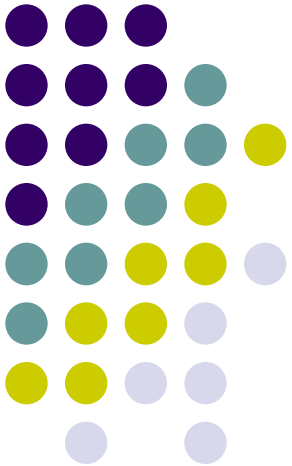
CYTOGENETIC METHOD

BALAN GOVARTHAN
SUNDARRAJAN ABIRAMI
LA-1 201(2)



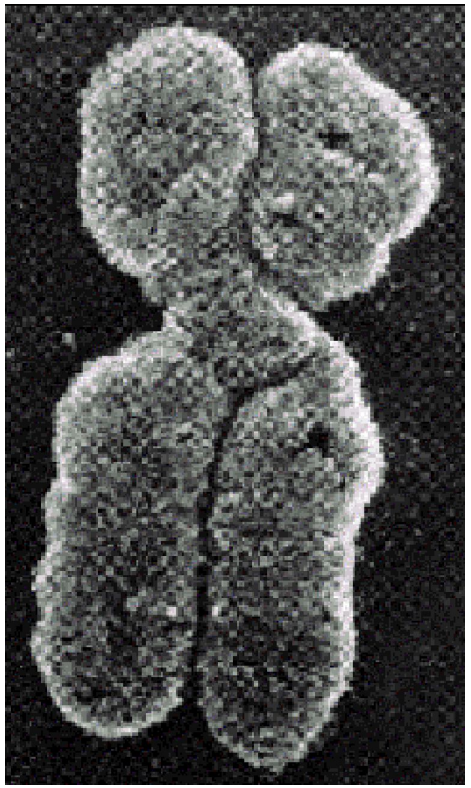
Cytogenetics = The study of chromosome number, structure, function, and behavior in relation to gene inheritance, organization and expression

Chromosome

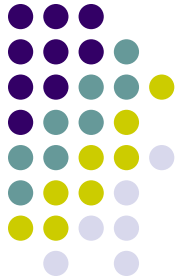
Chromo = colored in response to dye

Some = body

Chromosome of Eukaryotes have been the traditional subject for cytogenetic analysis because they are large enough to be examined with light microscope



Why Analyse Chromosomes and Genes?



Genetic errors arise from deletions or insertions of genetic material, abnormal numbers of whole chromosomes or genes, and even from misplacement of a single base in the DNA sequence.

Genetic abnormalities can range from relatively harmless to severe: from vitamin deficiencies and food allergies to cancer, birth defects and infant mortality.

Cytogenetic methods to detect chromosomal abnormalities underlying human birth defects usually involve analysis of mitotic chromosome

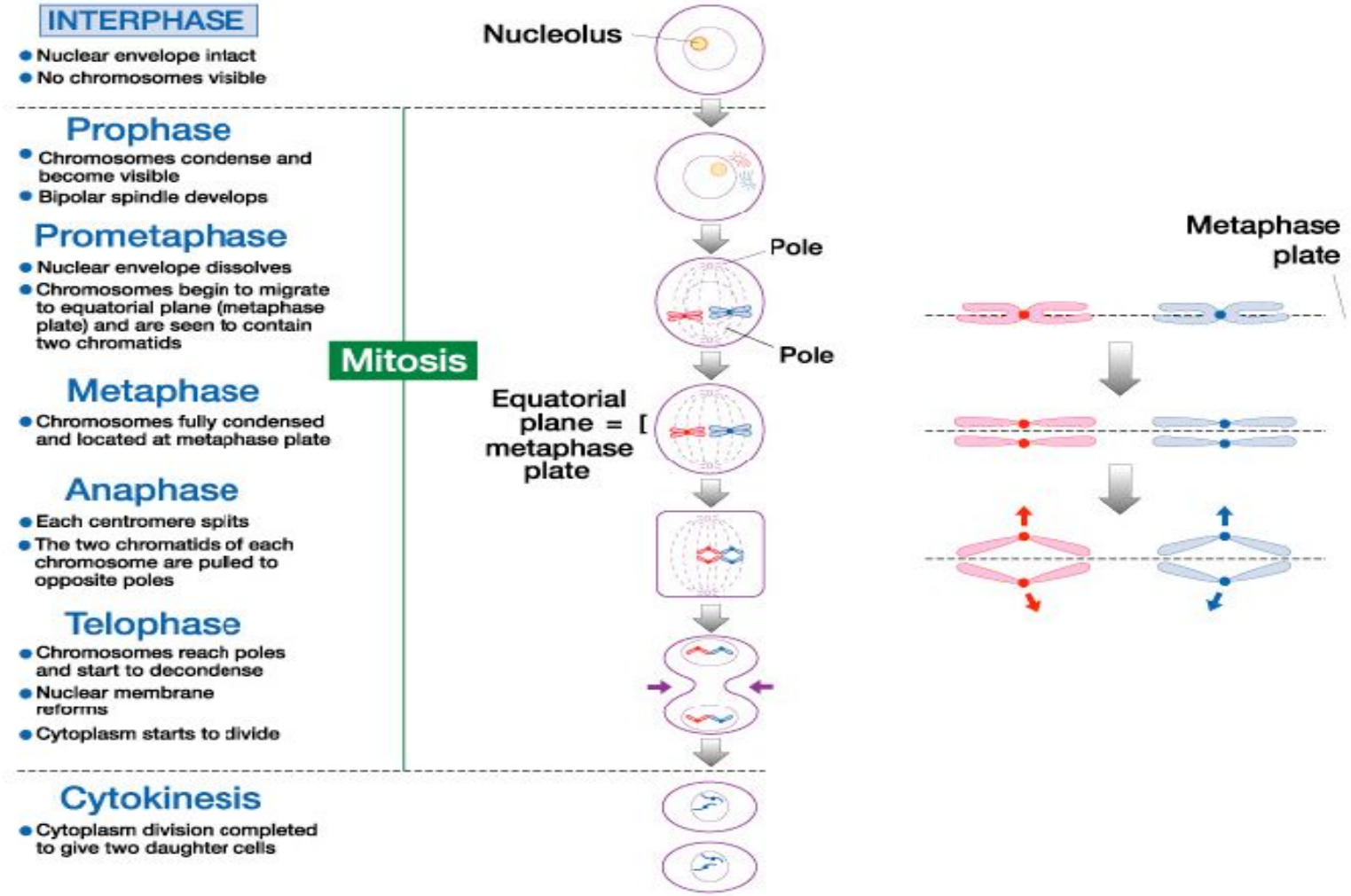


Figure 2-7 Human Molecular Genetics, 3/e. (© Garland Science 2004)

What tissues are appropriate for chromosome study?

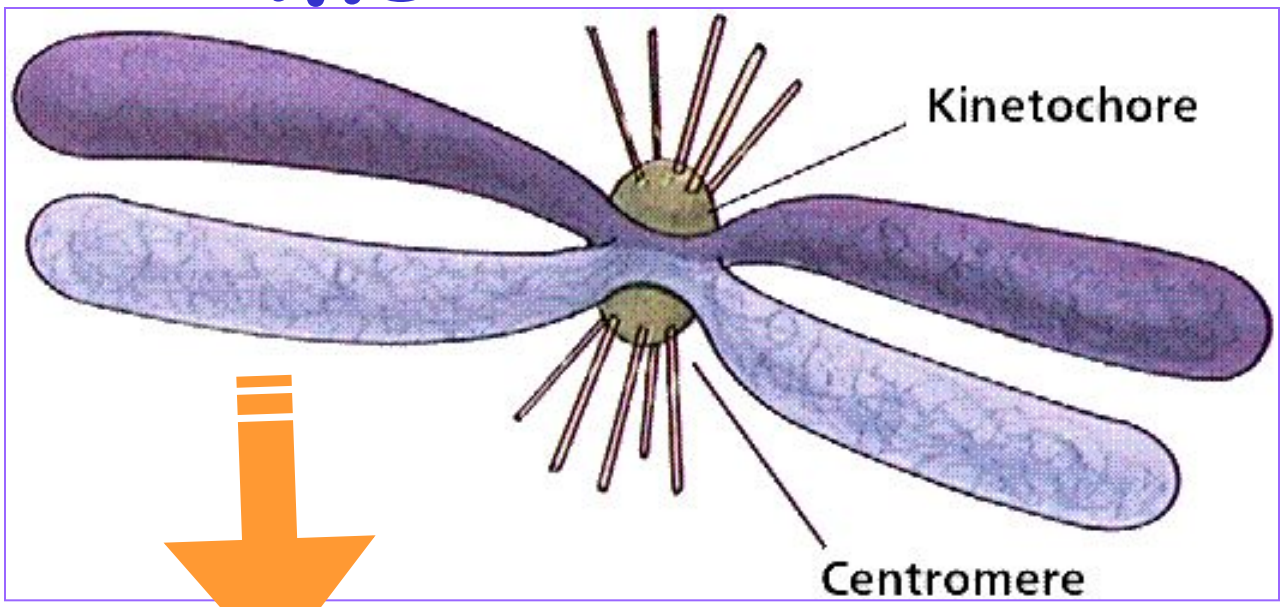
- A tissue that can be stimulated to undergo cell division in-vitro
- It is only during mitosis of the cell cycle that distinct chromosomes can be visualized with a light microscope

After culturing, in-vitro, a proportion of cells are arrested in mitosis, and are then "harvested" for chromosome analysis After harvesting, the cell preparations are dropped onto glass slides and stained. For most chromosome analyses, a G-banding technique is utilized for staining.

Metaphase spread

- The chromosomes are so named as they may be stained by certain dyes
- Chromosomes are composed of chromatin, which is composed of protein and DNA
- When cells are not dividing, the genetic material is decondensed
- Chromosomes become visible as distinct structures when the cell divides

Chromosome



Sister Chromatides

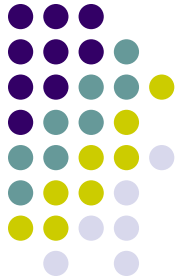
- Chromosomes of different species differ in number and information content
- Humans and several other species of organisms have 46 chromosomes

Karyotyping

Karyotype

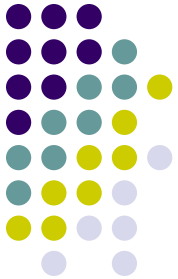
- A pictorial display of metaphase chromosomes from a mitotic cell
- Homologous chromosomes- pairs

Karyotype



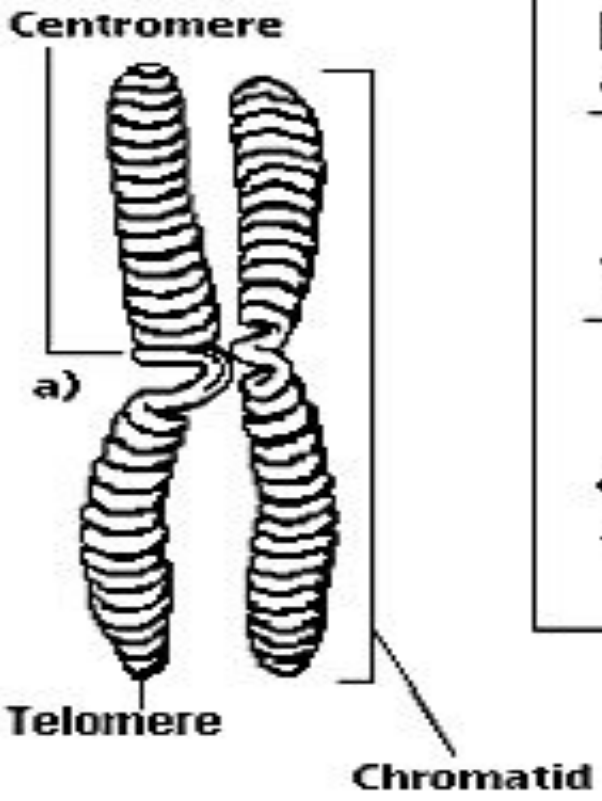
- Karyotyping is the analysis of chromosomes
- Cytogenetics is the study of chromosomes and inheritance
- Cytogenetics is based on studies of humans as well as *Drosophila* and other organisms

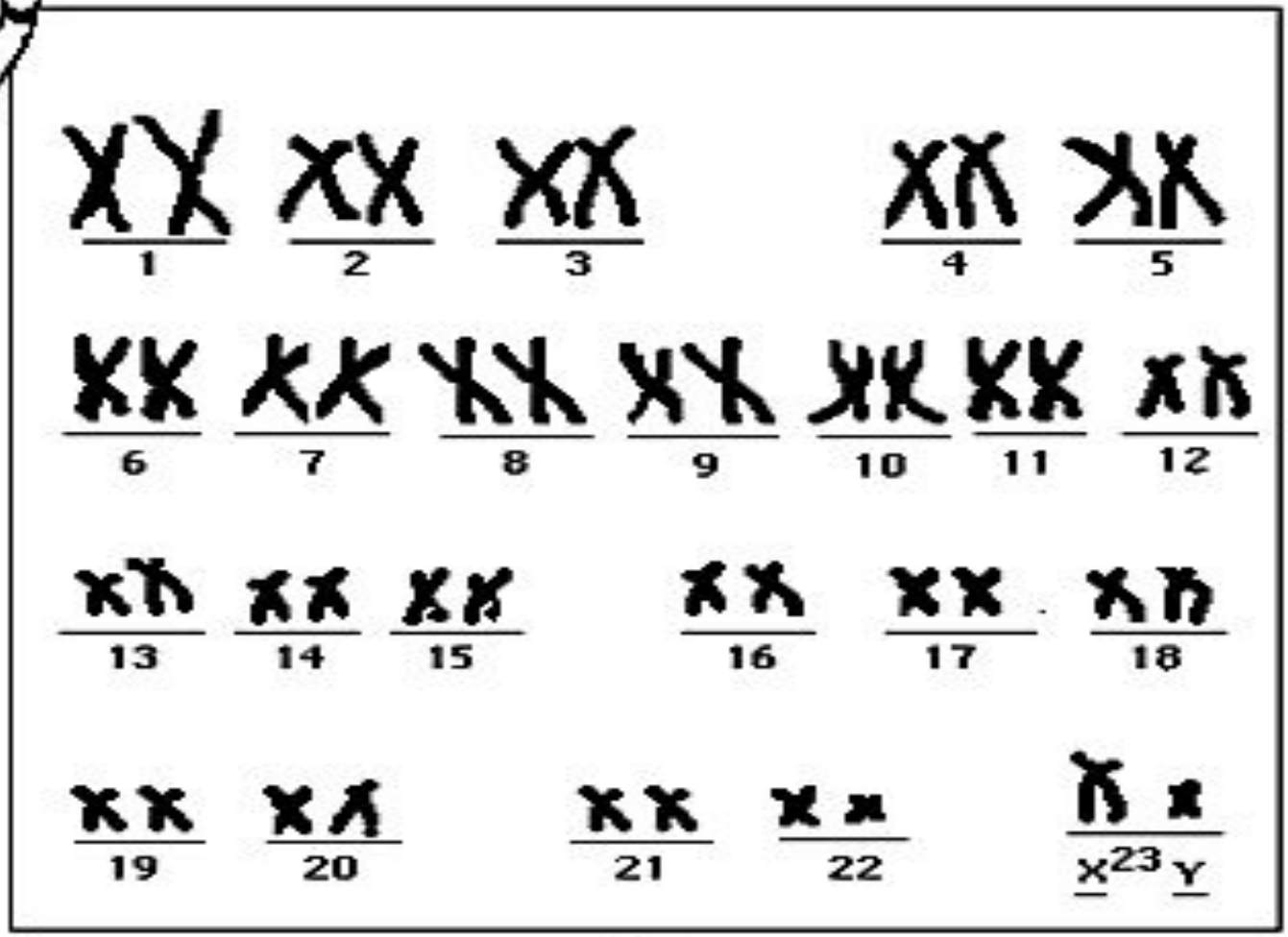
Preparing a karyotype



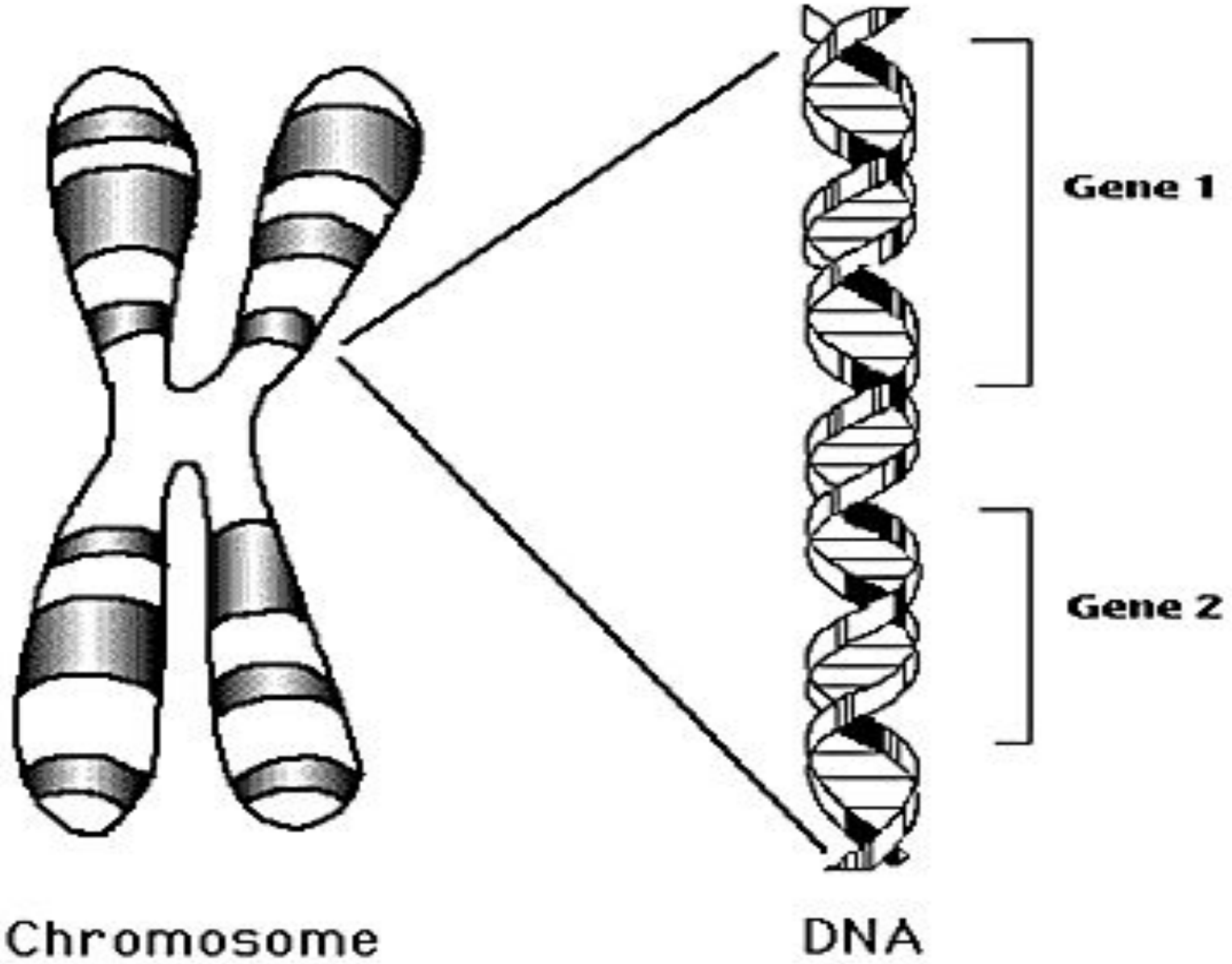
1. Harvested cells are first cltured
2. The cells are then treated with colchicine which arrests the cells in metaphase, and then treated and stained to observe the chromosomes
3. Chromosomes can be photographed or visualized using a computer, and then analyzed
4. Chromosomes are identified by size, position of the centromere, and banding and staining regions

HUMAN CHROMOSOMES





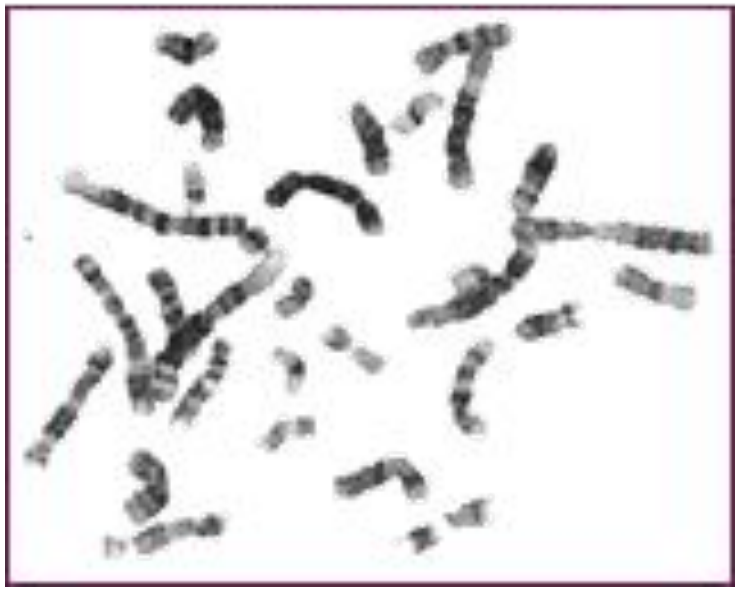
c)



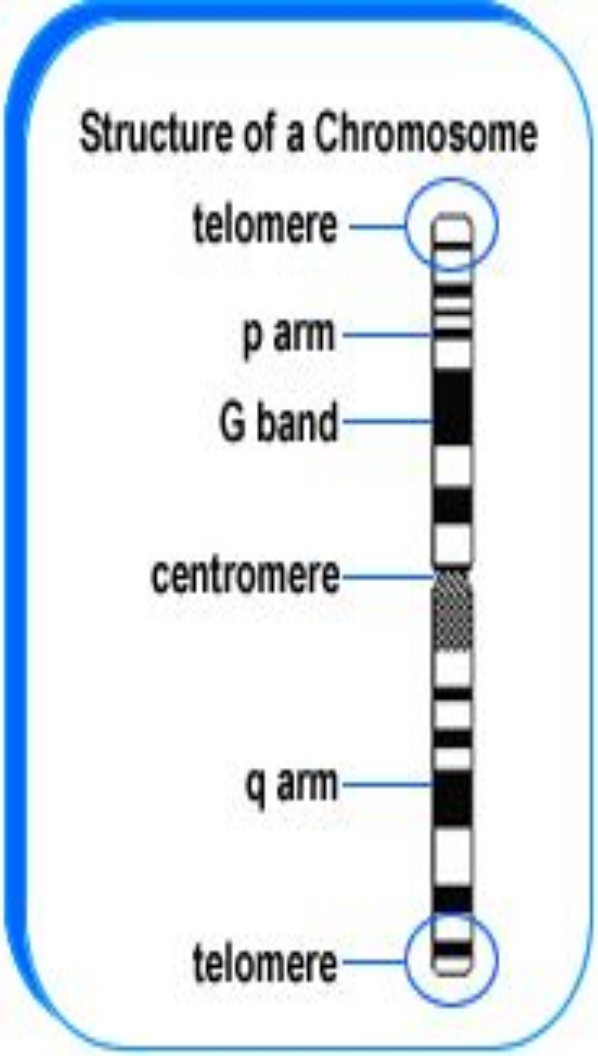
Genes

The analysis involves comparing chromosomes for their length, the placement of centromeres (areas where the two .chromatids are joined), and the location and sizes of G-bands

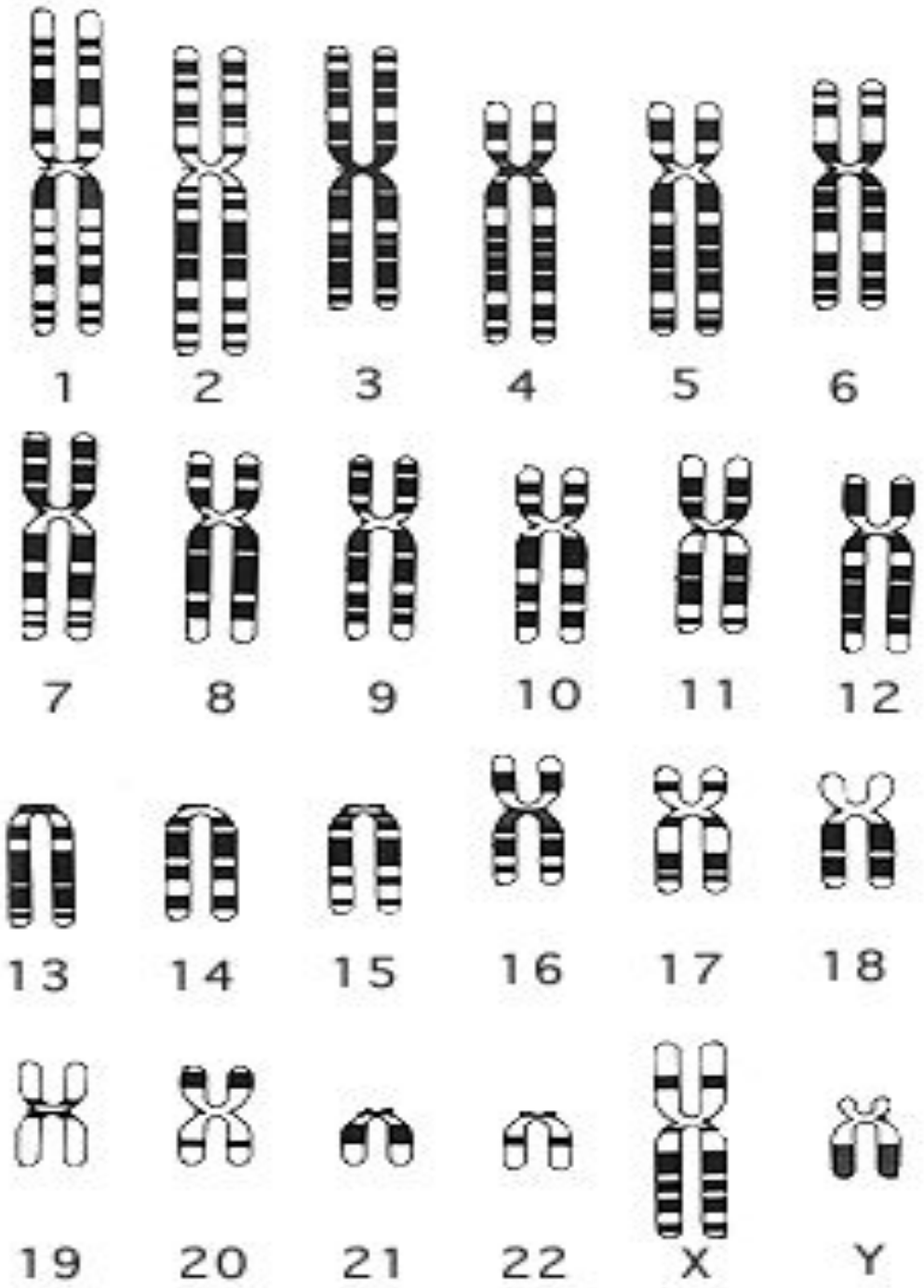
Chromosome smear



Identifying features of a chromosome



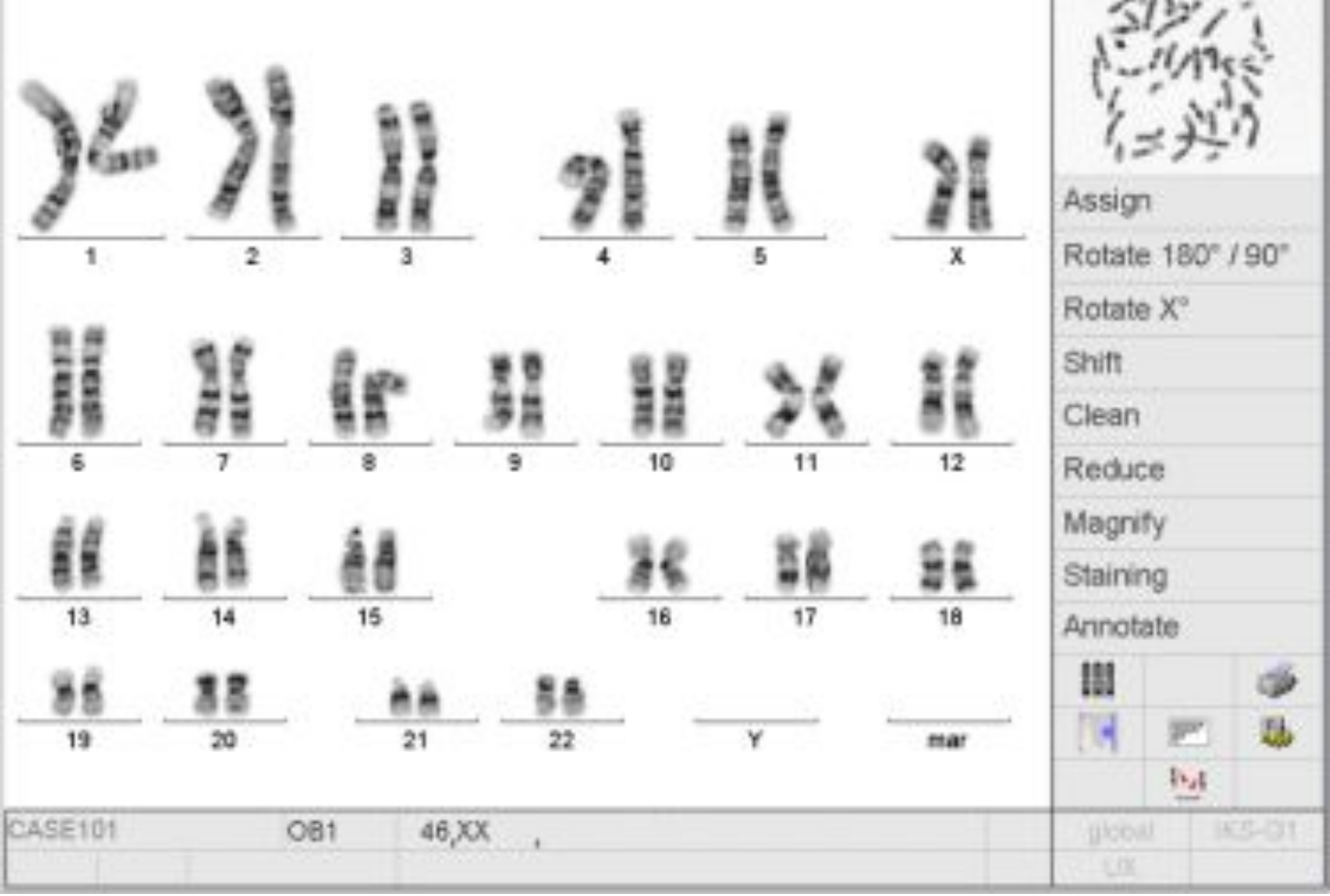
[A cartoon of a chromosome. The ends of the chromosome are called telomeres.
The centromeres is the narrowing of the chromosome
The chromosome has 2 arms – the smaller is called the p arm, the larger, the q arm.
The black bands are called G bands.]



Capture
Add. Capture
Obj. Threshold
Mask Meta.
Delete
Separate
Overlaps
Check Objects
Annotate

CASE101	Δ OB1 ∇	△ A ▽	46,XX ,	44	global	IKS-G1
					UX	GBAND

Metaphase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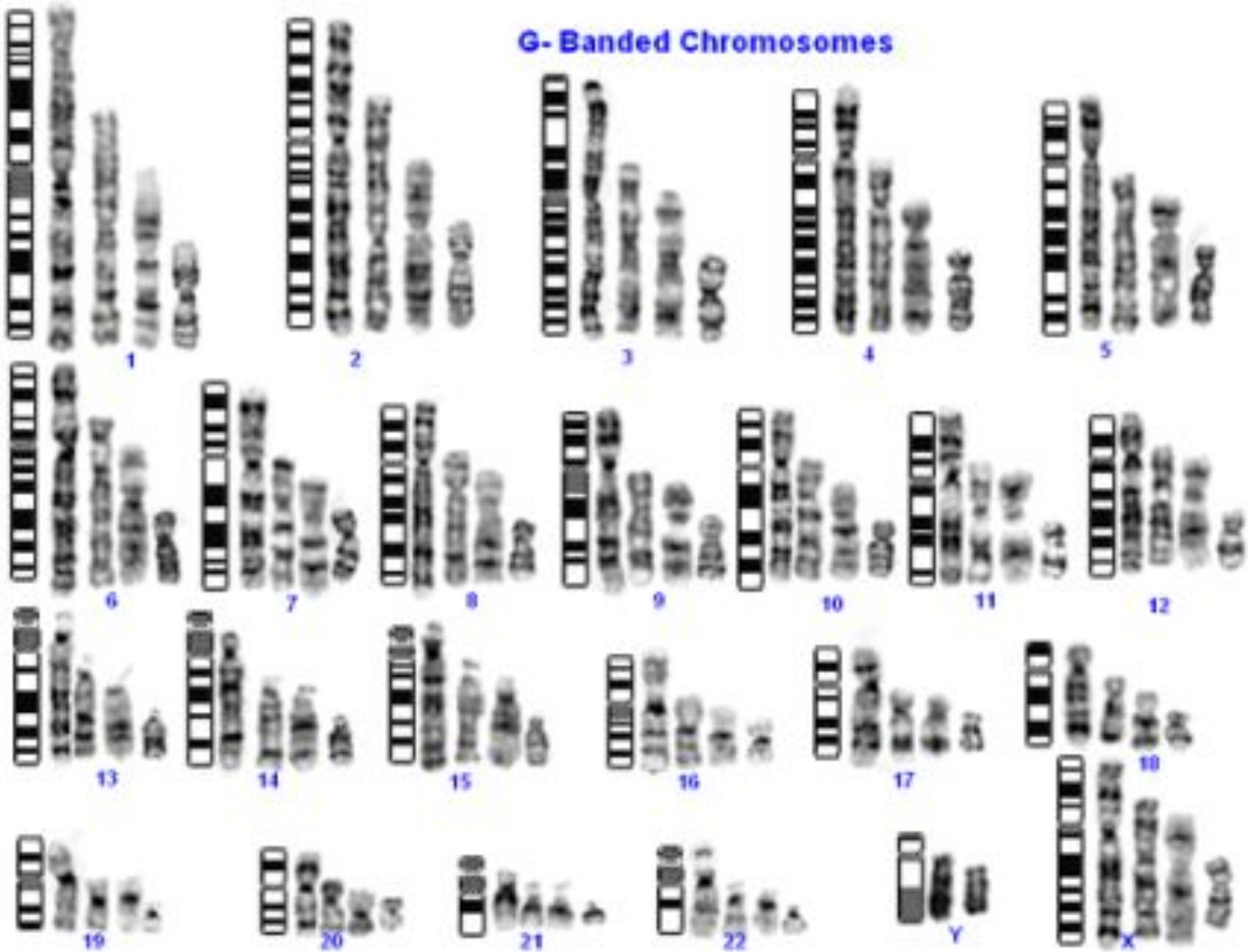
Y
mar
Assign
Rotate 180° / 90°
Rotate X°
Shift
Clean
Reduce
Magnify
Staining
Annotate
CASE101
OB1
46,XX

Karyotyped


G- Banded Chromosomes
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22
Y
X

Banding patterns on human mitotic chomosomes due to regions of condensed chomatin (darker - G bands) and less condensed chromatin (lighter - R bands)

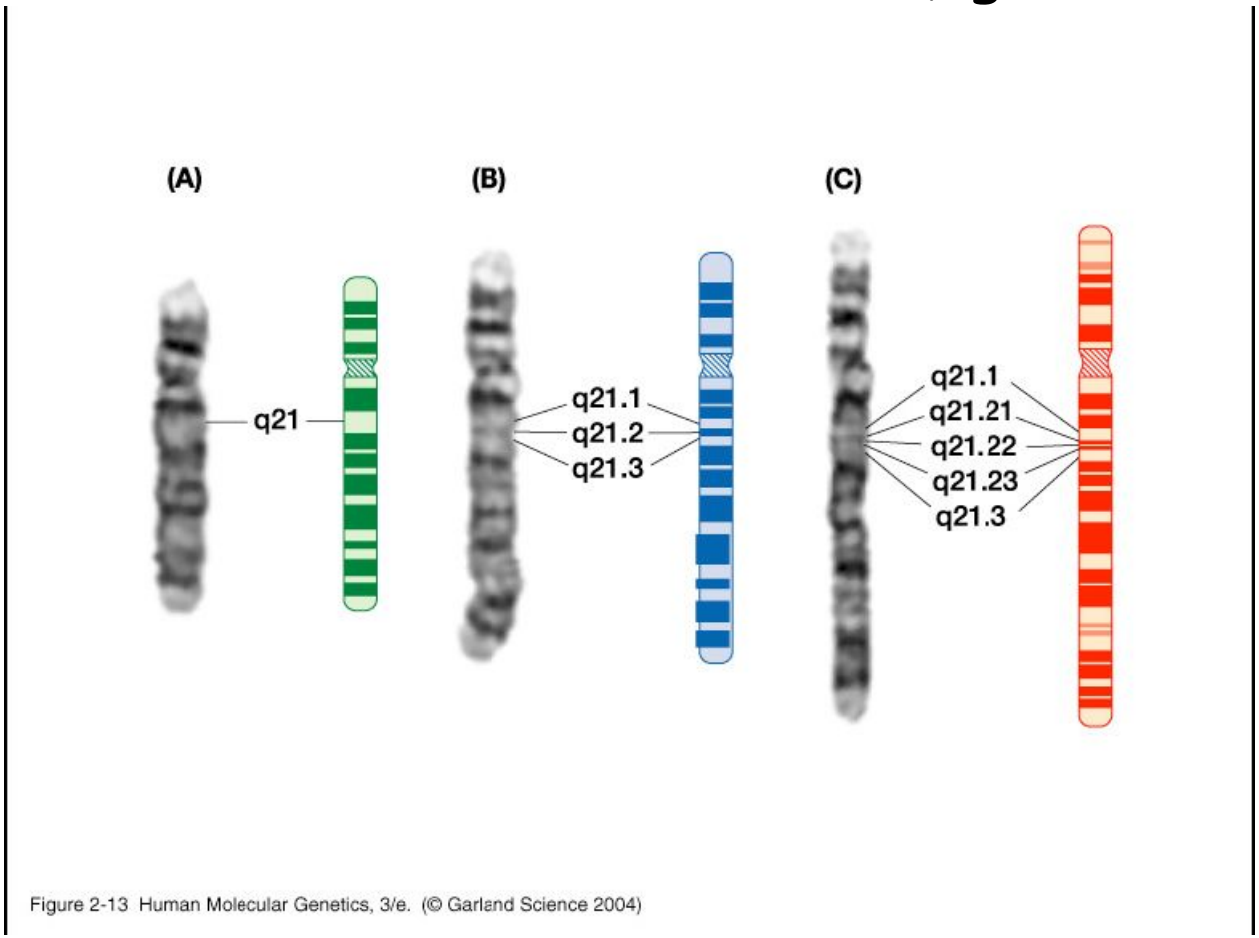


Figure 2-13 Human Molecular Genetics, 3/e. (© Garland Science 2004)

human chromosome 4 at varying resolutions due to exact mitotic stage, (or degrees of spreading - squashing - stretching)

Human chromosome number is determined by their length in “mitotic figures"

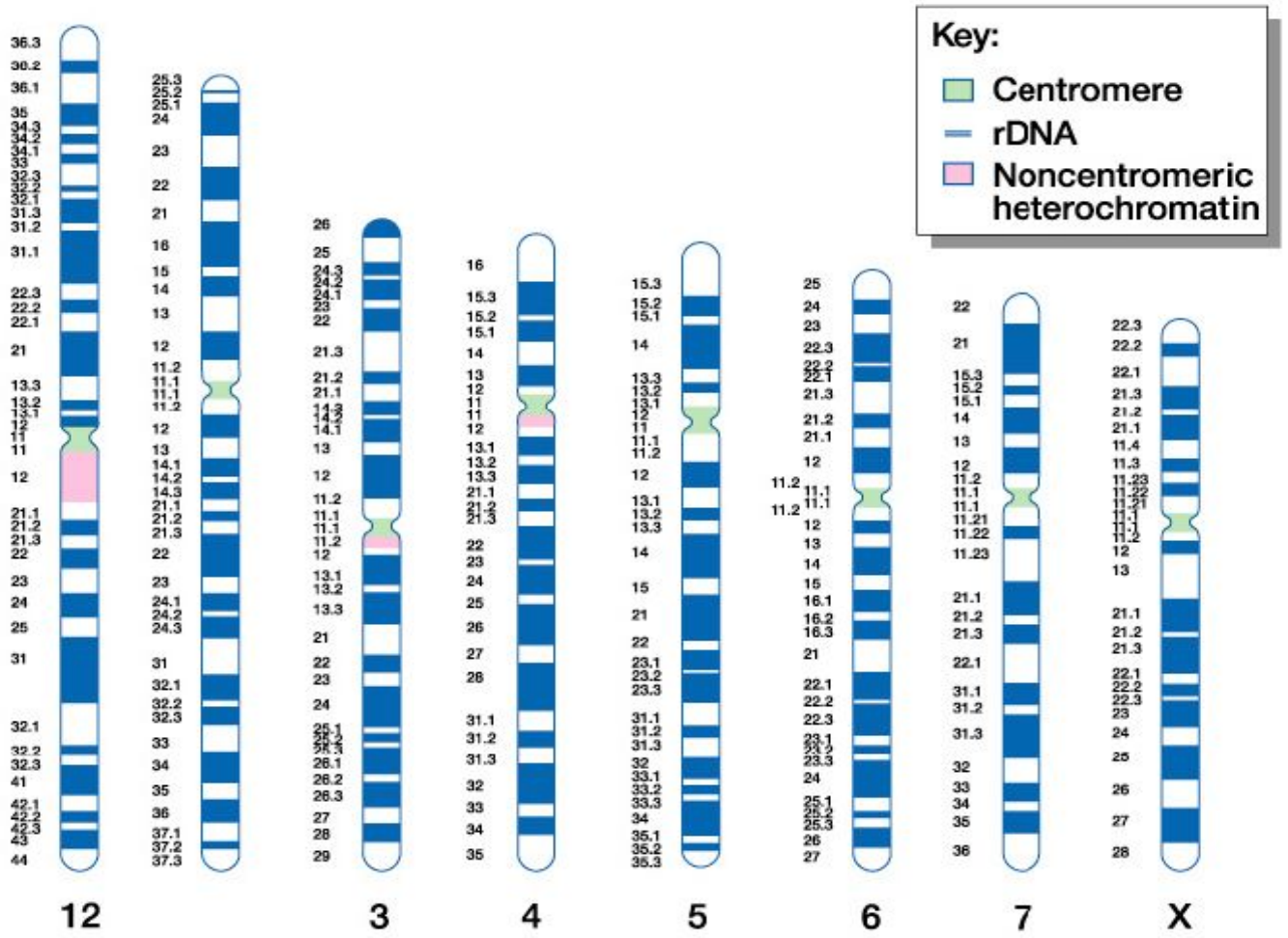
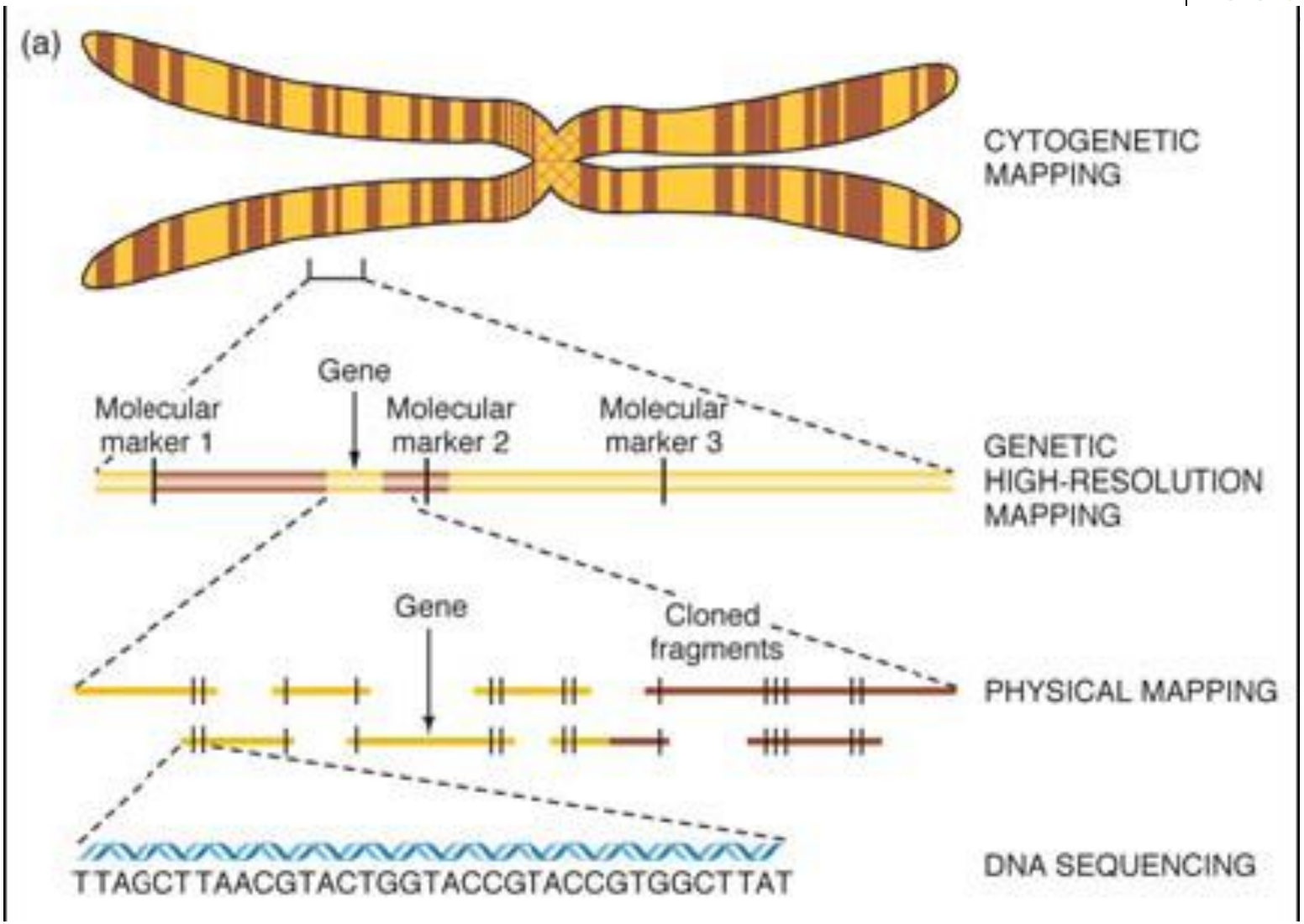
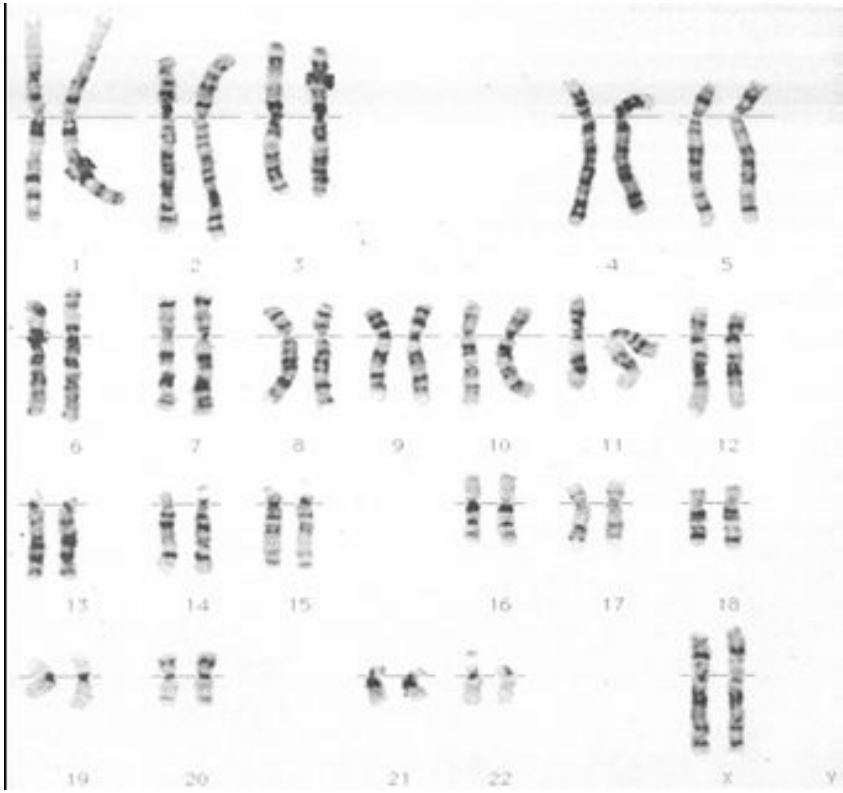


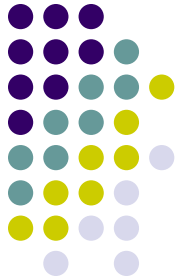
Figure 2-15 part 1 of 2 Human Molecular Genetics, 3/e. (© Garland Science 2004)


(a)
CYTOGENETIC MAPPING
Gene
Molecular marker 1
Molecular marker 2
Molecular marker 3
GENETIC HIGH-RESOLUTION MAPPING
Gene
Cloned fragments
PHYSICAL MAPPING
TTAGCTTAACGTACTGGTACCGTACCGTGGCTTAT
DNA SEQUENCING

International System for Cytogenetic Nomenclature, (ISCN,1995)

- Short arm of the chromosome = p
- Long arm of the chromosome = q
- Bands are numbered independently on the short and long arms
- Centromeres = p10,q10
- Band numbers increase as move from the centromere to the telomere





Hundreds of genes are encompassed within a single G-band.

Therefore, most constitutional chromosome abnormalities are associated with multiple congenital anomalies.

Therefore, deletion of a single gene cannot be detected by G-banding.

Conclusion

The evolution of cytogenetic techniques and the mapping of the human genome have provided scientists with a great deal of insight into the causes of numerous genetic disorders. Though rooted in early chromosome staining and gene mapping techniques, modern FISH, SKY, and CGH methods have far outshone their predecessors by providing an unprecedented .view of human chromosomes

-:Questions

What diseases can be detected through genetic testing?

What is the purpose of CYTOGENETIC?