map a cytogenetic map in which chromosome bands, each representing 1 million to 5 million bases, are stained and the investigator finds a correlation between people who show a particular trait and exhibit a similar staining pattern.
❖Another way to is produce a physical map using enzymes to cut pieces of DNA into fragments containing markers along with genes whose location is to be determined. By using computers to "walk" or overlay these fragments into their proper sequence we can produce a map of a long strand of DNA.
❖ The third technique is a method of mapping by crossover frequency (Genetic map).

Mapping and Sequencing the Human Genome

❖A primary goal of the Human Genome Project is to make a series of descriptive diagrams maps of each human chromosome at increasingly finer resolutions. Mapping involves (1) dividing the chromosomes into smaller fragments that can be propagated and characterized and (2) ordering (mapping) them to correspond to their respective locations on the chromosomes.

❖After mapping is completed, the next step is to determine the base sequence of each of the ordered DNA fragments.

❖The ultimate goal of genome research is to find all the genes in the DNA sequence and to develop tools for using this information in the study of human biology and medicine.

Genetic and Physical Maps

- genome mapping methods can be divided into two categories.
- Genetic mapping: uses genetic techniques to construct maps showing the positions of genes and other sequence features on a genome. Genetic techniques include cross-breeding experiments or, in the case of humans, the examination of family histories (pedigrees).
- Physical mapping uses molecular biology techniques to examine DNA molecules directly in order to construct maps showing the positions of sequence features, including genes.

Why map before sequencing?

- Major problem in large-scale sequencing:
  - Current technologies can only sequence 600–800 bases at a time. We need to sequence 3 billion bp in order to perfectly sequence human genome
- One solution: make a **physical** map of overlapping DNA fragments: Top-Down approach
  - Chromosomal libraries: 46 chromosomes/23 pairs
  - Genomic library for many fragments from each chromosome
  - Determine sequence of each fragment
  - Then assemble to form contiguous sequence

Map-less sequencing: Bottoms up Celera approach

- Alternative solution: fragment entire genome
  - Sequence each fragment
  - Assemble overlapping sequences to form contiguous sequence

Markers for genetic mapping

- The first genetic maps constructed in the organisms such as the fruit fly used genes as markers.
- Genes that could be studied show specific phenotypes like eye color, height.
- Some organisms have very few visual characteristics so gene mapping with these organisms has to rely on biochemical phenotypes.

What is Mapping?

- Mapping is identifying relationships between genes on chromosomes
  - Just as a road map shows relationships between towns on highway: fine maps
- Two types of mapping: genetic and physical

Genetic and Physical Mapping

--Genetic mapping is based on differences in recombination frequency between genetic loci meiosis.

--Genetic mapping requires that a cross be performed between two related organisms

Physical mapping

- Determination of physical distance between two points on chromosome
  - Distance in base pairs
- Example: between physical marker and a gene
- Need overlapping fragments of DNA
  - Requires vectors that accommodate large inserts
    - Examples: cosmids, YACs, and BACs

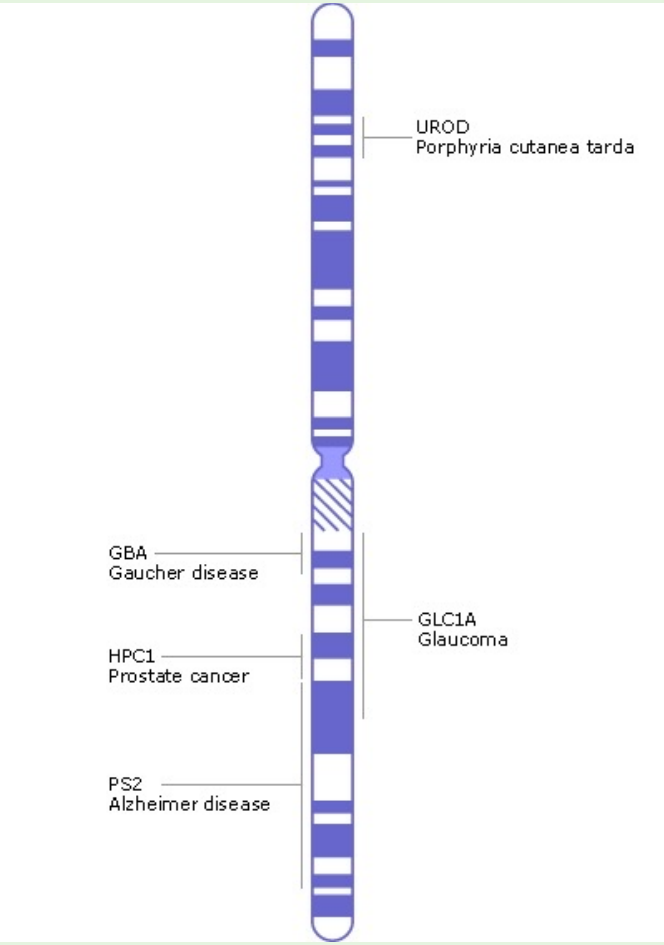
Importance of gene mapping

- Gene map is the anatomy of human genome. It is a perrequisite to understand functioning of human genome.
- Helps in analysis of the heterogeneity and segregation of human genetic diseases.
- Helps to develop methods for gene therapy.
- Provides clinically useful information about linkage

Chromosome 1

❖Contains over 3000 genes

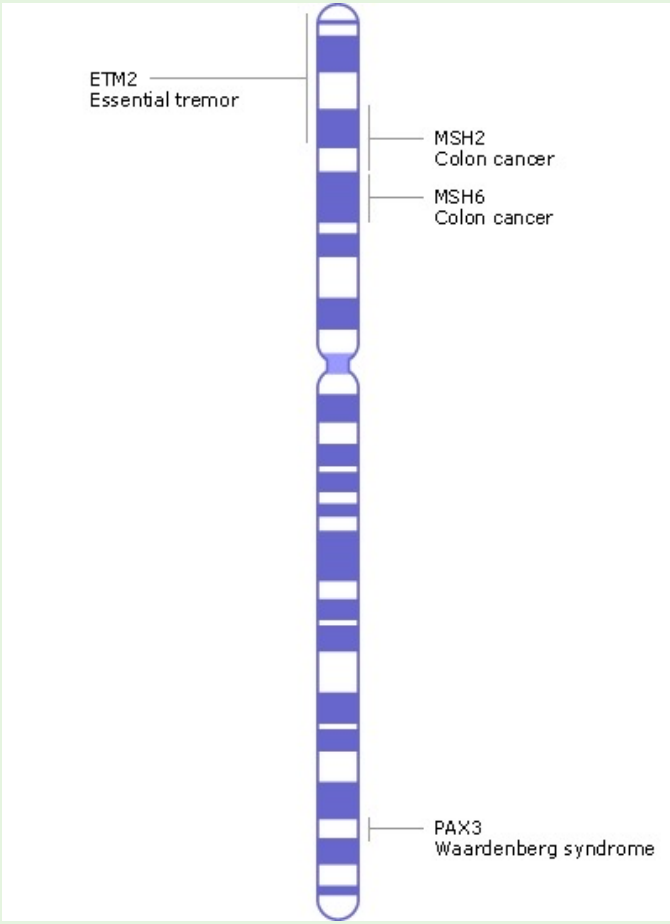
❖Contains over 240 million base pairs, of which ~90% have been determined



Chromosome 2

❖Contains over 2500 genes

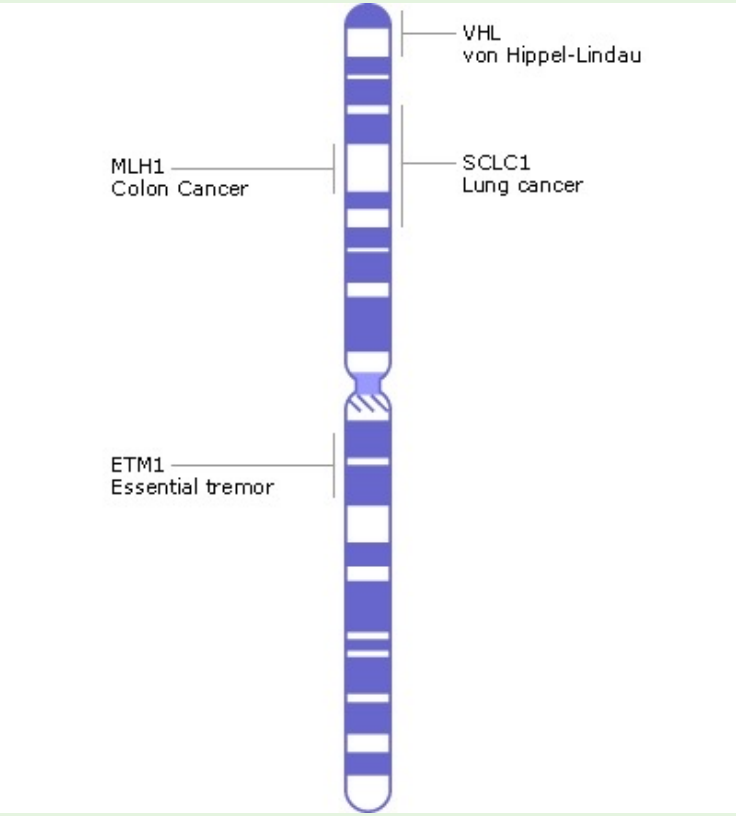
❖Contains over 240 million base pairs, of which ~95% have been determined



Chromosome 3

❖Contains approximately 1900 genes

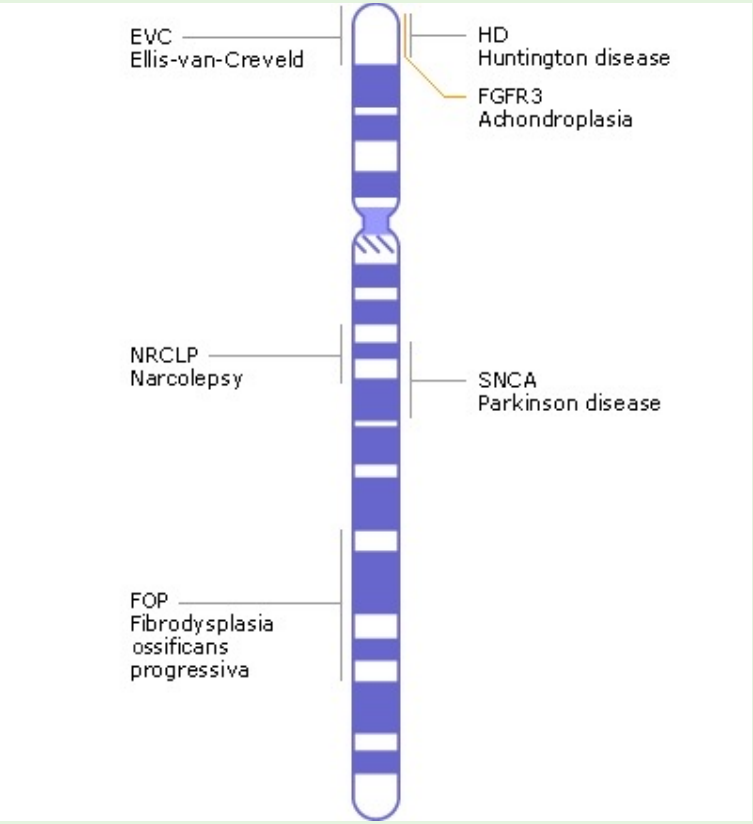
❖Contains approximately 200 million base pairs, of which ~95% have been determined



Chromosome 4

❖Contains approximately 1600 genes

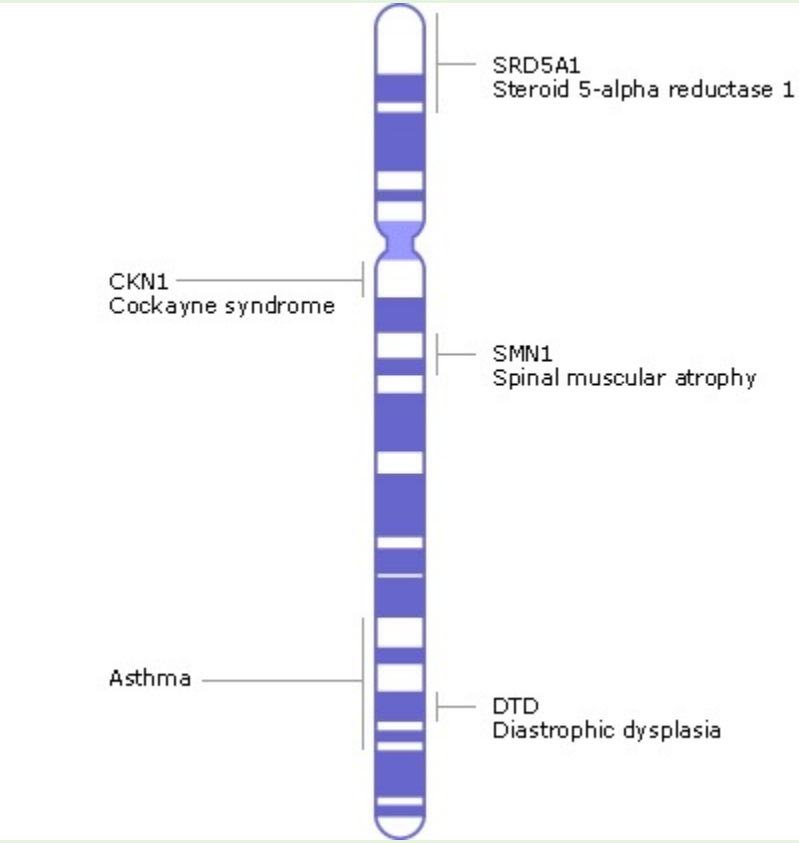
❖Contains approximately 190 million base pairs, of which ~95% have been determined



Chromosome 5

❖Contains approximately 1700 genes

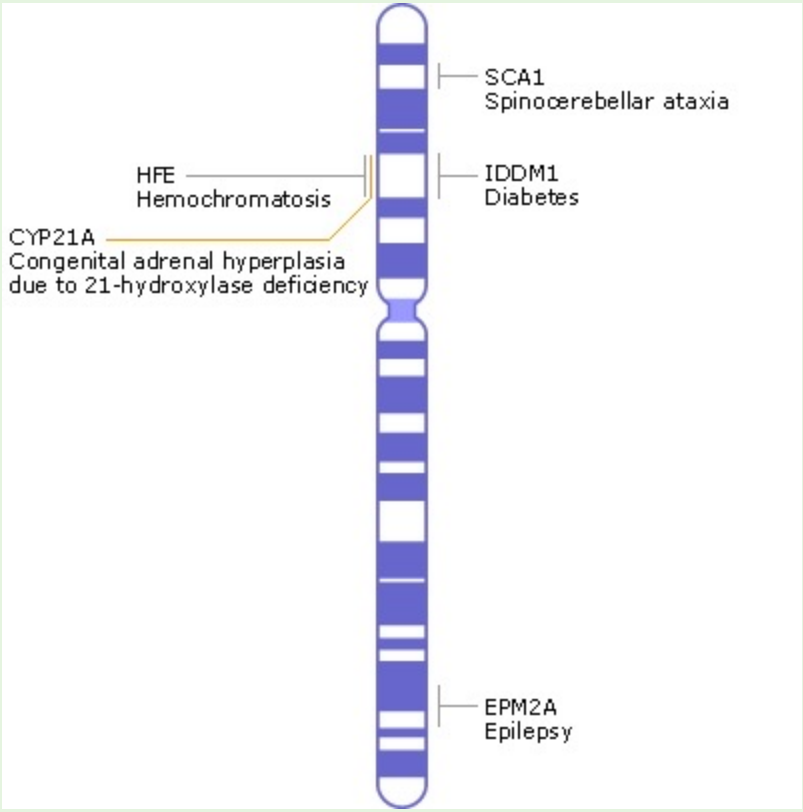
❖Contains approximately 180 million base pairs, of which over 95% have been determined



Chromosome 6

❖Contains approximately 1900 genes

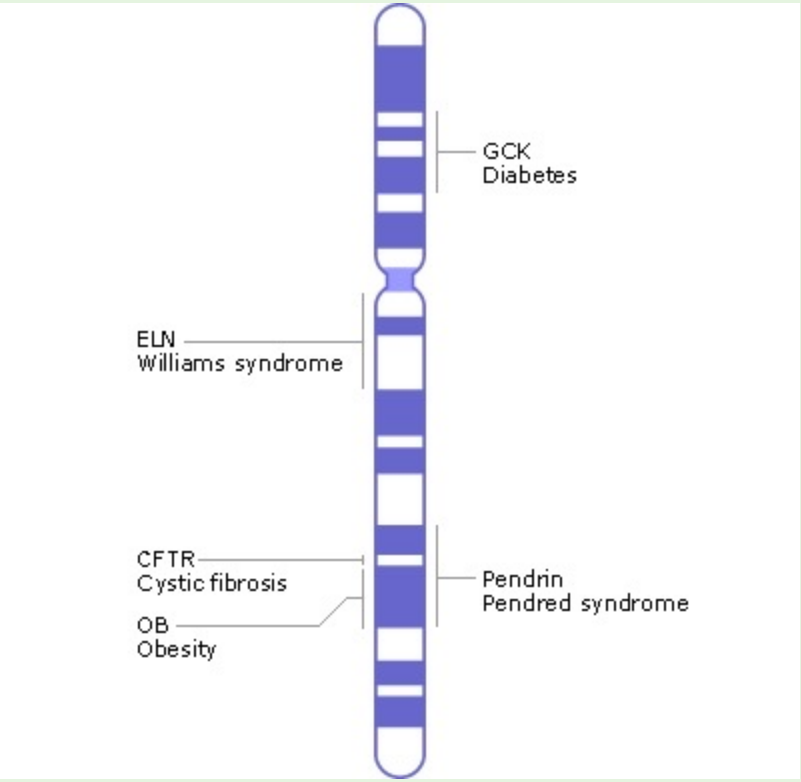
❖Contains approximately 170 million base pairs, of which over 95% have been determined



Chromosome 7

❖Contains approximately 1800 genes

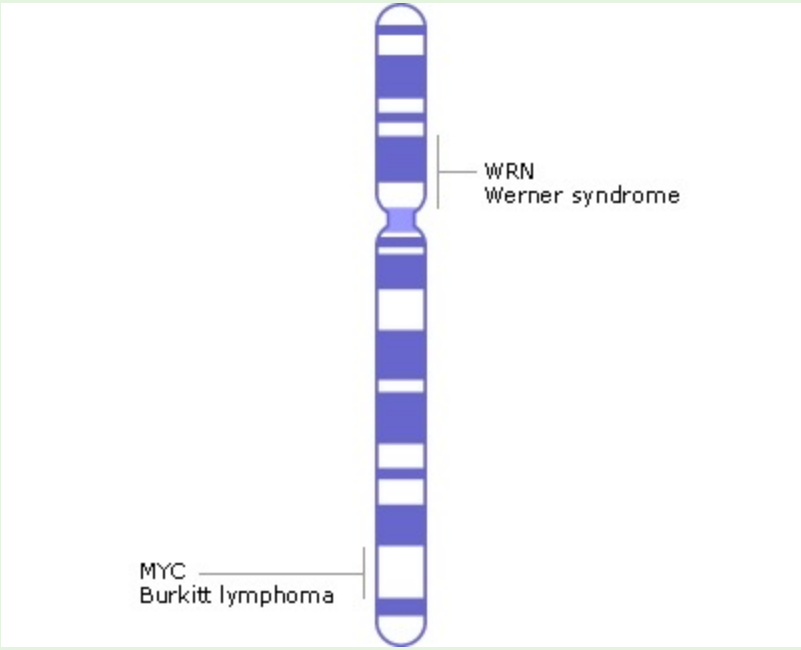
❖Contains over 150 million base pairs, of which over 95% have been determined



Chromosome 8

❖Contains over 1400 genes

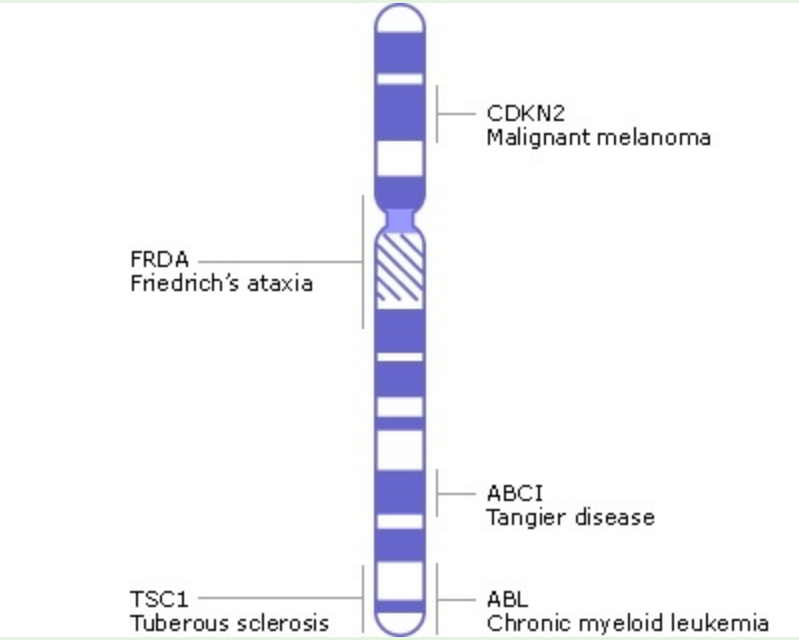
❖Contains over 140 million base pairs, of which over 95% have been determined



Chromosome 9

❖Contains over 1400 genes

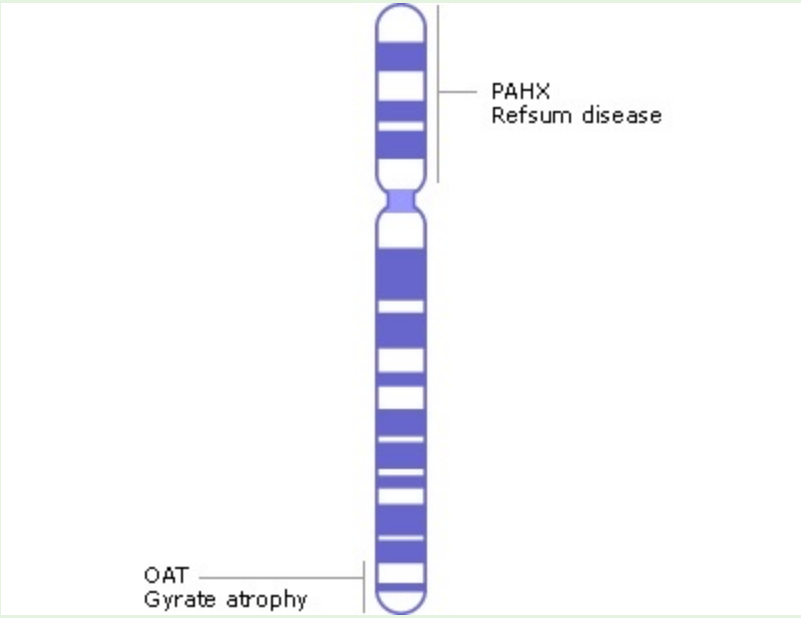
❖Contains over 130 million base pairs, of which over 85% have been determined



Chromosome 10

❖Contains over 1400 genes

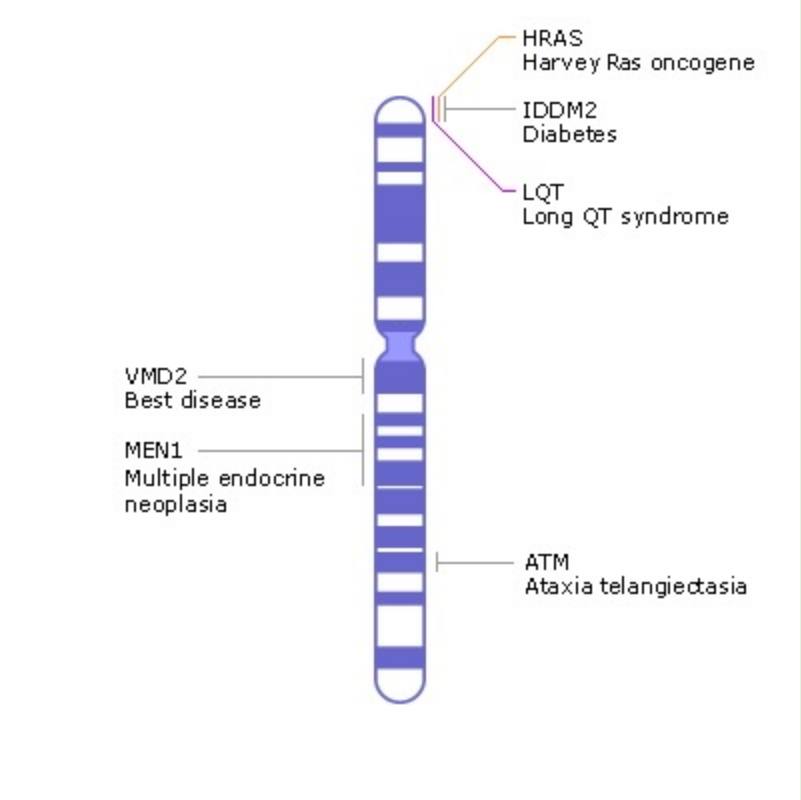
❖Contains over 130 million base pairs, of which over 95% have been determined



Chromosome 11

❖Contains approximately 2000 genes

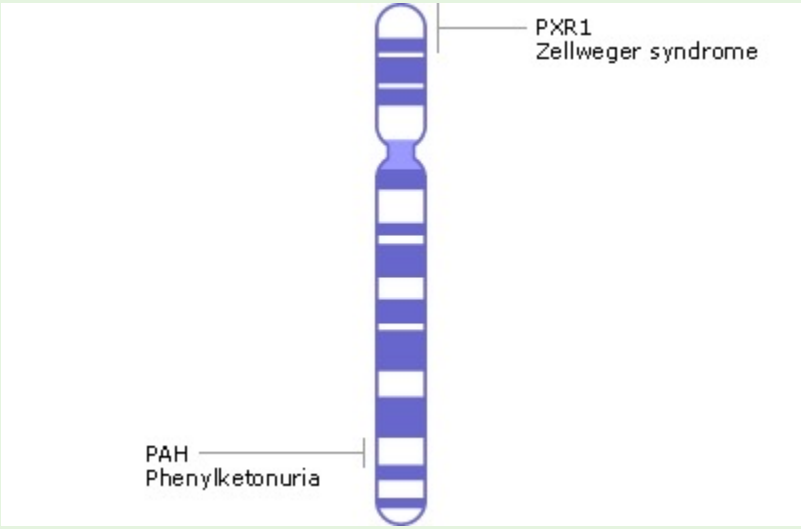
❖Contains over 130 million base pairs, of which over 95% have been determined



Chromosome 12

❖Contains over 1600 genes

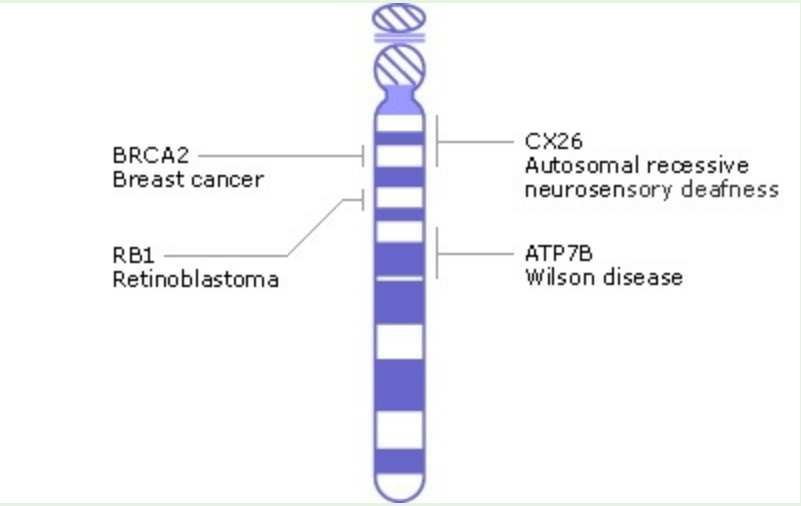
❖Contains over 130 million base pairs, of which over 95% have been determined



Chromosome 13

❖Contains approximately 800 genes

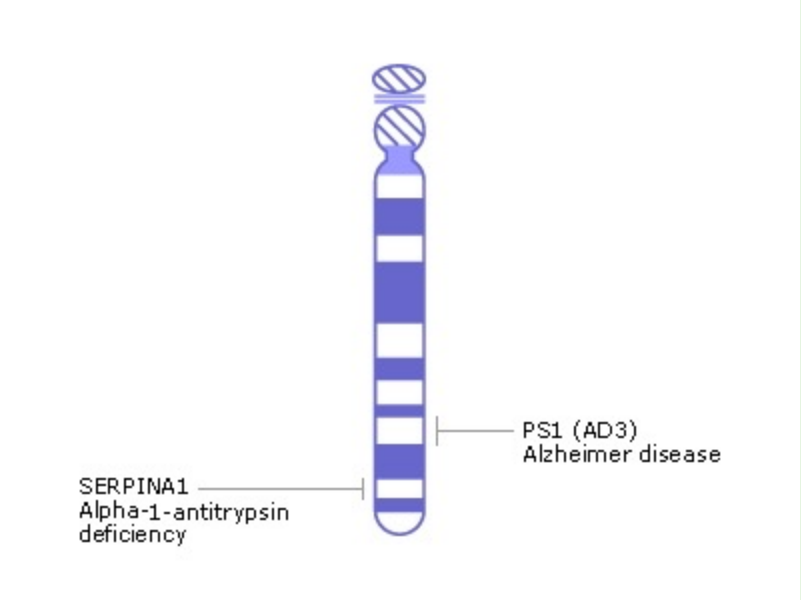
❖Contains over 110 million base pairs, of which over 80% have been determined



Chromosome 14

❖Contains approximately 1200 genes

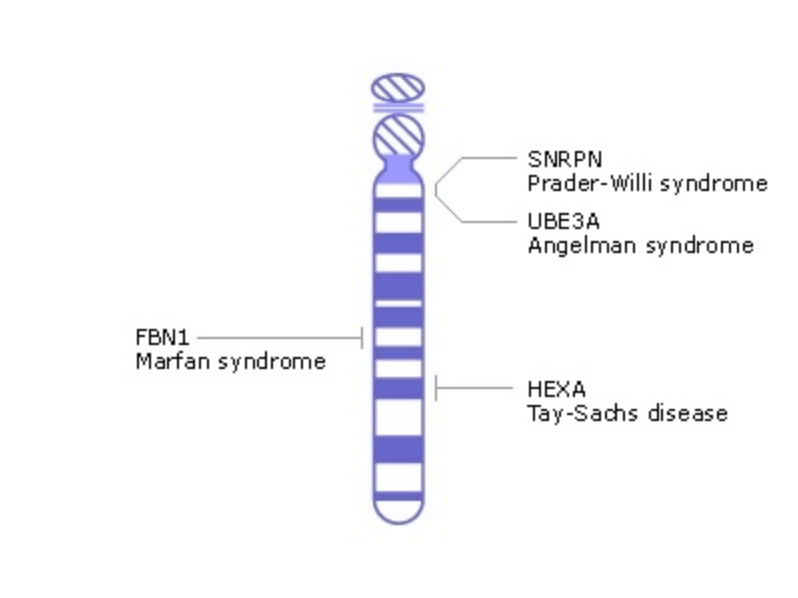
❖Contains over 100 million base pairs, of which over 80% have been determined



Chromosome 15

❖Contains approximately 1200 genes

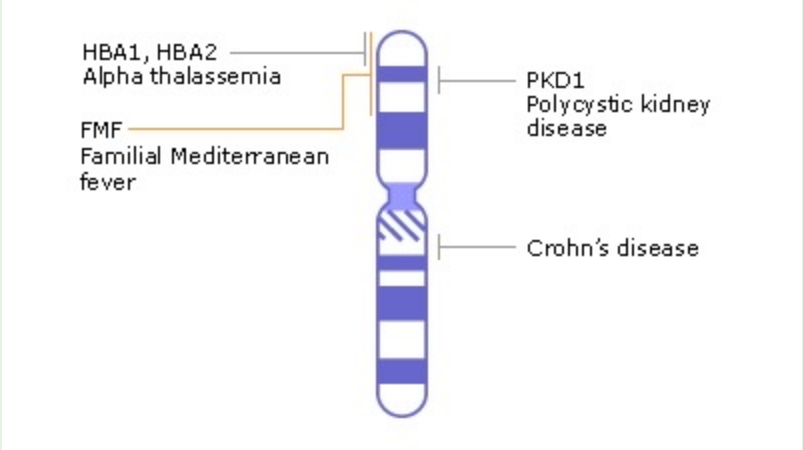
❖Contains approximately 100 million base pairs, of which over 80% have been determined



Chromosome 16

❖Contains approximately 1300 genes

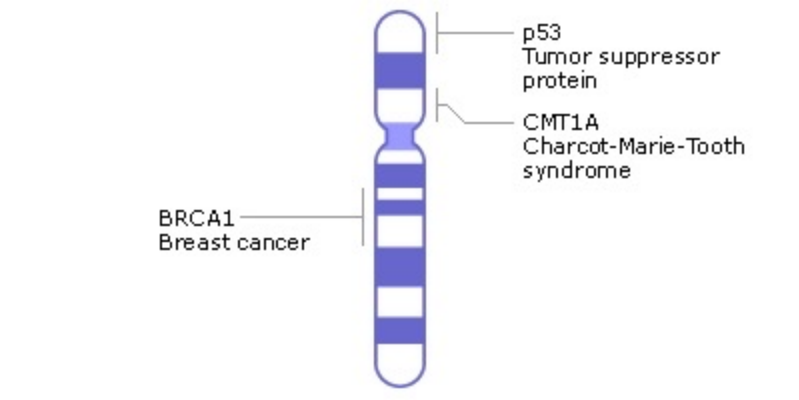
❖Contains approximately 90 million base pairs, of which over 85% have been determined



Chromosome 17

❖Contains over 1600 genes

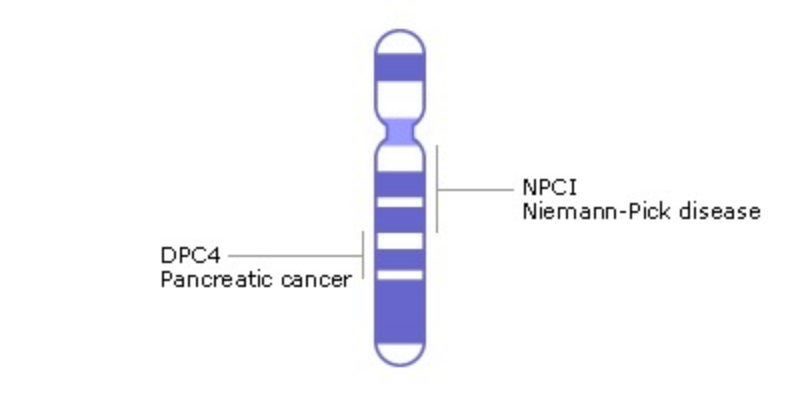
❖Contains approximately 80 million base pairs, of which over 95% have been determined



Chromosome 18

❖Contains over 600 genes

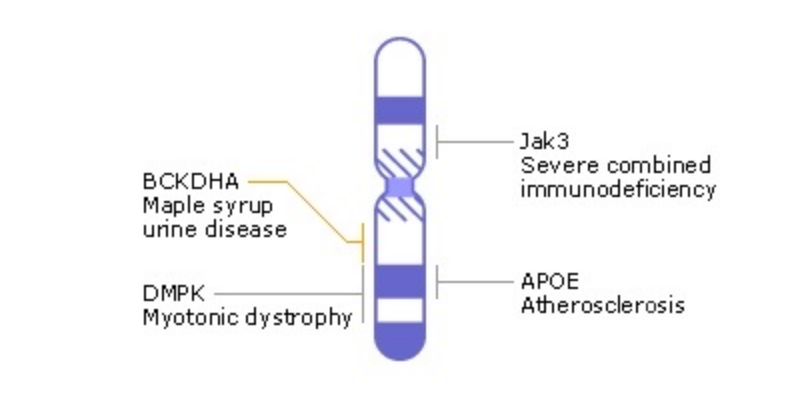
❖Contains over 70 million base pairs, of which over 95% have been determined



Chromosome 19

❖Contains over 1700 genes

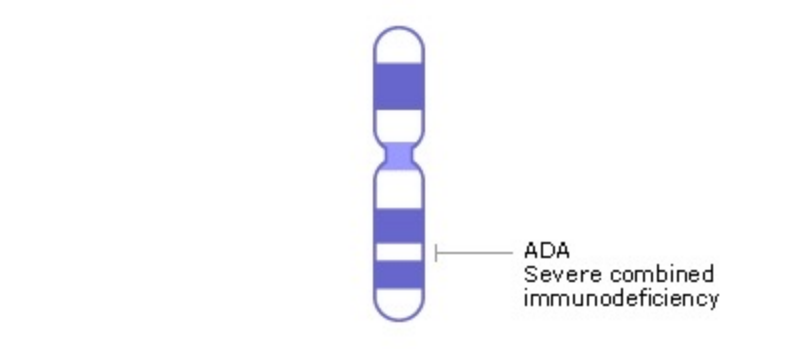
❖Contains over 60 million base pairs, of which over 85% have been determined



Chromosome 20

❖Contains over 900 genes

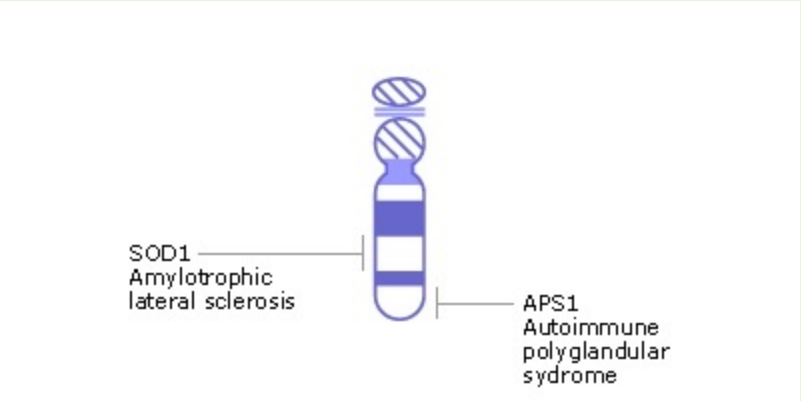
❖Contains over 60 million base pairs, of which over 90% have been determined



Chromosome 21

❖Contains over 400 genes

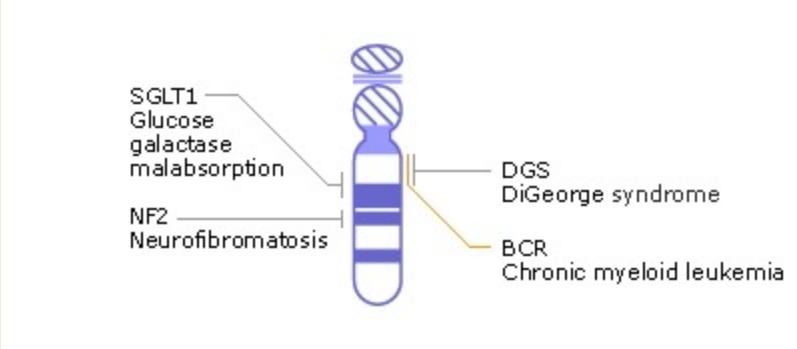
❖Contains over 40 million base pairs, of which over 70% have been determined



Chromosome 22

❖Contains over 800 genes

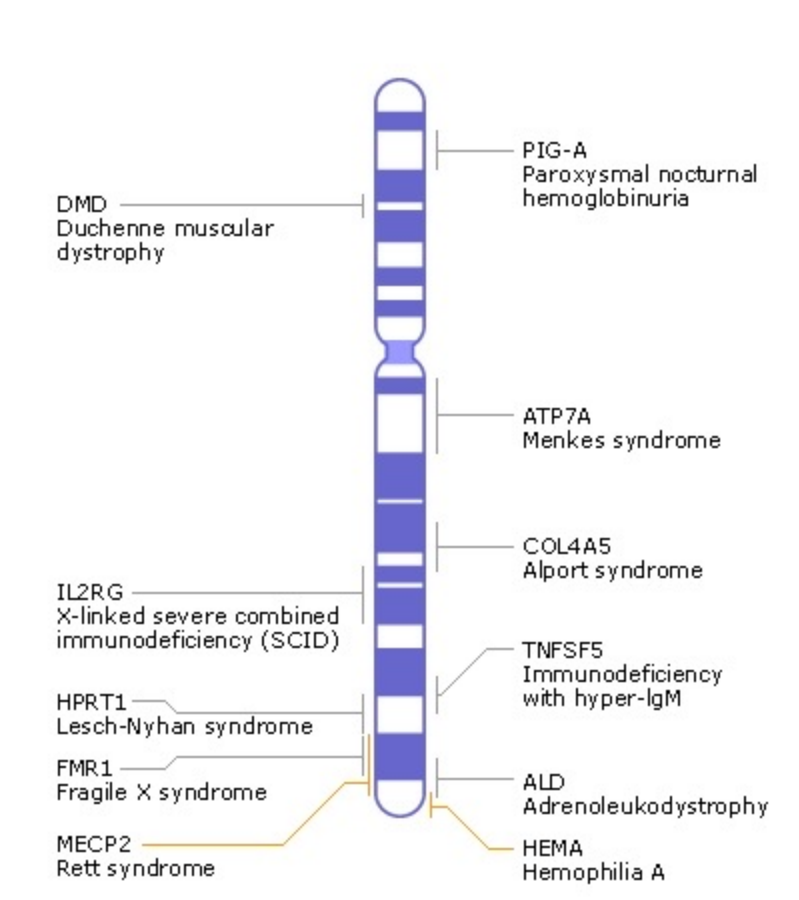
❖Contains over 40 million base pairs, of which approximately 70% have been determined



Chromosome X

❖Contains over 1400 genes

❖Contains over 150 million base pairs, of which approximately 95% have been determined



Chromosome Y

❖Contains over 200 genes

❖Contains over 50 million base pairs, of which approximately 50% have been determined