Role of Gene Therapy in Surgery

Essay

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سَنُرِيهِمْ آيَاتِنَا فِي الْآفَاقِ وَفِي أَنفُسِهِمْ حَتَّى
يَتَبَيَّنَ لَهُمْ أَنَّهُ الْحَقُّ أَوَلَمْ يَكْفِ بِرَبِّكَ أَنَّهُ
عَلَى كُلِّ شَيْءٍ شَهِيدٌ

فصلت: 53

Dedication

- **My mother**
- **My wife**
- **My brothers**
- **My friends**

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List of Abbreviations

RNA	ribonucleic acid
DNA	deoxyribonucleic acid
A	adenine
T	thymidine
G	guanine
C	cytocine
U	uracil
DHU	dihydrouridine
TC	pseudouracil residue
HSV	herpes simplex virus
EGF	epidermal growth factor
IGF	insulin like growth factor
TGF	transforming growth factor
PDGF	Platelts derived growth factor
VEGF	vascular endothelial growth factor
FGF	fibroblast growth factor
NGF	nerve growth factor
BDNF	brain derived neurotrophic factors
NT	neurotrophins
BMPs	bone morphogenic proteins
BMT	bone marrow transplantation
GM-CSF	granulocyte-macrophage colony-stimulating factor
TNF	tumor necrosis factor
IL-2	interleukin-2

Principles of gene therapy

All cellular functions depend on proteins, which consists of chains of amino acids. Only 20 different amino acids are commonly found in the proteins of all organisms.

The links in the chain of amino acids are termed peptide bond, and the chain themselves are called polypeptides. Proteins contain one or more polypeptides, and the structure and function of each depends on the sequence of amino acids making up the polypeptide chains. ***(Bradley et al,2001)***

Cells, therefore need:

1- Informations to produce proteins in regulated fashion.

2- The ability to convey this information to daughter cells during cell division.

The key to these requirements is provided by the DNA" deoxyribonucleic acid" double helix. ***(Bradley et al., 2001).***

Structure of Nucleic Acid

It consists of long chains of molecules called nucleotides each nucleotide molecule in turn consists of a nitrogenous base, a sugar moiety and phosphorus molecule. The nitrogenous bases are of two types "purine and pyrimidine." The purine bases are adenine and guanine, and the pyrimidine bases are

thymine, cytosine and uracil. There are two types of nucleic acids "Deoxyribonucleic acid or DNA and ribonucleic acid or RNA". DNA contains sugar called deoxyribose, and RNA contains sugar called ribose. DNA is mainly found in chromosomes "except mitochondrial DNA" and RNA is chiefly found in nucleolus and in cytoplasm. Among pyrimidine bases DNA has thymine and RNA has uracil, the rest of nitrogenous bases are common in both. ***(Emery A. E. H. and Rimoin D. L., 1983)***

DNA structure:

We realized that genes are composed of DNA and so it is essential at this stage to consider the structure of DNA

Watson-Crick Model:

J.D. Watson, Crick and M.H.F. Wilkins proposed a structure of DNA molecule based on X ray diffraction studies, for which they were awarded the Nobel Prize.

They suggested that DNA molecule consists of two chains of nucleotides in the form of double helix. Each chain has a backbone of sugar-phosphate molecules "fig.1".

The two chains are held together by hydrogen bonds between nitrogenous bases. The DNA chains have polarity due to orientation of sugar- phosphate molecules. The 5` end of the

chain is terminated by a 5` carbon atom of a sugar molecule and the 3` end of the chain is terminated by a 3` carbon atom. In the two strands of DNA double helix the 5`end of one strand is opposite to the 3` end of the other. In short, the strands are said to be anti parallel.

The bases in DNA molecule pair with specificity. Adenine always pairs with thymine and cytosine with guanine. The two strands of DNA molecule separate at a nuclear division and each strand then builds up its complement. This is called REPLICATION ***(Weatherall D. J., 1991)***

The process of DNA replication commences simultaneously at multiple sites along the length of DNA strand and then progresses in both directions.

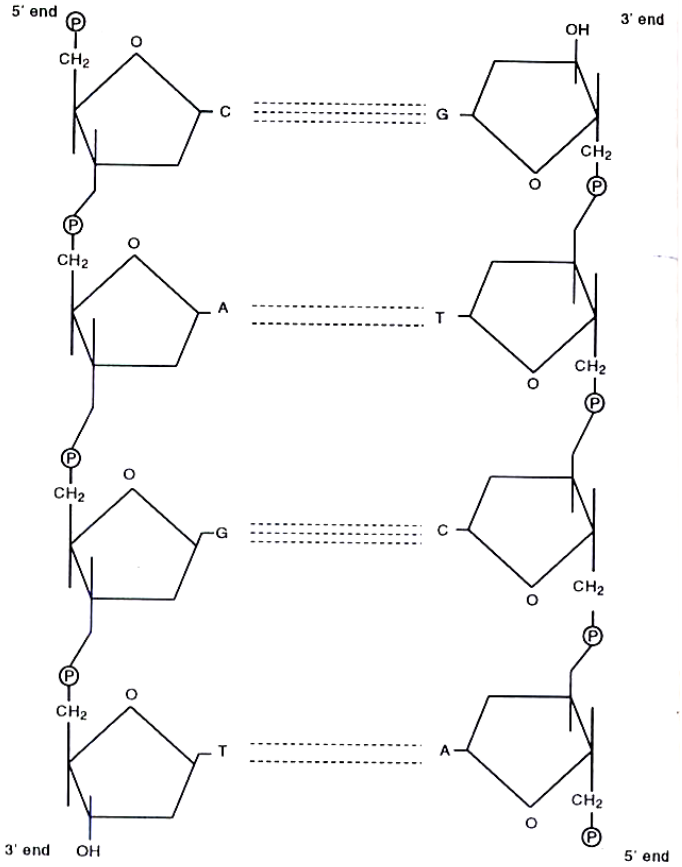

Figure (1): Diagrammatic representation of sugar phosphate backbone and nucleotide pairing in DNA duplex. A-adenine, C cytosine, G guanine, T thymine, and P phosphate.

(After Emery A. E. H. and Rimoin D. L., 1983)

Chromosomes

The width of chromosomes is much larger than the diameter of DNA molecule. with this consideration there must be tight coiling of DNA helices. The Solenoid model of the chromosome structure was proposed by Finch and Kluge. It is believed that a total length of DNA in chromosomes, if extended, run into meters while a total length of human chromosome complement is about half a millimeter. This means that there may be several orders of DNA coiling in chromosomes.

They are as under:

1- Primary coiling of DNA double helix.

2- Secondary coiling around histone beads i.e. nucleosomes.

3- Nucleosomes undergo tertiary coiling to form chromatin fibers

4- Chromatin fibers in turn form loops.

5- These loops further coil tightly to form a chromosome which we observe under a microscope "fig 2" ***(Emery A. E. H. and Rimoin D. L., 1983)***