Molecular Biology (3)

The human genome

Mamoun Ahram, PhD
Bilal Azab, PhD
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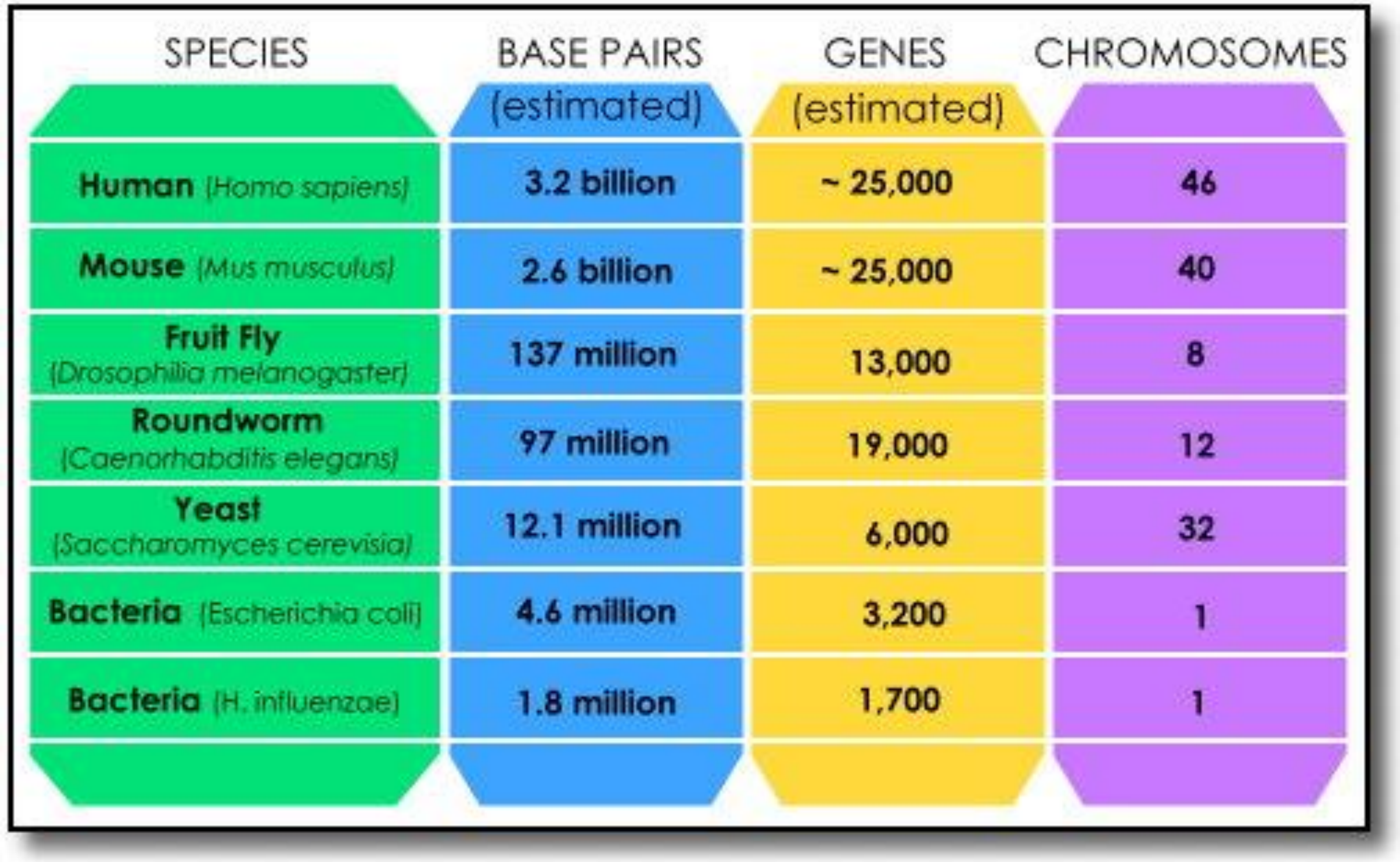
Resources

- This lecture
- Cooper, Ch. 5, pp.159-162, 166-171



SPECIES	BASE PAIRS (estimated)	GENES (estimated)	CHROMOSOMES
Human (*Homo sapiens*)	**3.2 billion**	**~ 25,000**	**46**
Mouse (*Mus musculus*)	**2.6 billion**	**~ 25,000**	**40**
Fruit Fly (*Drosophilia melanogaster*)	**137 million**	**13,000**	**8**
Roundworm (*Caenorhabditis elegans*)	**97 million**	**19,000**	**12**
Yeast (*Saccharomyces cerevisia*)	**12.1 million**	**6,000**	**32**
Bacteria (Escherichia coli)	**4.6 million**	**3,200**	**1**
Bacteria (H. influenzae)	**1.8 million**	**1,700**	**1**

Nucleotides per genomes

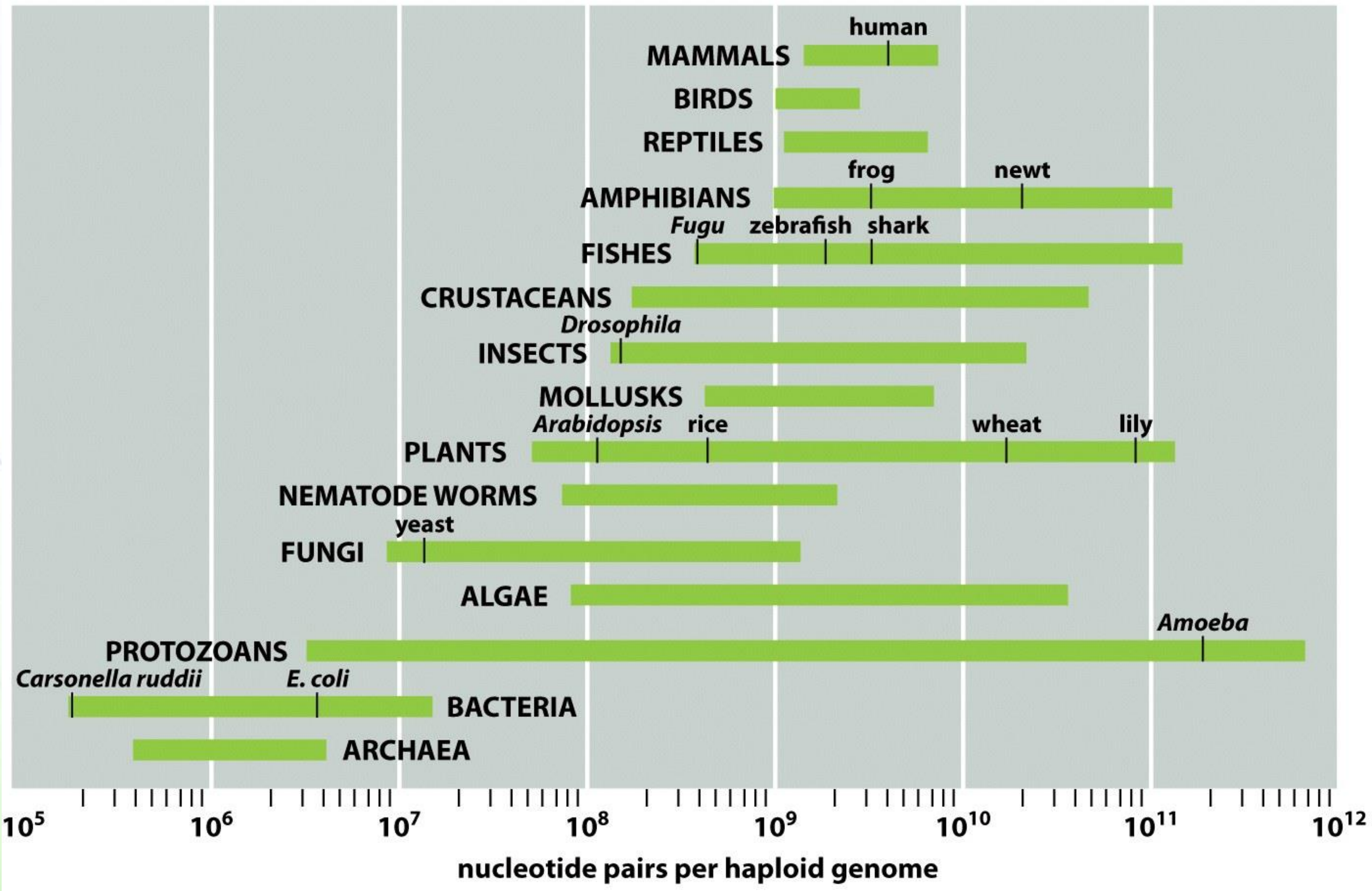
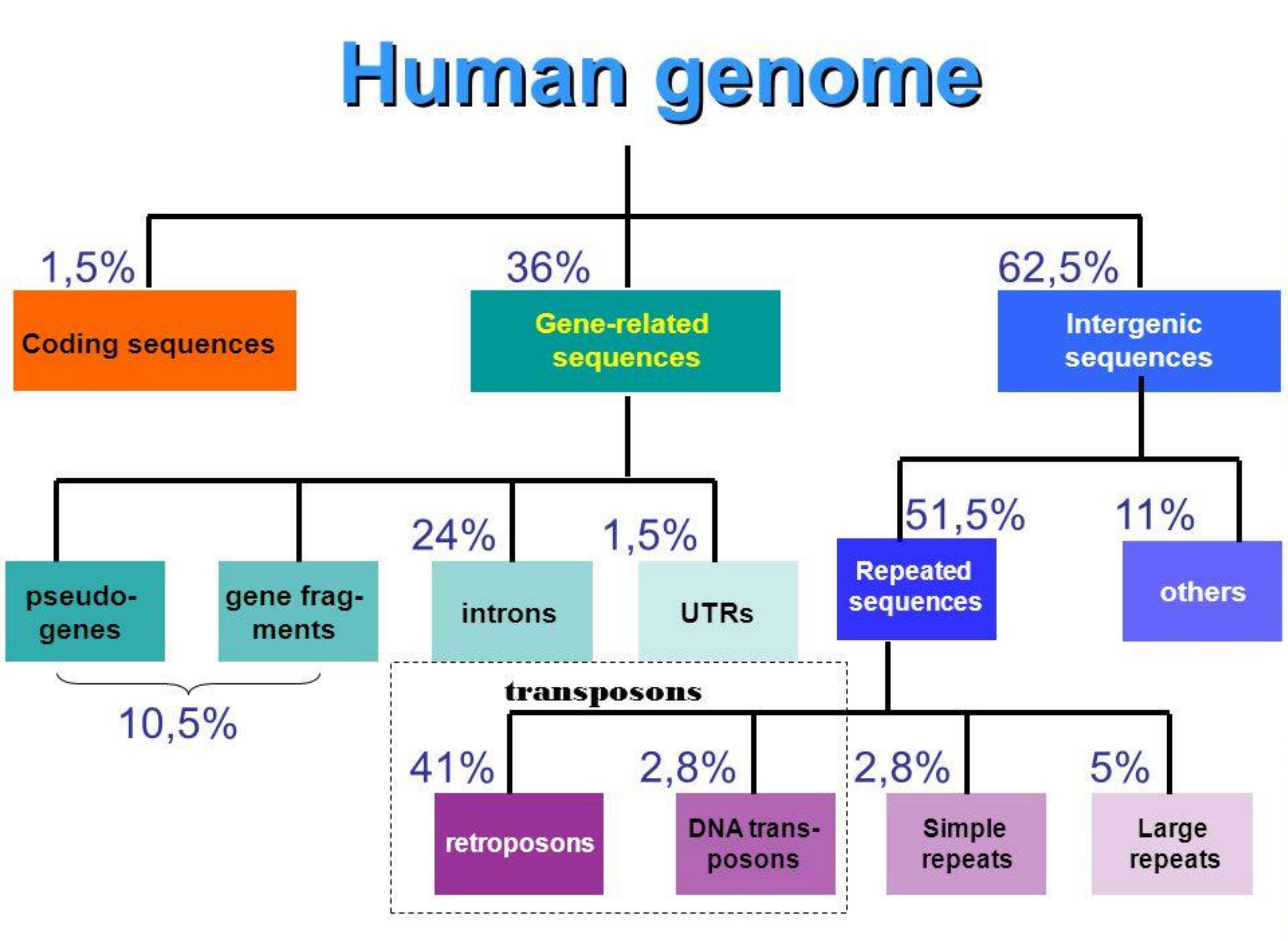


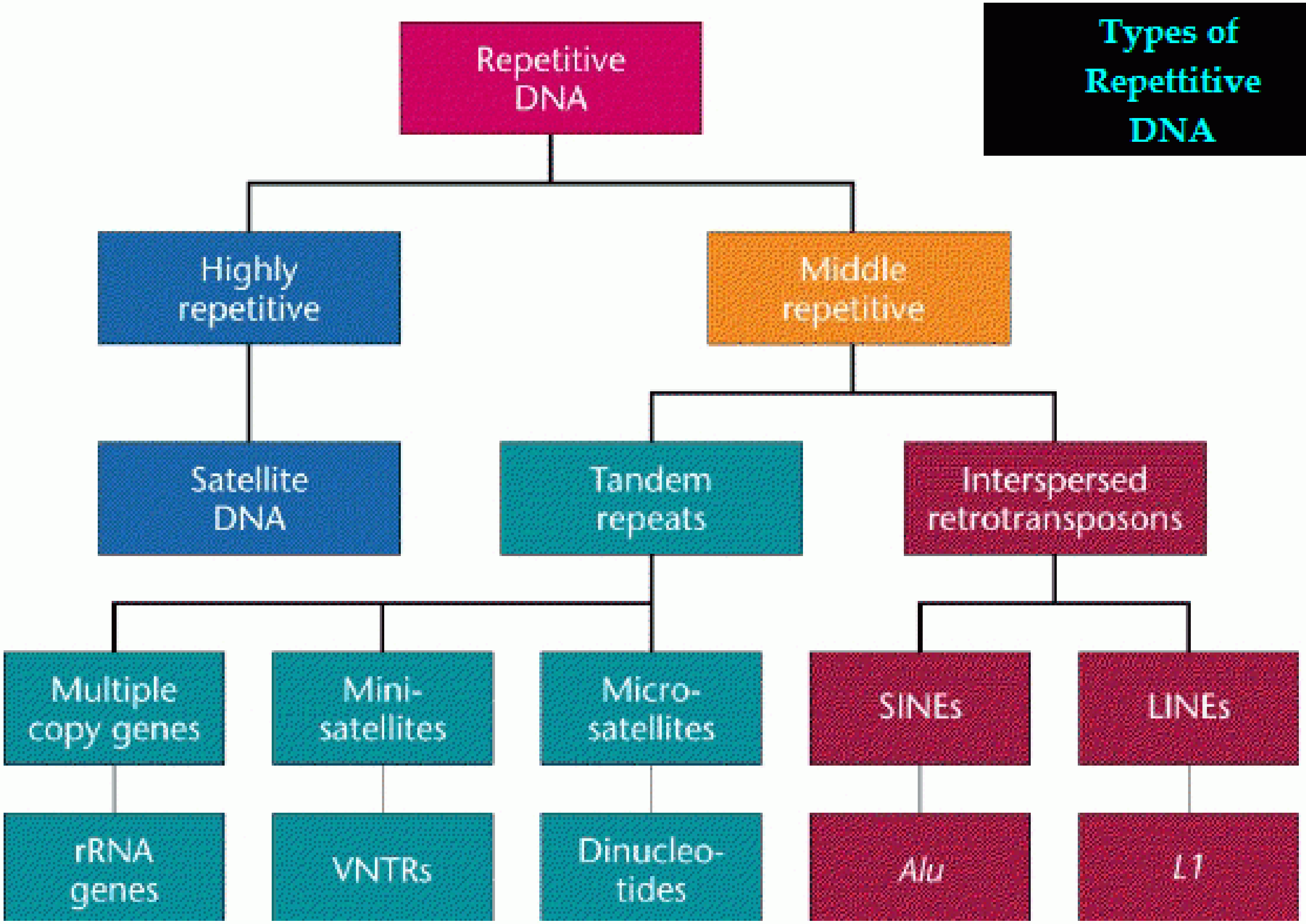
Figure 1-41 Essential Cell Biology 3/e (© Garland Science 2010)

Components of the human genome



Repetitive DNA sequences

Types of Repettitive DNA

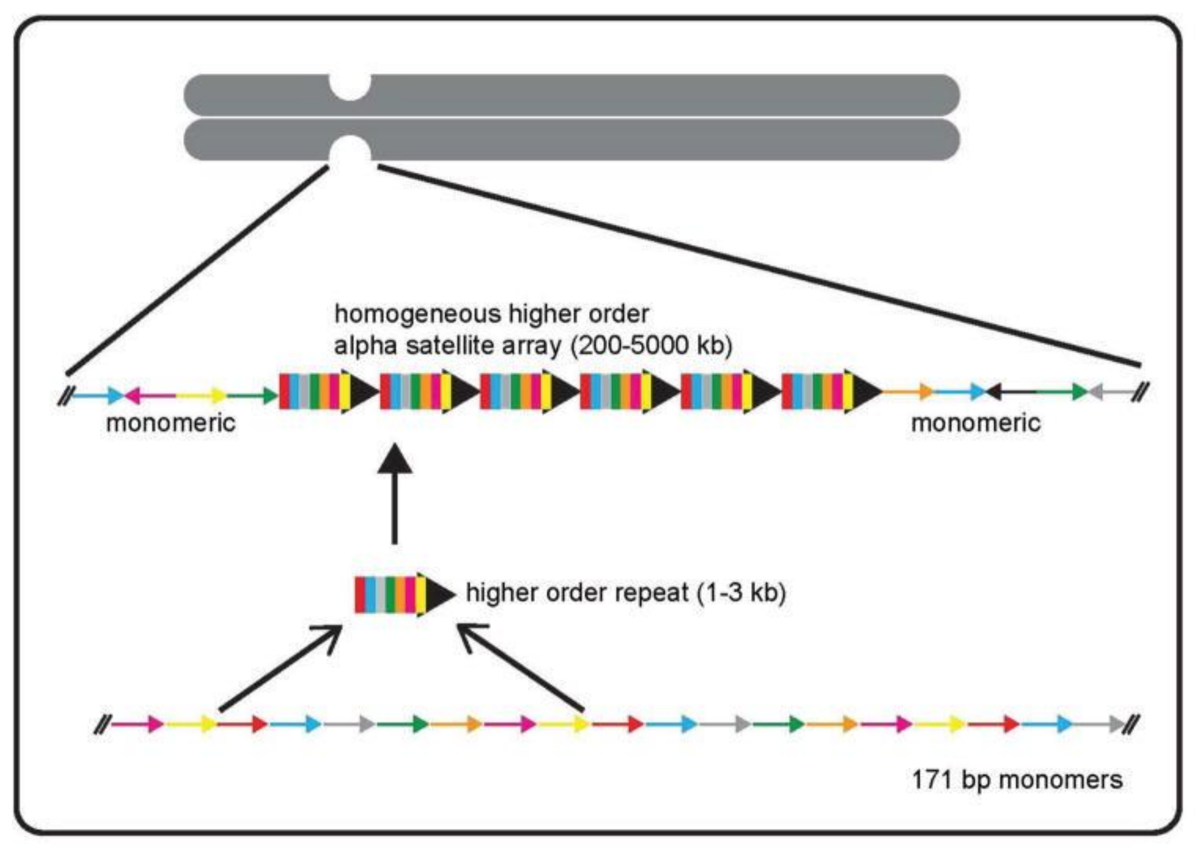


Repetitive DNA sequences

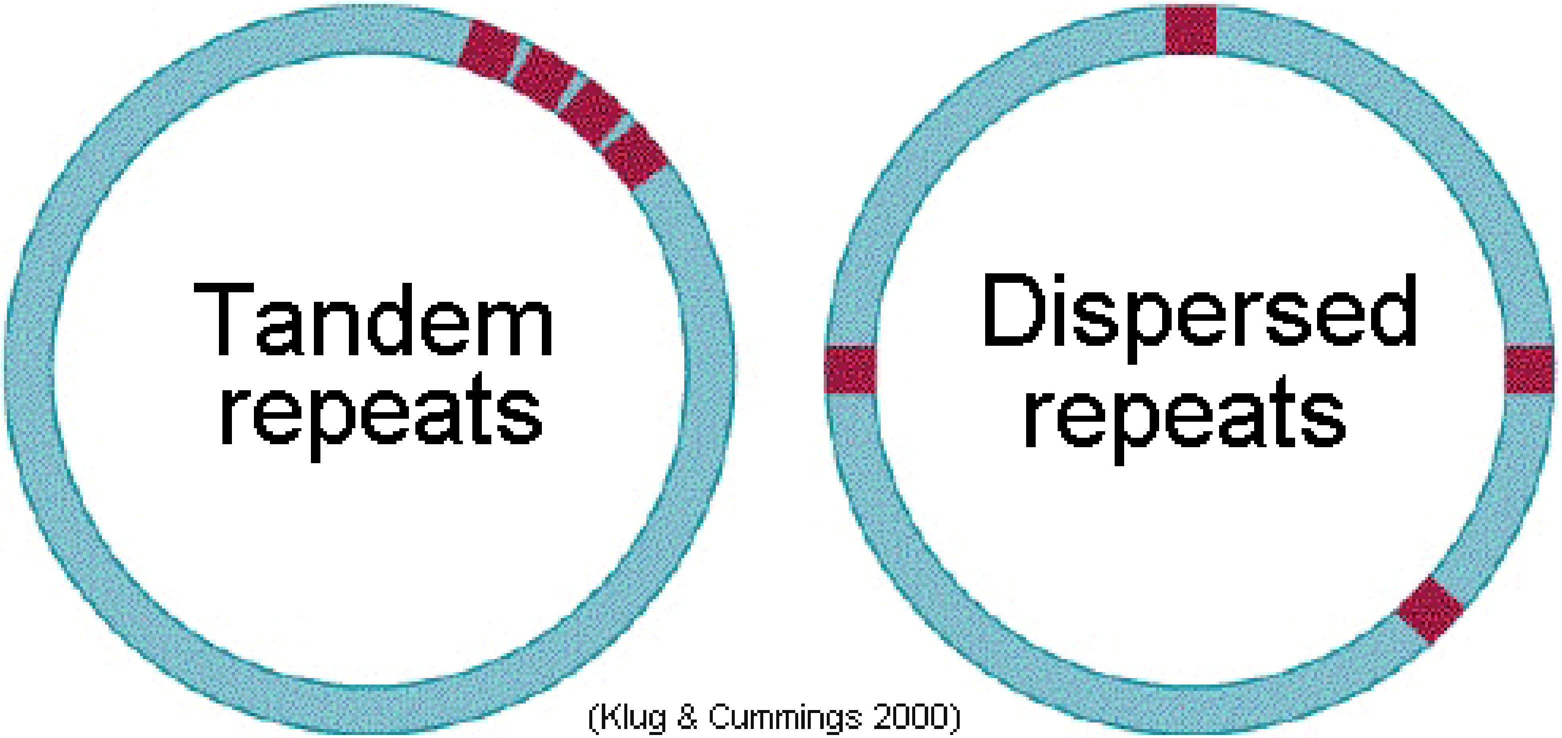
Repetitive DNA

Highly repetitive

Satellite DNA



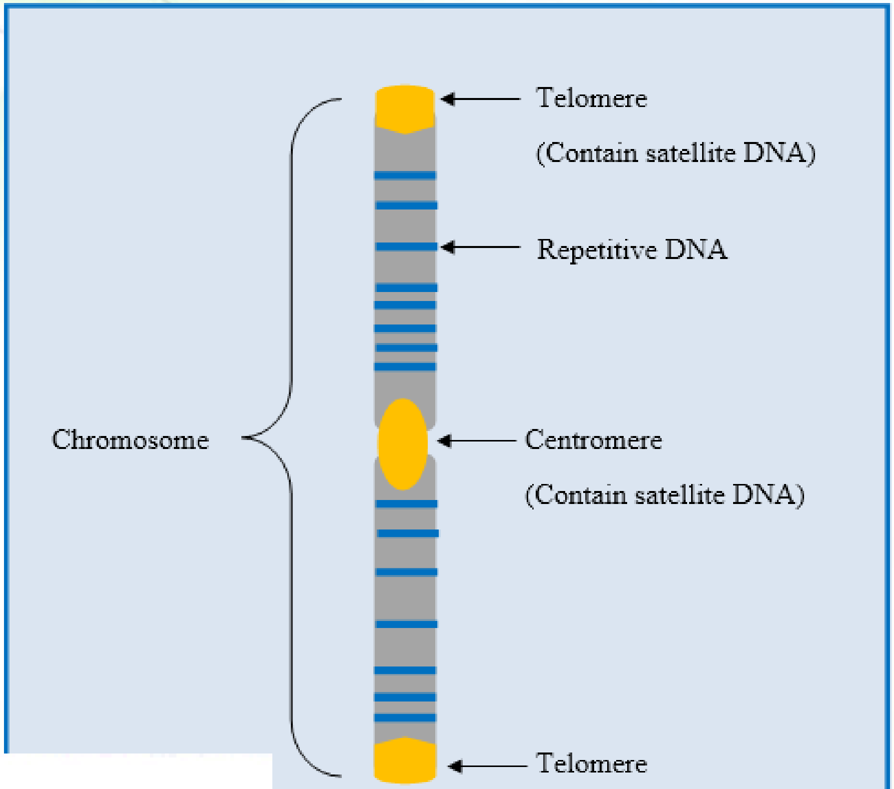
Tandem vs. dispersed

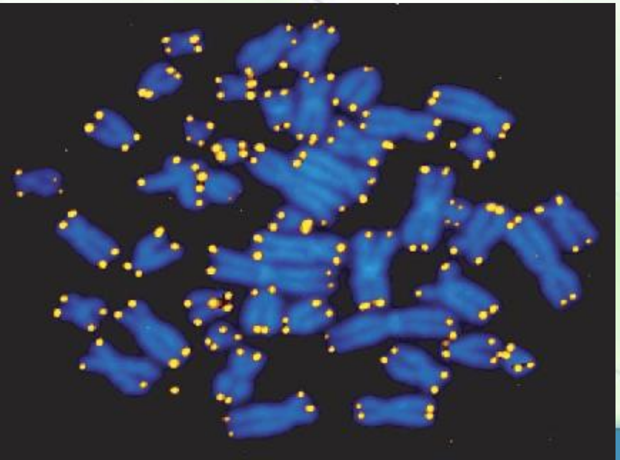


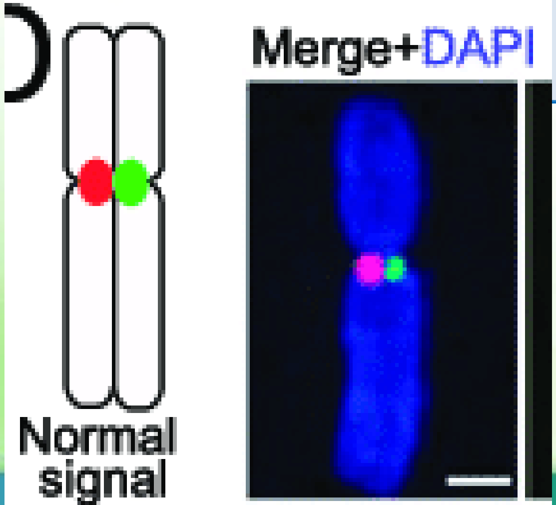
(Klug & Cummings 2000)

Satellite (macro-satellite) DNA

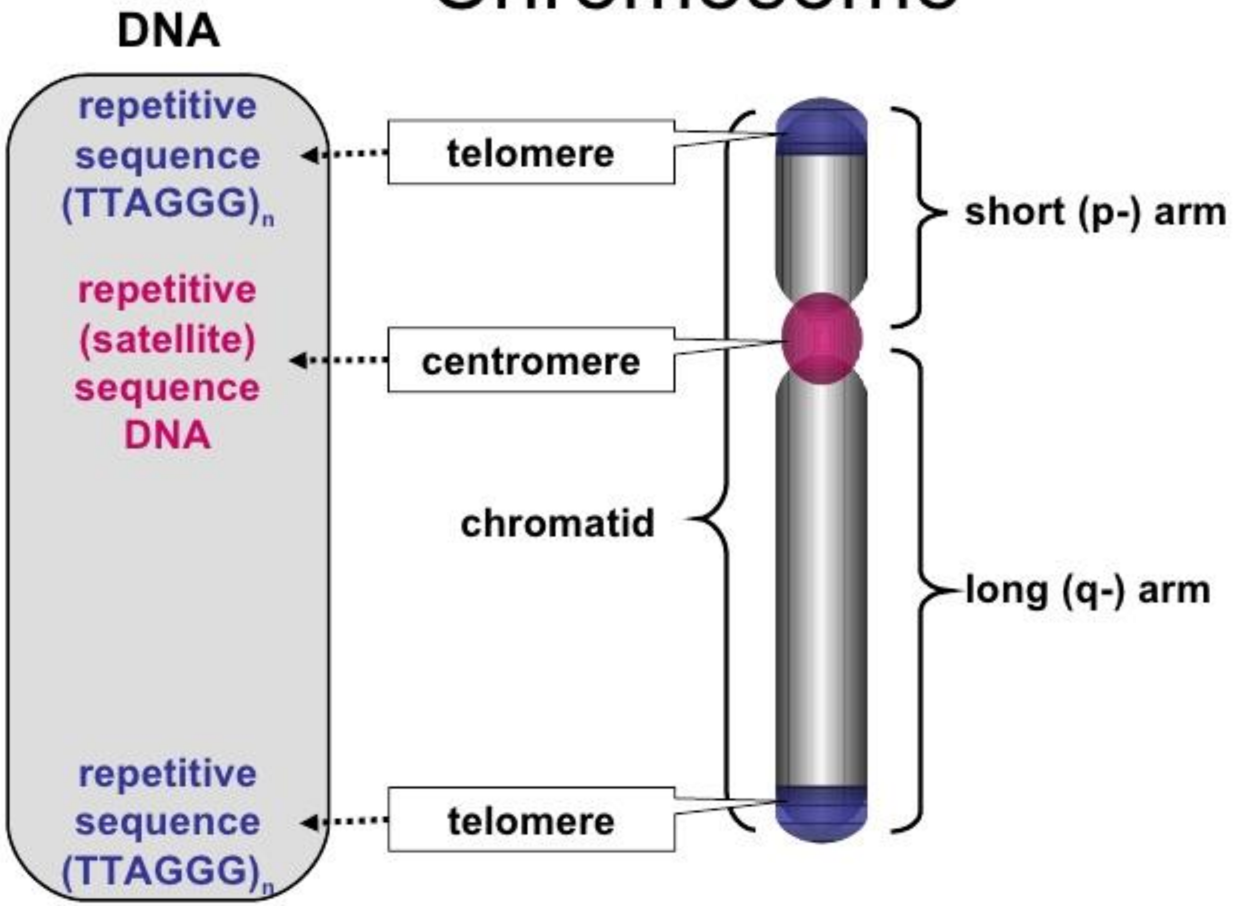
- Regions of 5-300 bp repeated 10^6-10^7 times (10% of genome)
- Centromeric repeats (171 bp) unique to each chromosome (you make chromosome-specific probes) by **fluorescent in situ hybridization**.
- Telomeric repeats







Chromosome



DNA

repetitive sequence $(TTAGGG)_n$

repetitive (satellite) sequence DNA

repetitive sequence $(TTAGGG)_n$

telomere

centromere

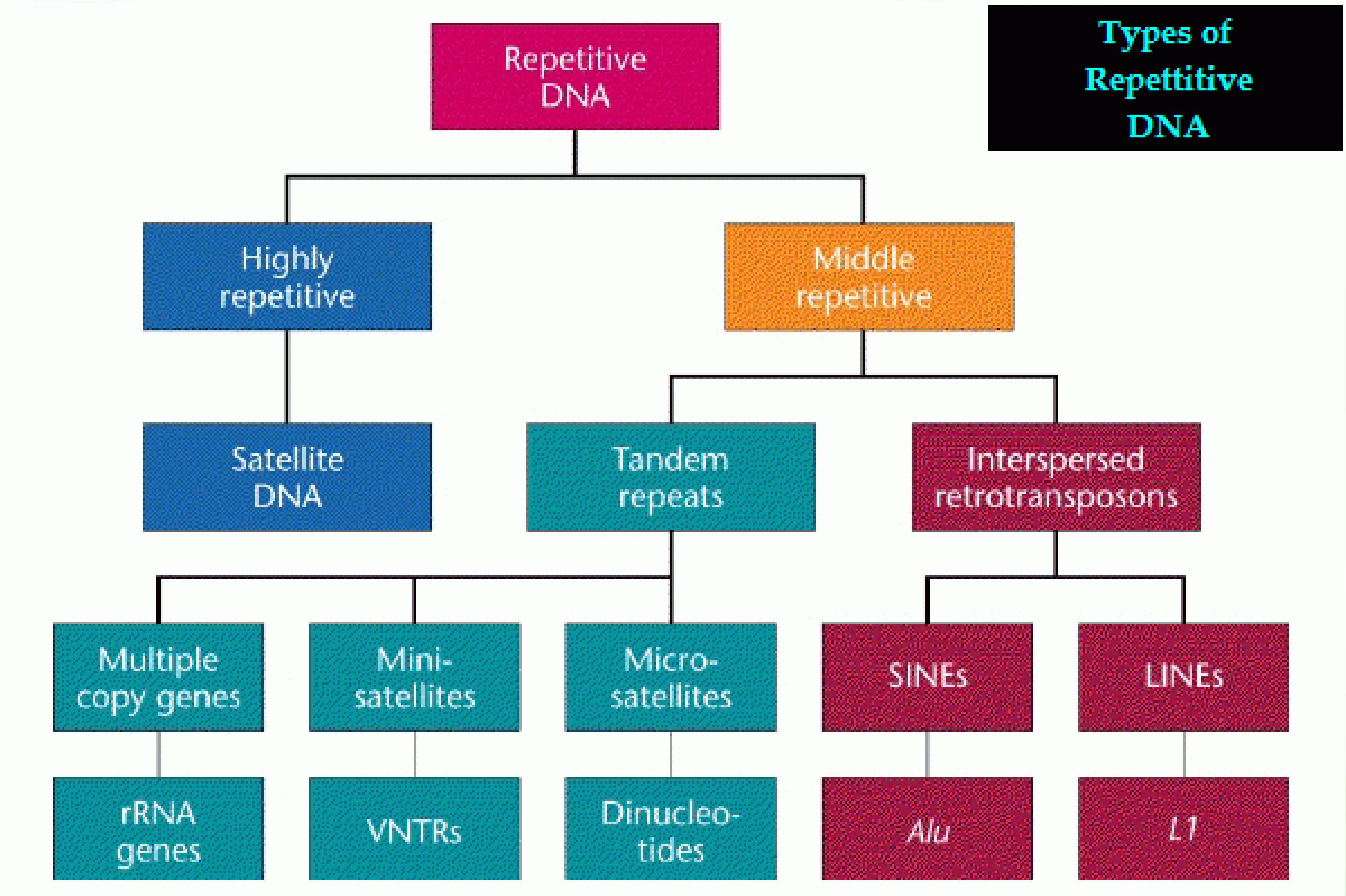
telomere

chromatid

short (p-) arm

long (q-) arm

Repetitive DNA sequences

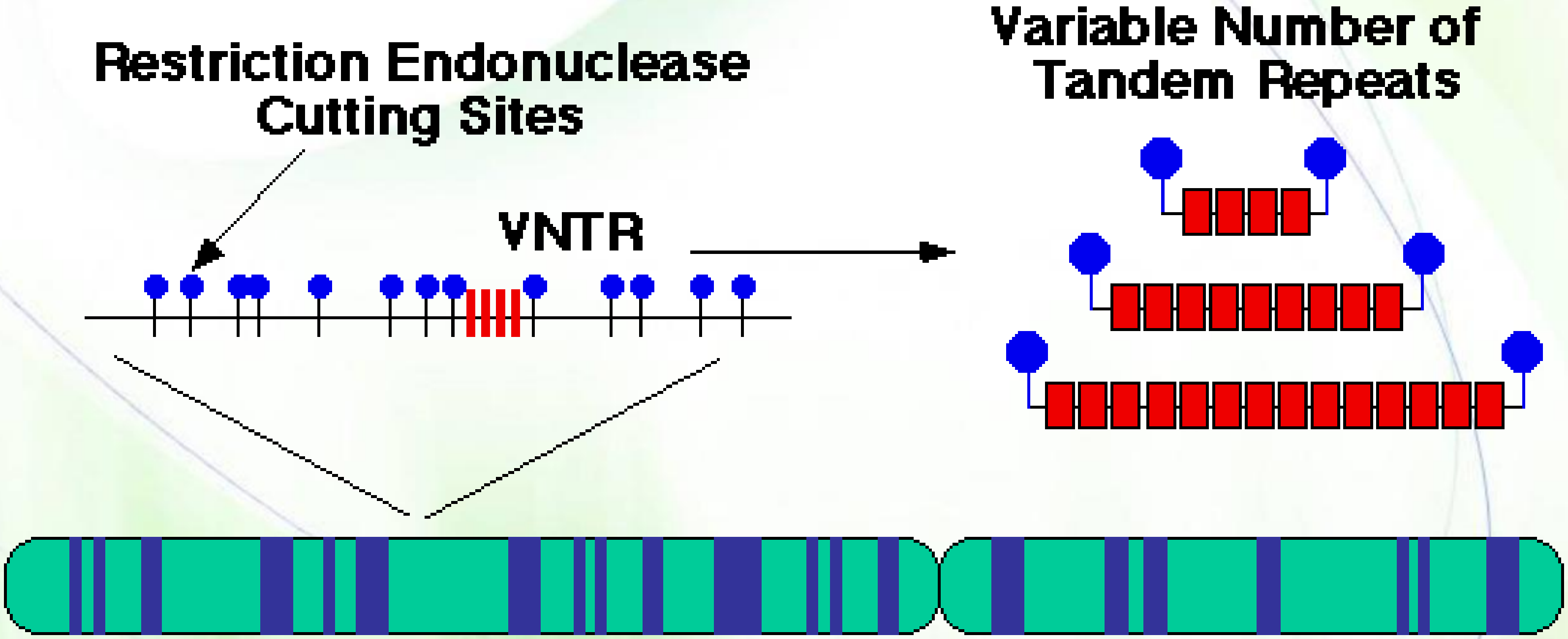


Types of Repettitive DNA

- Repetitive DNA
  - Highly repetitive
    - Satellite DNA
  - Middle repetitive
    - Tandem repeats
      - Multiple copy genes
        - rRNA genes
      - Minisatellites
        - VNTRs
      - Microsatellites
        - Dinucleotides
    - Interspersed retrotransposons
      - SINEs
        - *Alu*
      - LINEs
        - *L1*

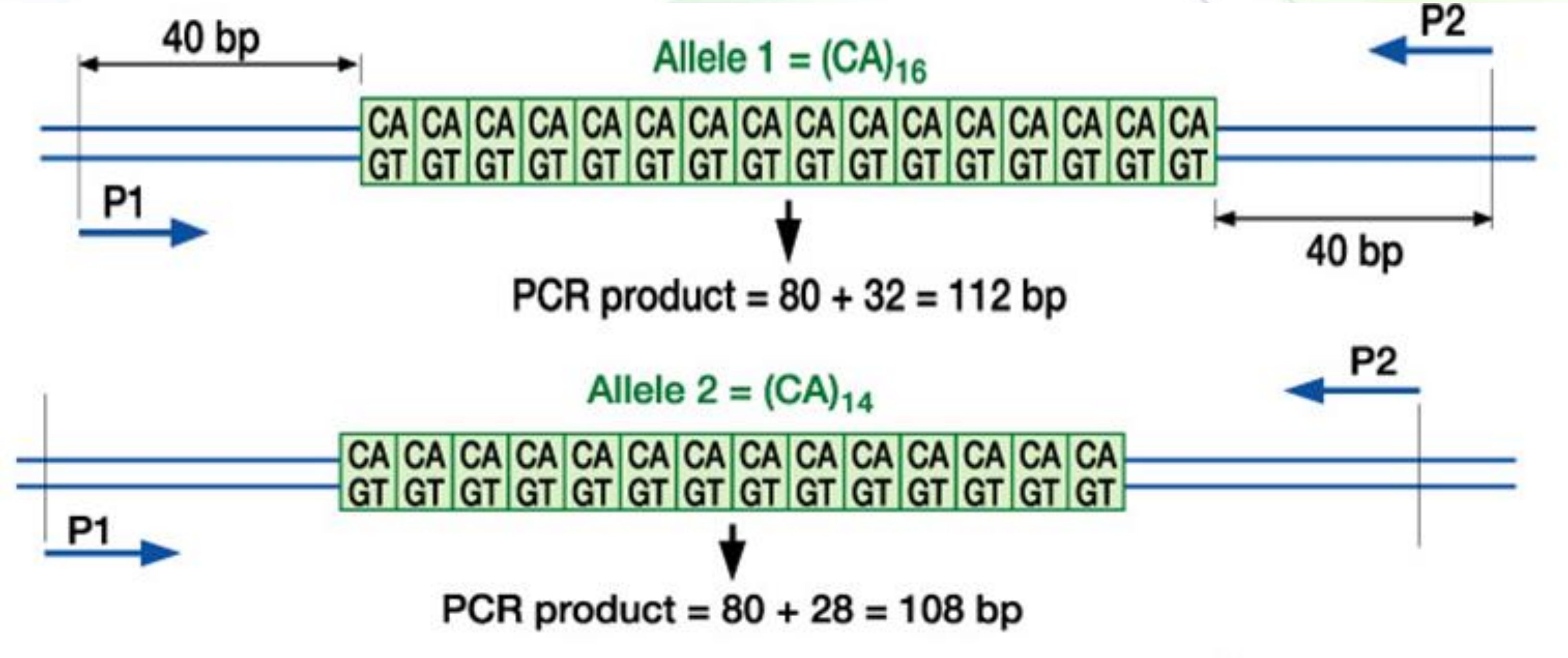
Mini-satellite DNA

- Mini satellite sequences or VNTRs (variable number of tandem repeats) of 20 to 100 bp repeated 20-50 times



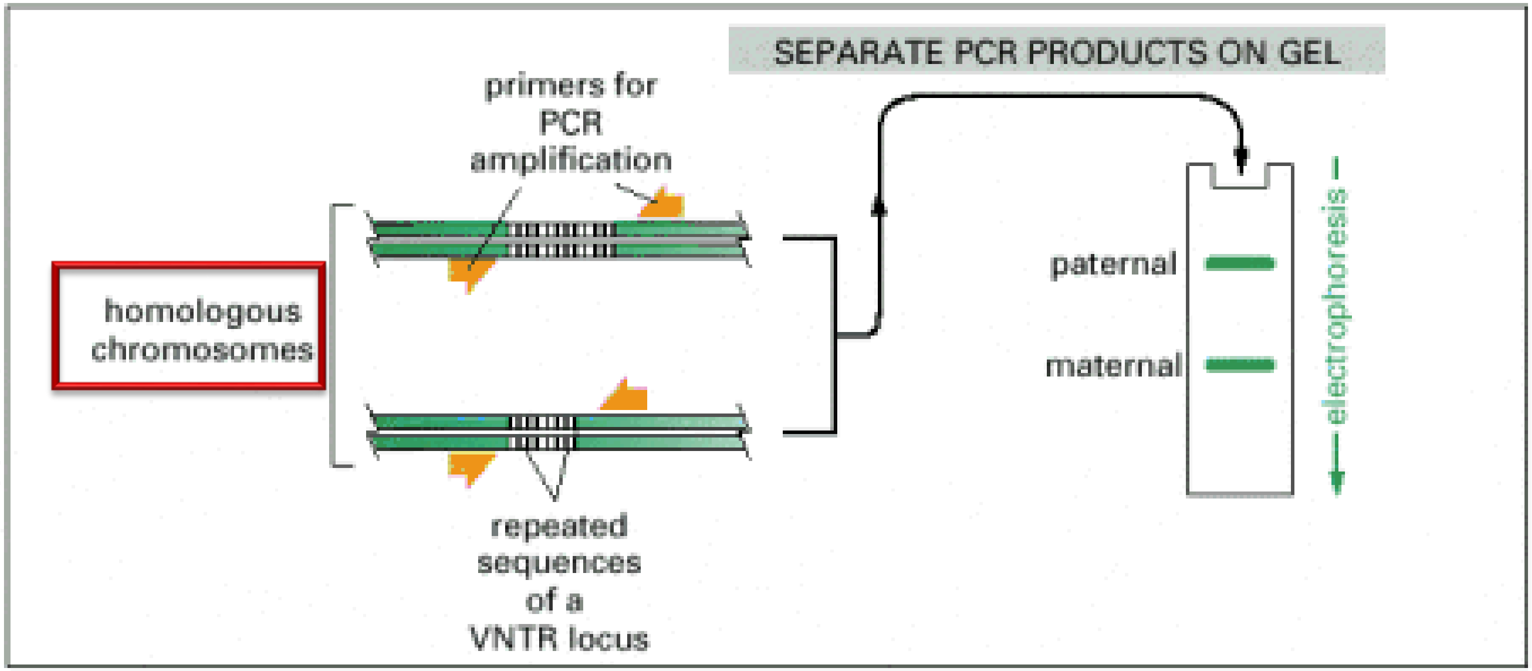
Micro-satellite DNA

- STRs (short tandem repeats) of 2 to 10 bp repeated 10-100 times

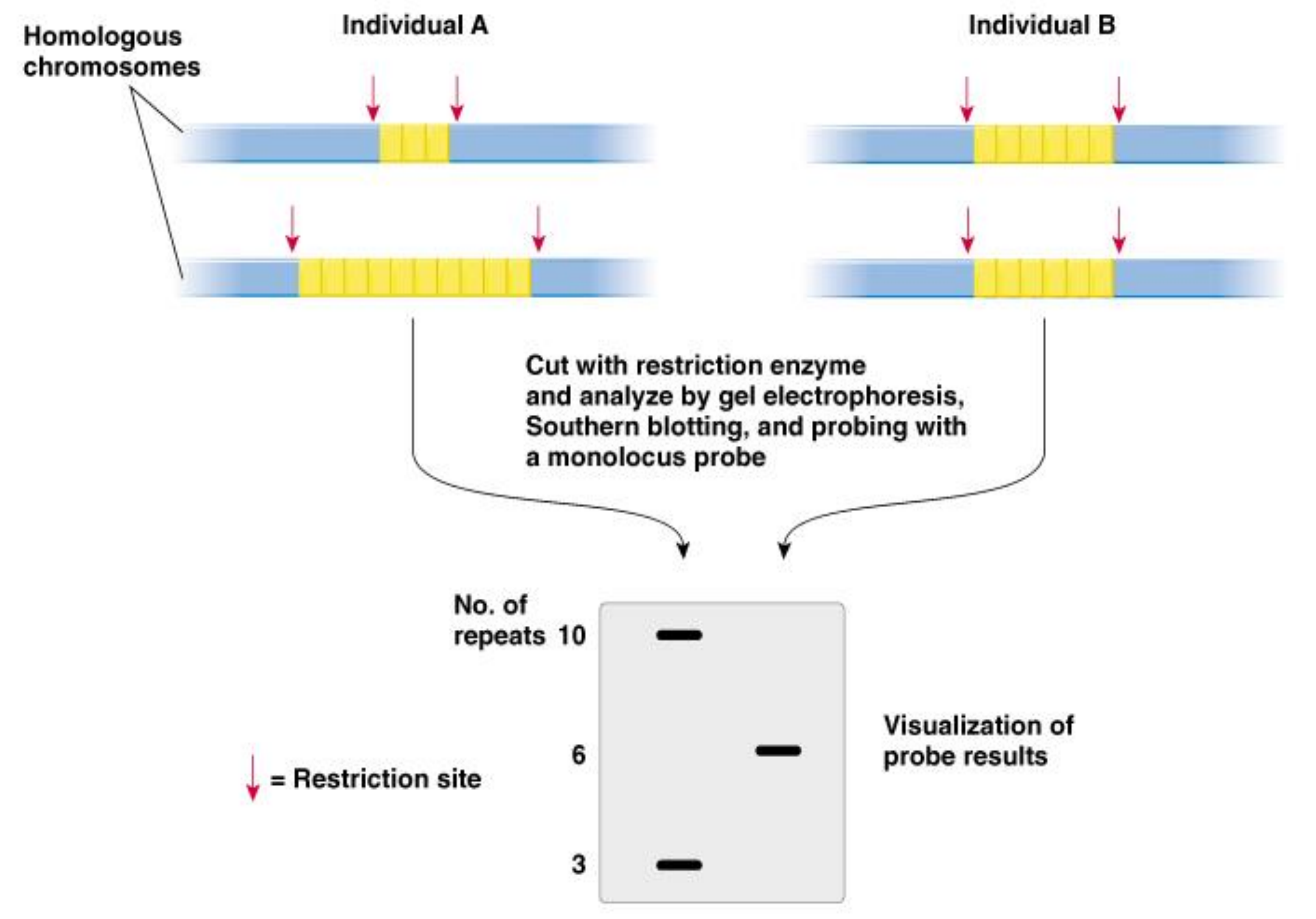


Polymorphisms of VNTR and STR

- STRs and VNTRs are highly variable among individuals (polymorphic)
  - Thus, they are useful in DNA profiling for forensic testing

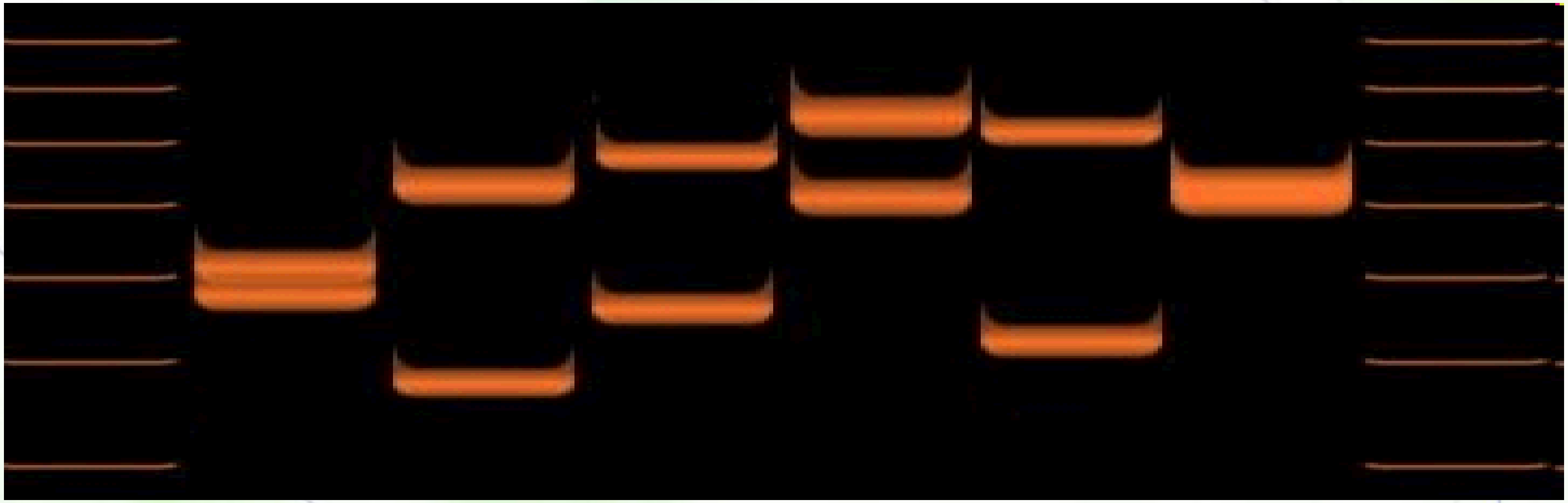


Microsatellites and VNTRs as DNA Markers



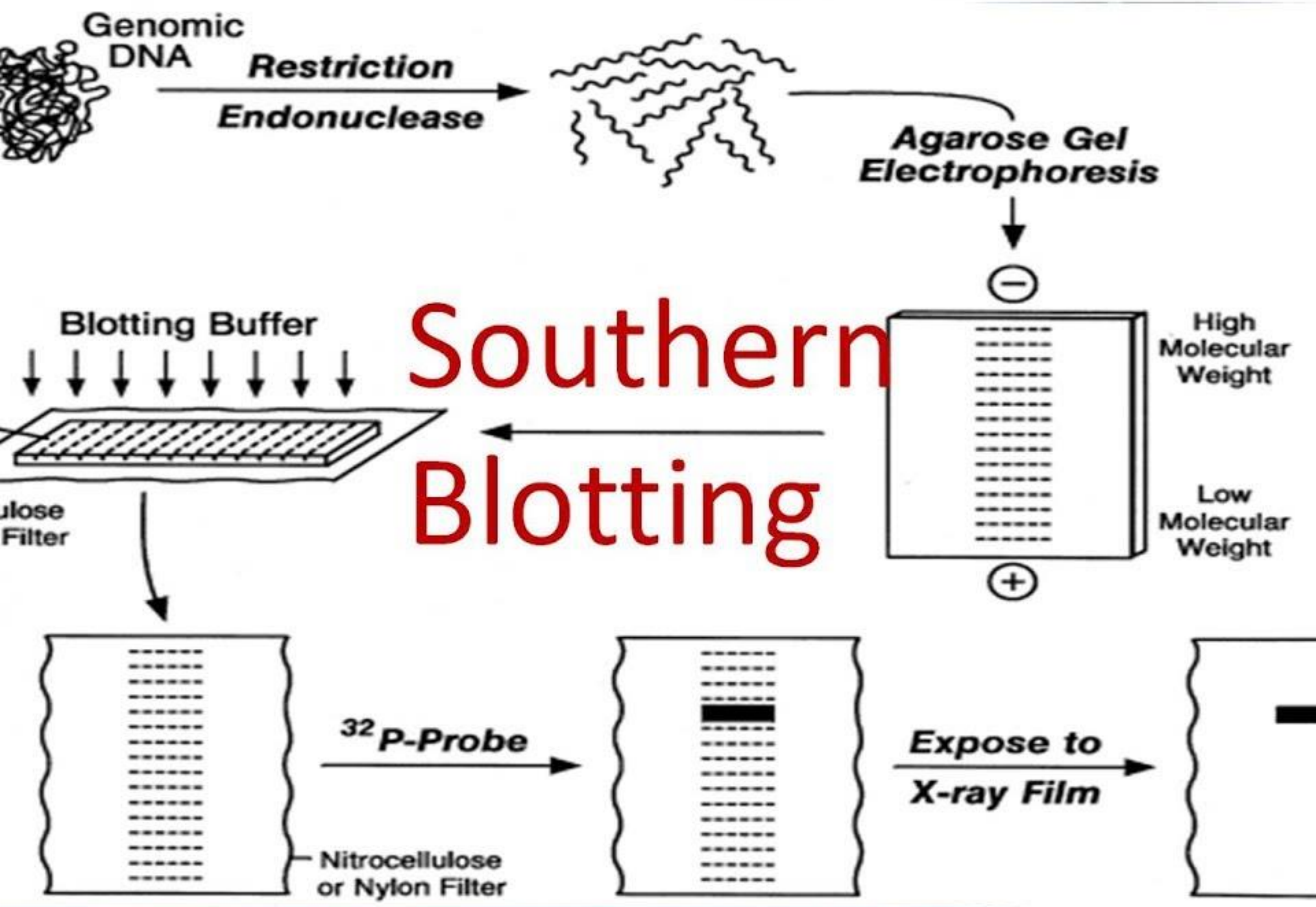
VNTR in medicine and more

- The picture below illustrates VNTR allelic length variation among 6 individuals.

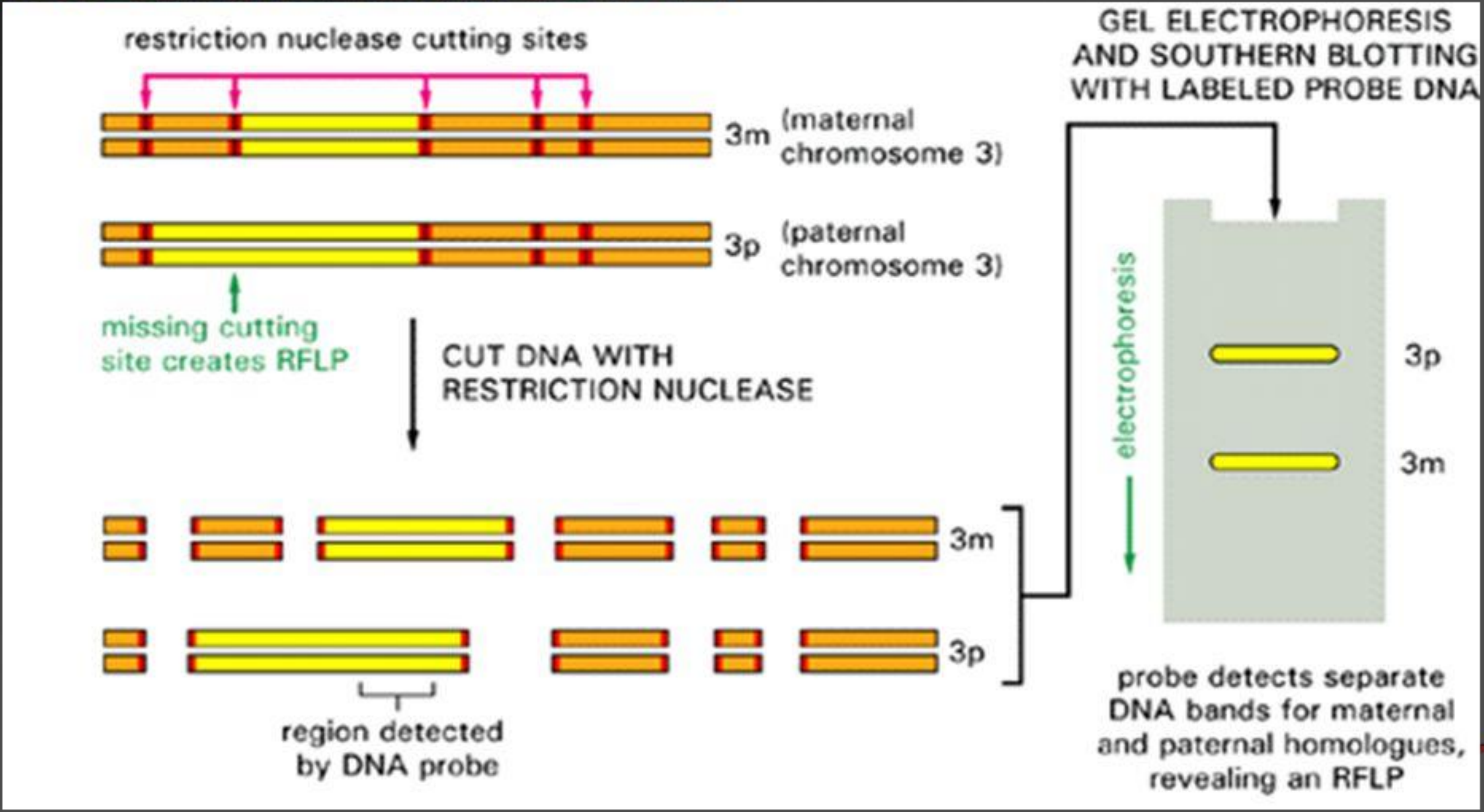


The likelihood of 2 unrelated individuals having same allelic pattern extremely improbable

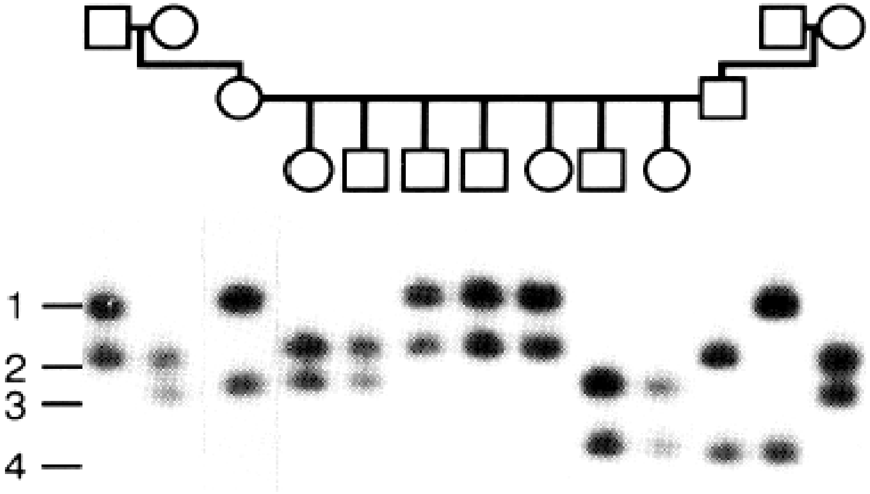
Southern Blotting



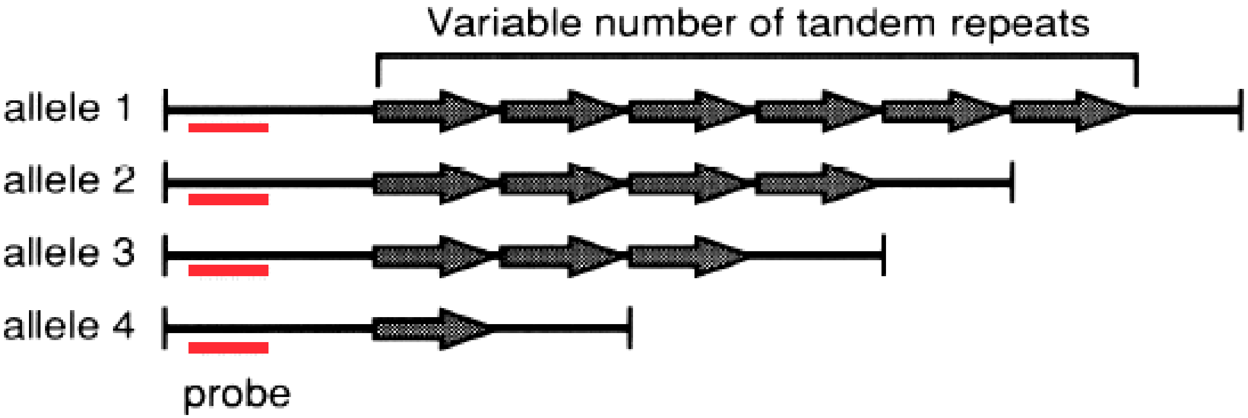
Detection of an RFLP by Southern blotting



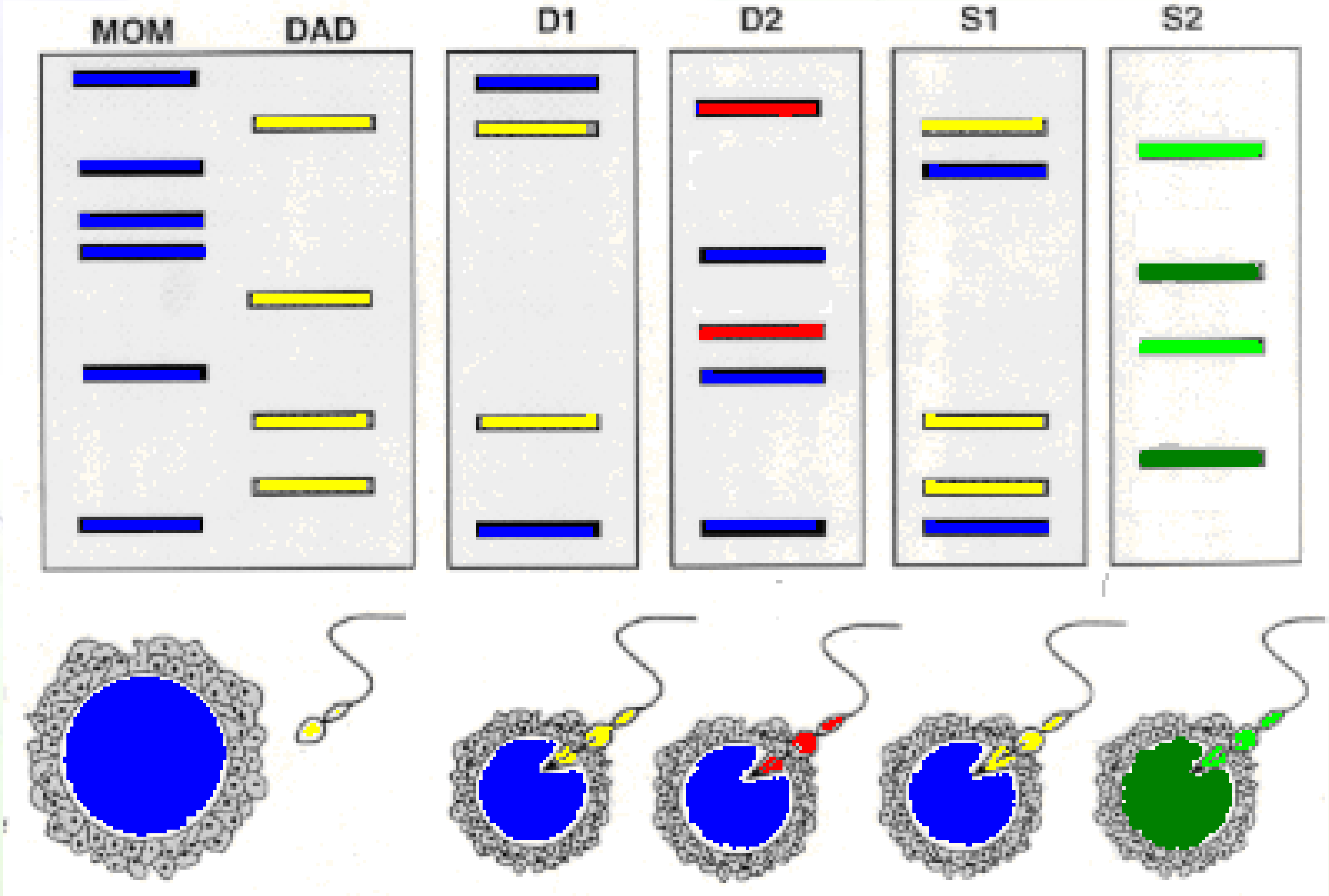
Real example



single-locus probe but multiple alleles



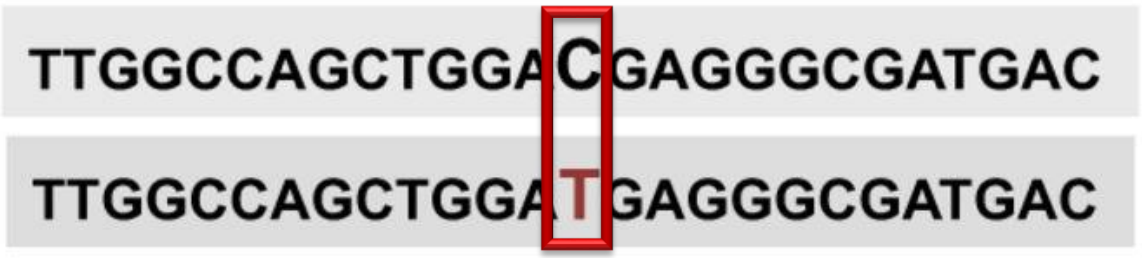
Thompson & Thompson Genetics in Medicine, p. 130, 1991

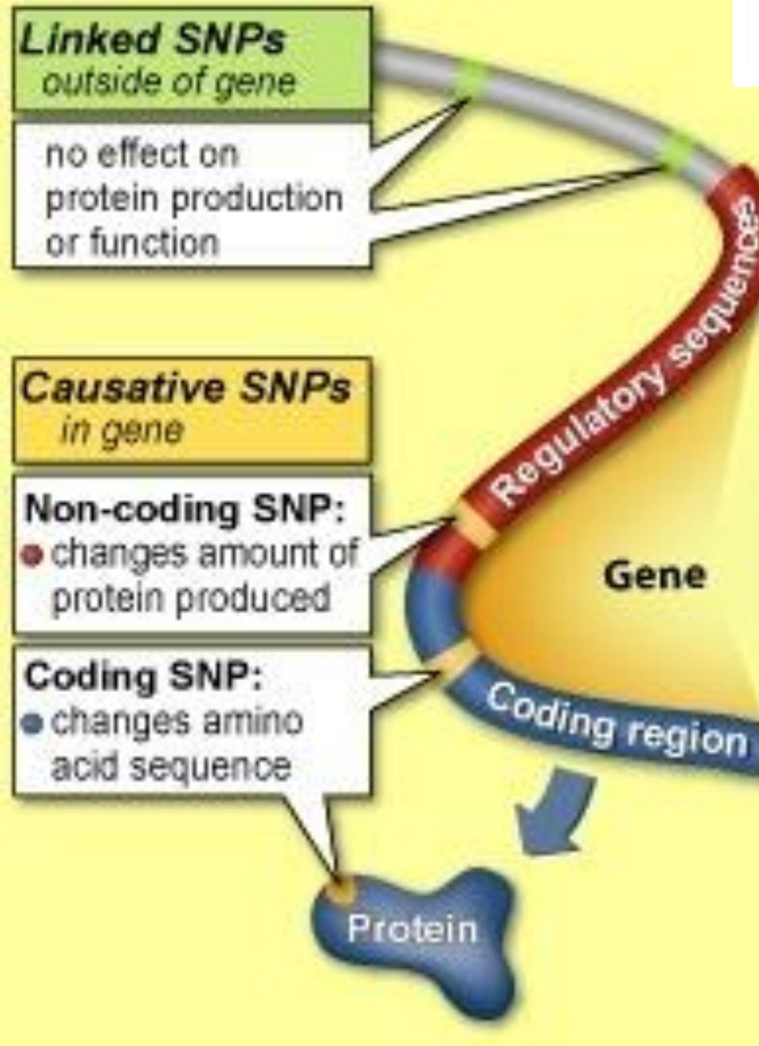

MOM
DAD
D1
D2
S1
S2

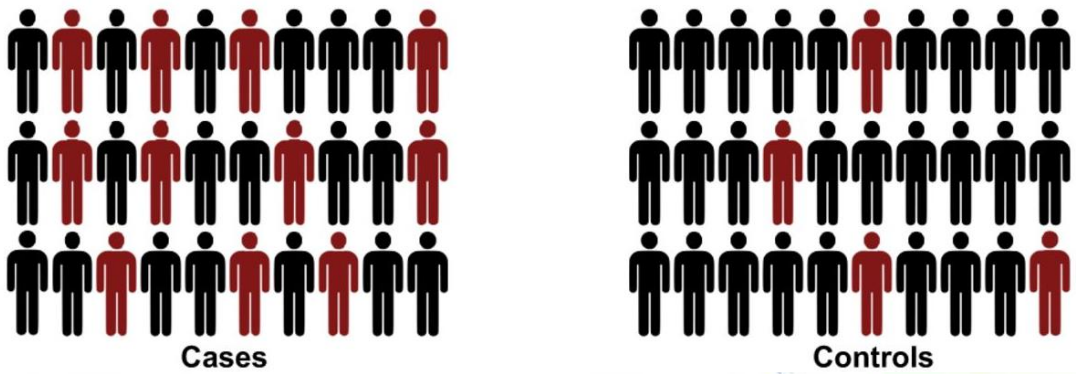
Single nucleotide polymorphism (SNPs)

- Another source of genetic variation
- Single-nucleotide substitutions of one base for another
- Two or more versions of a sequence must each be present in at least one percent of the general population
- SNPs occur throughout the human genome - about one in every 300 nucleotide base pairs.
  - ~10 million SNPs within the 3-billion-nucleotide human genome
  - Only 500,000 SNPs are thought to be relevant

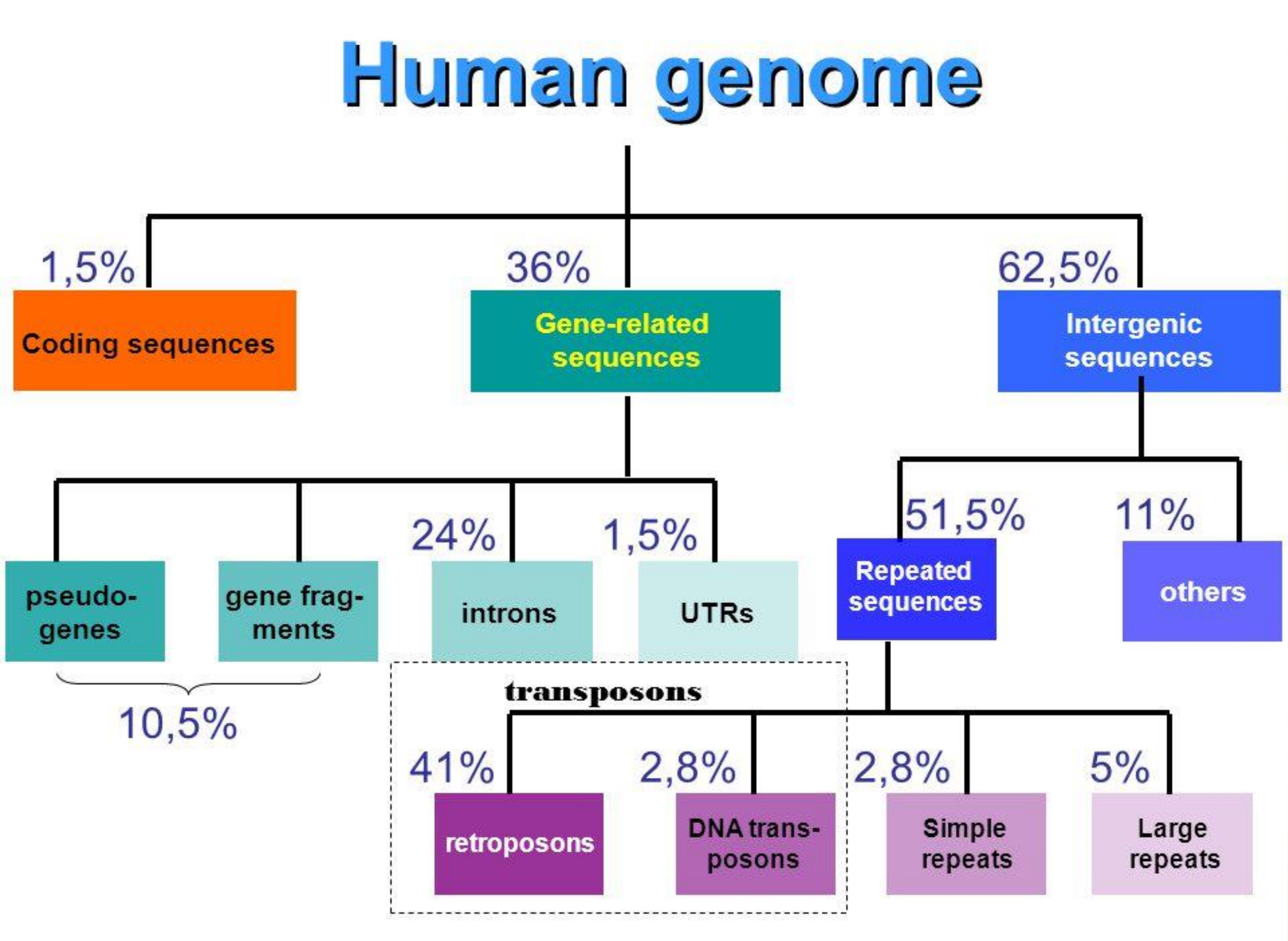
Categories of SNPs





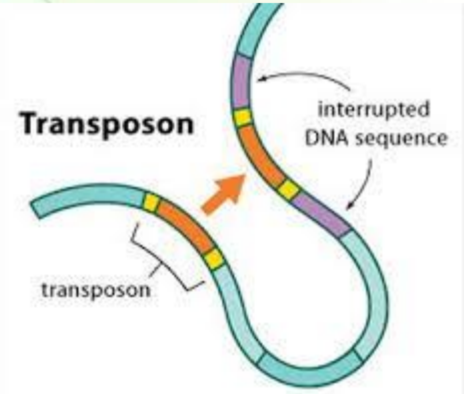


Components of the human genome

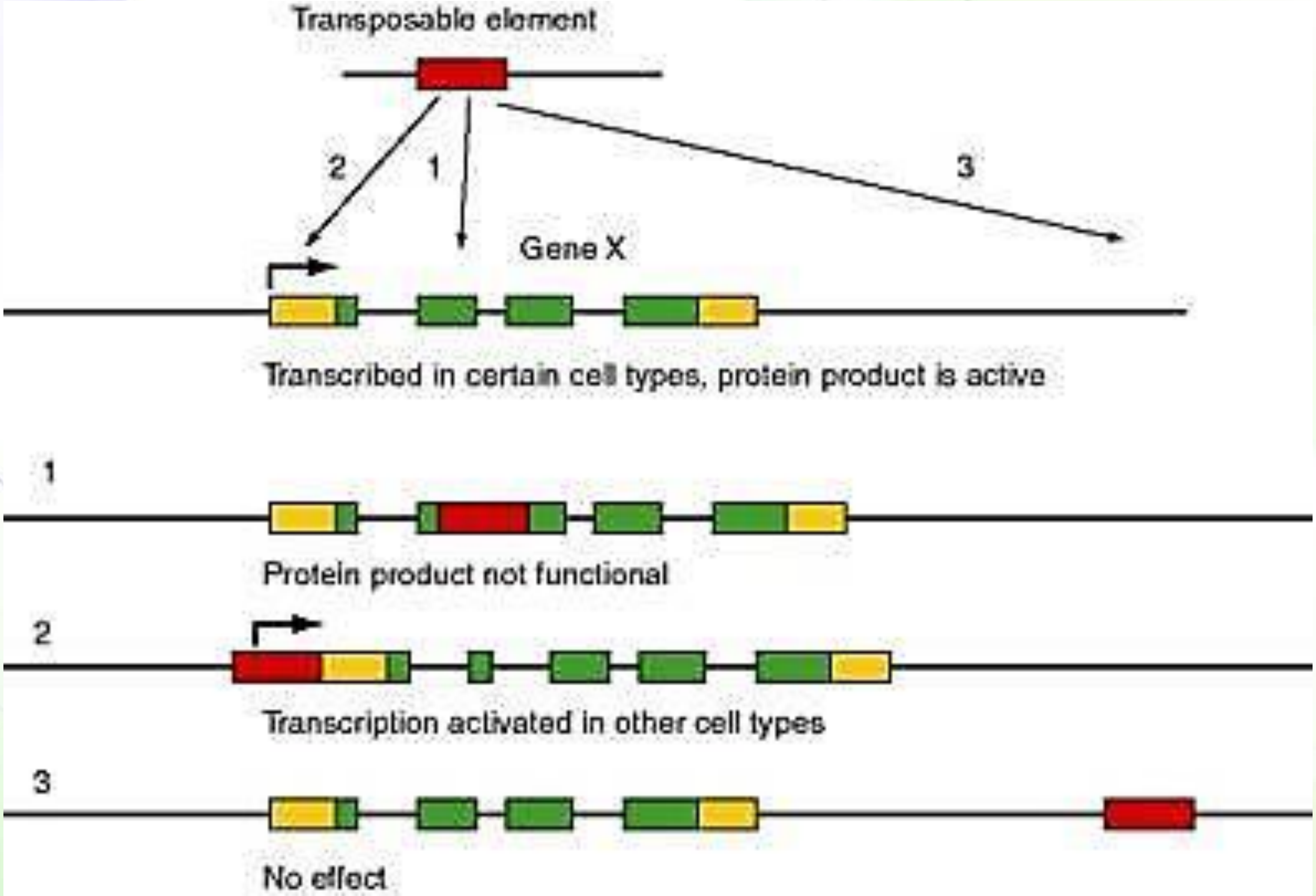


Transposons (jumping genes)

- They are segments of DNA that can move from their original position in the genome to a new location.



- Two classes:
  - DNA transposons (2-3% of human genome)
  - RNA transposons or retrotransposons (40% of human genome).
    - Long interspersed elements (LINEs)
    - Short interspersed elements (SINEs) – An example is Alu (300 bp)
- Diseases often caused by transposons include hemophilia A and B, severe combined immunodeficiency, porphyria, predisposition to cancer, and Duchenne muscular dystrophy.


Transposable element
2
1
3
Gene X
Transcribed in certain cell types, protein product is active
1
Protein product not functional
2
Transcription activated in other cell types
3
No effect