MOLECULAR BASIS OF THE CHROMOSOME, THE GENE AND GENE EXPRESSION

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Cell is the basic structural and functional unit in all living organisms. All cells arise from the division of preexisting cells. However, the first cell or cells had a spontaneous origin and evolution. Nucleus is a normal constituent of all living cells. Chromosomes that are made up of chromatine are confined to the cell nucleus, the number of chromosomes depend on the kind of organism. Hereditary material of an organism is orderly arranged in one or more chromosomes so that the chromosome is a complex and highly ordered organelle Genetic transmission with the behaviour of the chromosomes in meiosis provides the physical basis for Mendelian inheretance where the transmission and continuity of traits from one generation to the next is followed by the determination of phenotypic ratios.

The DNA-histone complex or the nucleosome is the basic unit of structure of the chromosomes. These two components are present in roughly equal amount by weight. DNA or deoxyribonucleic acid is highly stable molecule conserved from one cell generation to the next. DNA is a polyanion with a continuous sequence of acidic phosphate and it is thought to be neutralized and stabilized by the histones with the basic nature that act as polycations.

The structure of DNA which is the molecule in which all precoded genetic information of an organism is stored , was discovered in 1953. Each molecule of DNA is a double helix with 2 strands that are identical to each other and are running in opposite direction. Each strand is a polymer of 4 nucleotide namely Adenine (A) , Guanine(G) , Thymine(T) , and Cytocine (C). Two strands are attracted to each other and held together because there is specific H_2 bonding between A of one strand with T of the other and C of one strand with G of the other (Fig.1)

G C A T T G
C G T A A C   Two strands

Fig. 1. Two strands of DNA.

As a matter of fact the base sequence of one strand is complementary to the base sequence of the other strand. Therefore, each strand has necessary information to determine the structure of the other. Different DNA molecules differ in their length and in sequence of base pairs.

Histones are a single class of proteins but 5 major types have been identified with each type having minor variants in structure but not necessarily so in function. It has been shown that the histones are nonspecific as to DNA nucleotide sequence or to species. Four of the five major histones that are involved in maintaining the structure of the chromosome are named as H_1, H_2, H_3, and H_4 Histones H_3 and H_4 are the most conservative and histone H_1 is the least conservative during the evolutionary process.

The basic unit of structure of chromosome is the nucleosome. The nucleosome consists of a core of eight histone molecules made up of two molecules each of H_2A_1, H_2B_1,H_3, and H_4 (Fig.2) DNA is wrapped arround this core of 8 histones with a stretch of linker DNA to which the histone H_1 is attached (Fig.3) So a nucleosome can be defined as a unit of about 200 nucleotide pairs of DNA organized into a globular structure by two moecules each of the four major histones. The histone H_1 links the nucleosomes with each other to make a chain (Fig.4) the nucleosome is the first stage of contraction above the level of the naked DNA double helix and its formation introduces a sixfold reduction in the length of the DNA strand. An additional reduction in length by fivefold or sixfold can be achieved by grouping of nucleosomes due to the binding action of histone H_1. Therefore, in chromosomes DNA molecules are kept in a tightly compact and organized state occupying only a few microns. On the other hand, it is **reasonable** to assume that only one double helix of DNA extends from one end of the chromosome to the other.

Existence of genes had been established with the discovery of Mendal's work since 1865. By means of wide variety of physical, chemical, and biological techniques, now it has been shown that relatively small regions of base pairs in the long DNA molecules which form chromosomos function as genes. Furthermore a gene has definite molecular boundaries, a beginning and an end, and a particular sequence of nucleotides in between and it can serve as a template for replication and transcription. Genes are functional entities of DNA which are not structurally distinguishable. Either the nucleotide sequence of one gene may entirely be included in the nucleotide sequence of another gene or the nucleotide sequence of two or more gnes may be overlapped or the nucleotide sequence of a gene may be independent.

Transcription and the translation are the first and second steps, respectively in a chain of biochemical events whereby a gene gains phenotypic expression through the formation of protein, Each specific protein of a cell is controlled by one or more genes unique for that protein. However, all the genes of an organism are not expressed all the time. Genes are expressed only when it is necessary. Different genes function in different cells at different times, and in different environmental conditions. Therefore, transcription which is the first step of gene expression is a highly selective process copying only certain portions of the genome at any one time.

Proteins are synthesised on ribosomes which are in the cytoplasm of the cell. The coded informations in DNA is sent to ribosome by messenger molecules made up of RNA (Ribonucleic acid) which is complementary to DNA. Therefore, mRNA(messenger RNA) should be synthesised on DNA by copying the necessary base sequence and this process is called transcription. Transcription involves only one of the two strands for any given gene or at any given region of the chromosome. But strand-switching can occur and mRNA for a different gene may be coppied from the other strand. The reaction of transcription is catalysed by the enzyme RNA polymerase When only a portion of a genome is being transcribed selectively, there must be a system to make it fully functional and responsive. A model that explains this selective transcription has been presented in terms of the 'operon' concept in micro organisms. According to this concept (1) there must be someway to repress those genes which are not been transcribed, (2) there must be a mechanism of derepression so that genes can be expressed when it is necessary ; (3) there must be a recognition site on DNA for the RNA polymerase to begin its transcriptional activities; and (4) there must be a termination signal for transcription to stop. The regions

of DNA that determines protein structure are
structural genes. Transcription of these str l
genes are controlled by regulatory genes or l-
ling elements of DNA to which individual stru
genes or groups of them are linked. Controlli
ments are termed as operater, promoter, and ter er
In a negative control system of the operon, the
repressor must be removed from the operator regi or
RNA polymerase to bind with the promoter region to
initiate transcription. In a positive control system,
a specific protein should bind to the promotoer as a
prerequisit for the proper binding of RNA polymerase
to initiate transcription. Once the transcription i
initiated the RNA polymerase travels along DNA and
synthesise mRNA until the terminater sequence is
found, which signals the enzyme to dissociate from
DNA. The controlling system of selective transcription in micro organisms as described by the operon
concept has not yet been found in higher organisms.
However, there must, of course, be serveral kinds
of recognition sites on DNA for the RNA polymerases,
a system for selective transcription, and a termination point for the process in higher organisms too.
It is believed that histones are the general repre ors
of DNA while the nonhistone chromosomal proteins
are the derepressors that involve in the promotio
of transcriptional process. It is shown that an
molecule called heterogeneous RNA (HnRNA) is als
involved between DNA and mRNA in the transcripti
process of higher organisms. In this system, firs
to HnRNA and then HnRNA to mRNA are thought to be
transcribed.

The process of protein synthesis on mRNA by converting the information to protein structure wit the use of ribosomes is called translation. Protein are linear polymers of aminoacids. The sequence of nucleotides in genes codes for the sequence of amino acids in proteins. Each aminoacid in protein is cod by three adjoining nucleotides in DNA. This set of three bases is called a triplet. Front end, the lea and the tail end, the trailer of the mRNA are not translated during the translational process. Leade sequence is the binding site of ribosomes. Ribosome bind at the leader sequence and travel along the mRNA passing triplets with addition of aminoacids in a sequence coded by the triplets until a nonsense triplet is found which signals for termination. Thus the final product of a gene, the protein, is synthesized in order to carry out the gene expression.

The knowledge of gene, gene expression, and other related techniques open the door for genetic engineering, where genes are manipulated. In the near future, agriculture seems to be the one that is likely to be benifitted most due to the impact brought about by genetic engineering.

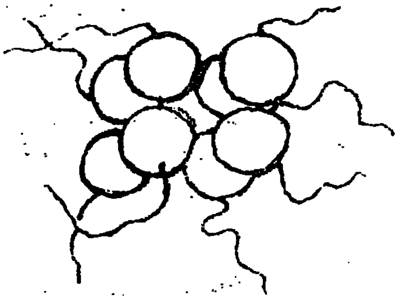

Fig. 2. The nucleosome without DNA

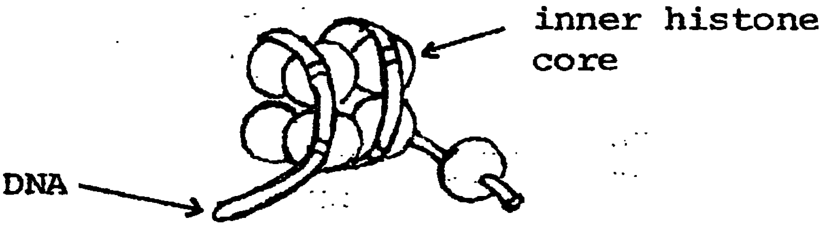

Fig.2. Single nucleosome.

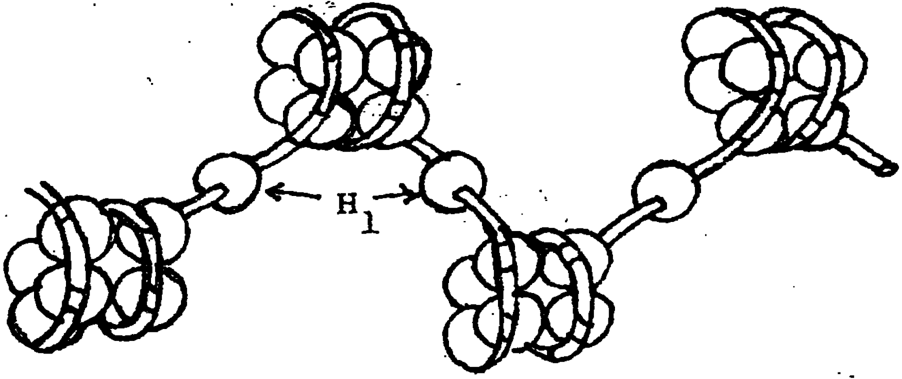

Fig.4. A chain of our nucleosomes.

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