HUMAN GENETICS

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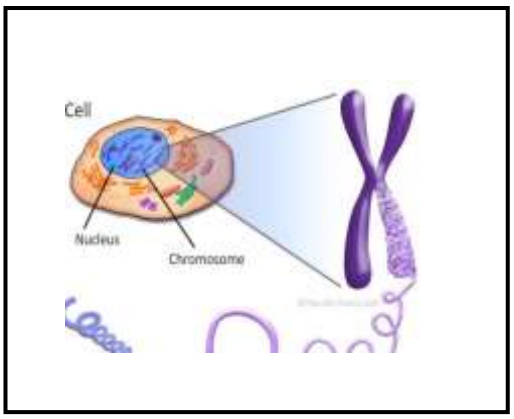
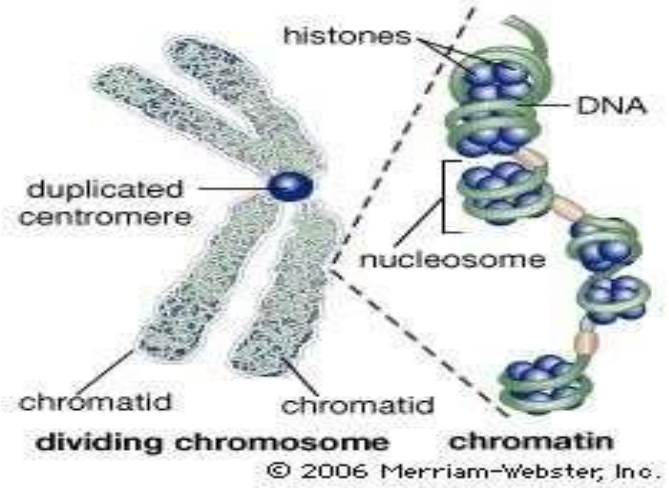


Chromosomes and chromosomal abnormalities

- Chromosomes, composed of protein and DNA, are distinct dense bodies found in the nucleus of cells
- The total number of bases in all the chromosomes of a human cell is approximately six billion and individual chromosomes range from 50 to 250 million bases.
- The DNA sequence for a single trait is called a gene.
- Each chromosome contains a few thousand genes, which range in size from a few thousand bases up to 2 million bases
- The compact DNA forming a chromosome is composed of acidic chromosomal proteins called histones, and other heterogeneous proteins, non-histones. This DNA and protein complex is called chromatin. Histones are of five major types, and are termed as H1, H2A, H2B, H3 and H4, and they help in proper packaging of the chromatin. Two copies of these four histones form an octamer around which DNA winds. Each histone is associated with 140 base pairs, making two turns. Each DNA core complex is spaced by 20-60 base pairs. Thu the appearance of chromatin is like a beaded string. The complex of DNA and histones is called a **nucleosome**.

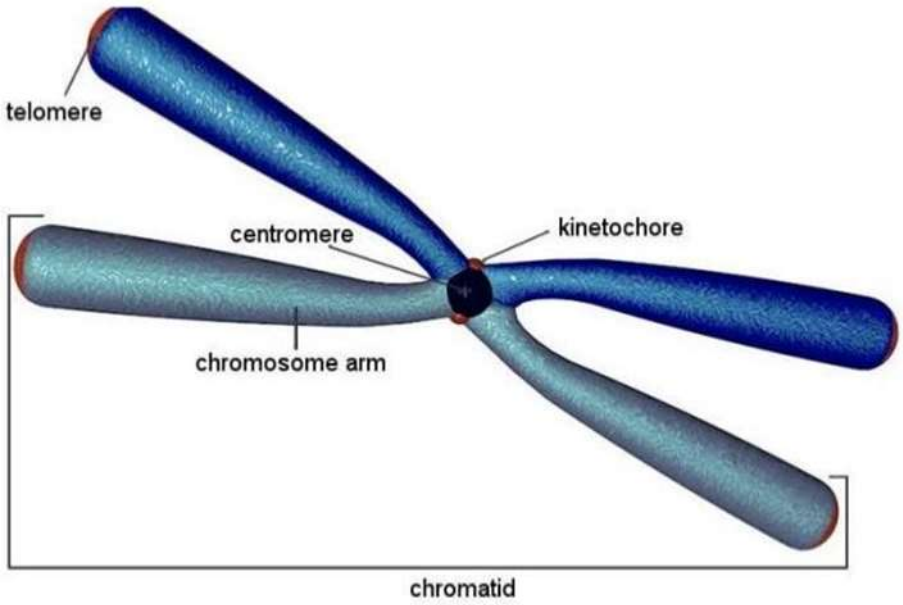


The gametes contain a single set of chromosomes, namely 22 autosomes and one sex chromosome. This single set of chromosomes is called haploid or 1n, in contrast to the chromosome set of a somatic cell, which is diploid, or 2n.

Homologous chromosomes have genes at loci in the same sequence though slightly different forms may be present due to polymorphisms on the two different chromosomes. This alternative form of a gene found on the same homologous chromosome is called an **allele**

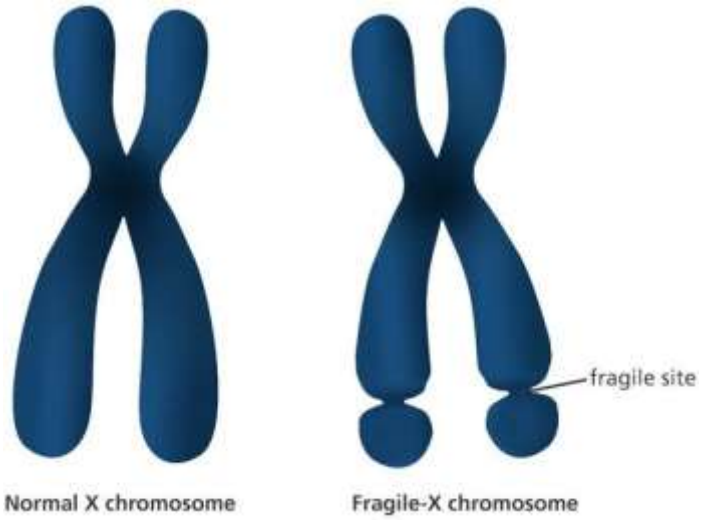
During metaphase, chromosomes differ from each other in their morphology. Each chromosome is composed of two chromatids joined together at the primary constriction by a centromere. During cell division, the centromere is responsible for cell division. The centromere divides the chromosome into a short and long arm. The part of the chromosome above the centromere is called short arm (p) and the part below is called long arm (q). The chromosomes are grouped from A to G on the basis of the length of the chromosome and position of the centromere

The terminal end of a chromosome is called a **telomere**. Telomeres are specialized structures comprising DNA and protein, which cap the ends of eukaryotic chromosomes. Besides primary constrictions at the centromere, some of the metaphase chromosomes have secondary constrictions. These secondary constrictions on the acrocentric chromosomes are the site for synthesis of ribosomal material in the interphase nucleus. These regions are termed the Nucleolus Organizer Regions (**NORs**).



Hereditary Fragile Sites

Several chromosomes have been seen to have fragile sites. They are often harmless on autosomes except for some syndromes and are of significance in chromosomal instability syndromes. The fragile site on the X chromosome at Xq27.3 is associated with the fragile X syndrome. This is the most common familial form of mental retardation, and is inherited as an X- linked disorder.



CHROMOSOMAL ABNORMALITIES

Chromosome abnormalities are changes resulting in a visible alteration of chromosomes.

A chromosomal abnormality may be present in all cells of the body (constitutional abnormality) or may be present only in certain cells or tissues (somatic abnormality).

Chromosomal abnormalities, whether constitutional or somatic, fall into two categories, numerical and structural abnormalities

Numerical abnormalities occur when the normal human chromosomal complement of 46 gets addition or loss of one or more chromosomes in the diploid number (2N). This is termed as aneuploidy. If a chromosomal complement has multiples of haploid number (1N) it is termed as polyploidy.

Euploid		Chromosome numbers are multiples of the haploid set (2n)
Polyploid	Triploidy Tetrploidy	Chromosome numbers are greater than diploid (3n, triploid)
Aneuploid	Monosomy Trisomy Tetrasomy	Chromosome numbers are not exact multiples of the haploid set (2n1 trisomy; 2n1 monosomy)
Mosaic		Presence of two different cell lines derived from one zygote (46XX/45X, Turner mosaic)
Chimaera		Presence of two different cell lines derived from fusion of two zygotes (46XX/46XY, true hermaphrodite)