

Genetics Lectures 2 & 3

1. Clinical Importance of Cytogenetics

Cytogenetics plays a crucial role in clinical medicine and research. Chromosomal abnormalities occur in approximately 0.6–1% of live births. They are strongly associated with major clinical conditions such as spontaneous miscarriages (33–67%), congenital anomalies, developmental disorders, and cancers. In fact, a large proportion of tumor cells (especially leukemia and solid tumors) show chromosomal abnormalities. This highlights the importance of cytogenetic analysis in diagnosis, prognosis, and management of diseases.

2. Why Study Human Chromosomes?

Chromosome analysis helps explain many medical conditions. It is essential in identifying causes of infertility, recurrent pregnancy loss, birth defects, and malignancies. Cytogenetics allows localization of DNA on chromosomes, detection of structural abnormalities, and monitoring of chromosomal changes during treatment. It is also widely used in genetic counseling.

3. Tissues Used for Chromosome Studies

The choice of tissue depends on the condition being studied. Peripheral blood lymphocytes are the most commonly used because they are easy to obtain and minimally invasive. Bone marrow is used mainly in hematological malignancies. During pregnancy, chorionic villus sampling is used in early stages, while amniotic fluid analysis is used later. Other tissues such as skin or organ biopsies may also be used when needed.

4. Karyotype and Karyogram

A karyotype refers to the number and appearance of chromosomes in a cell. Normal human karyotypes are 46,XX (female) and 46,XY (male). A karyogram is a visual representation where chromosomes are arranged in homologous pairs based on size, centromere position, and banding pattern. Chromosomes are typically arranged from largest (chromosome 1) to smallest (chromosome 22), followed by sex chromosomes.

5. Chromosome Banding Techniques

Banding techniques are essential for identifying chromosomes and detecting abnormalities. The most commonly used method is G-banding (Giemsa staining). In this method, dark bands represent heterochromatin (AT-rich, gene-poor, inactive), while light bands represent euchromatin (GC-rich, gene-rich, active). Other techniques include R-banding (reverse of G-banding), Q-banding (fluorescent), C-banding (centromeric), and T-banding (telomeric).

6. G-Banding Details (High Yield)

G-banding produces approximately 300–400 bands per haploid set. Each band may represent millions of base pairs and contain hundreds of genes. The technique involves treating chromosomes with trypsin to partially digest proteins, followed by staining with Giemsa. This allows visualization of distinct banding patterns that are unique for each chromosome.

7. Chromosome Culture Process (Step-by-Step)

1. Sample collection (blood, bone marrow, etc.)
2. Add mitogen (PHA) to stimulate cell division
3. Arrest cells in metaphase using colchicine
4. Centrifuge to obtain cell pellet
5. Add hypotonic solution to swell cells
6. Fix cells and wash
7. Drop cells on slide to burst and spread chromosomes
8. Stain with Giemsa

9. Observe under microscope

This process ensures chromosomes are clearly visible and analyzable.

8. Chromosome Structure

Each chromosome consists of a centromere, telomeres, and chromosomal arms (p and q). The centromere is essential for chromosome segregation and contains alpha-satellite DNA. Telomeres are repetitive DNA sequences (TTAGGG)_n located at chromosome ends and protect them from degradation and fusion. Subtelomeric regions lie adjacent to telomeres and are highly variable and clinically significant.

9. Telomeres and Aging

Telomeres shorten with each cell division, which is associated with aging. When telomeres become critically short, cells stop dividing and undergo apoptosis. However, cancer cells maintain telomere length using telomerase, allowing unlimited replication and contributing to tumor progression.

10. Chromosome Classification

Chromosomes are classified based on centromere position into metacentric (middle), submetacentric (off-center), and acrocentric (near end). Acrocentric chromosomes (13, 14, 15, 21, 22) have satellite regions containing ribosomal RNA genes, which are essential for ribosome formation.

11. High-Resolution Banding

High-resolution banding is performed at earlier stages (prophase or prometaphase), when chromosomes are less condensed. This allows visualization of up to 800 bands, improving the detection of subtle chromosomal abnormalities that cannot be seen in standard metaphase banding.

12. Key Exam Concepts

- Metaphase is the best stage for chromosome visualization
- G-banding is the most commonly used technique
- Telomeres protect chromosome ends and shorten with age
- Centromere is essential for chromosome segregation
- PHA stimulates cell division
- Colchicine arrests cells in metaphase
- High-resolution banding detects subtle abnormalities