Genetics and cell **:-**

To understand gentic and cell ,we must know the role of genes in normal cell cycle (the process of dividing and growth of cell), there are two types of genes regulate the cell cycle. Protoncogenes are these genes which responsible about the growth of cell while tumor suppressor genes are responsible about regulate suppressed the growth of cell .Other two types of genes have an important role in defense about cell if any damage take place. The first type is genes regulate apoptosis, which lead to cause dying for harm cells in order not to threat the other cells and tissue. While the second type is, DNA repair genes that all genes have mention above under the control of this type of genes that DNA repair genes look for presence of any mistake in DNA during division. When they find one, they either fix it or kill the cell by apoptosis (programmed process of cell death) . Therefore, it maintains the cells (morphologically, structurally and physiologically) and this normal regulate path of cells.

As these genes (DNA repair genes and genes regulate apoptosis) are mainly responsible for regulating the normal cell cycle, these genes are also responsible about causes of cancer that both genes are responsible about the irregular division which out of control and the cancer. When proto-oncogenes undergo an mutate effect it will be oncogenes leading the cells to be under uncontrolled division by encoding for liberation highly amount of growth stimulatory protein which active in this side. Whereas if tumor suppressor genes mutated it will lose its work and the essential protein of this genes which prevent the transforming cell and being cancer cells.

The role of genes regulates apoptosis; the process is relevant in many aspects of biological differentiation and development, including the process of

carcinogenesis. Genes important in apoptosis that according to Underwood,(2004) there is (Bcl-2 family) which its work divided into two types either genes stimulating this process like (Bax, Bad) by unknown mechanism or other include the bcl-2 gene which appears to suppress apoptosis in many tissue culture systems and *in vivo*. The *p53* gene, which encodes a transcription factor that appears to have multiple roles in regulating cell growth, including a role in apoptosis and the *fas* gene, which is a member of the TNF (tumor necrosis factor) receptor super family .*Fas* gene appear to be involved particularly in lymphocytic apoptosis . It is interesting to note some autoimmune diseases appear to be caused by defects in the apoptotic pathway, leading to over proliferation and abnormal prolongation of the life span of lymphocytes that are self-reactive. Therefore, one of the characterized of cancer cells is the immortality by stimulating Bcl-2 or inhibiting the Bax, Bad and then the cell continue in division with what have of mutation and genetic damage .Another effect which cause the immortality of cancer cells is due to the enzyme which called Telomerase (a sequences of pieces capping DNA) protect the cell from damage that the cell lose a fragment of DNA in each processes until being short and cannot division. It is thought that the absence of telomerase activity and the resultant continual loss of telomeric sequences through rounds of replication play a primary role in the senescence of normal cells[)]. This may provide a natural protection against the uncontrolled growth of cells. One method of defeating this control is by reactivating telomerase. Another way of bypassing this control might be by the acquisition of a new telomere without regard to the underlying sequence, as they have suggested in tumor. Such an event may serve to explain human tumor cells that do not show telomerase activity or telomere extension. Identifying and understanding the mechanisms by which cells can

escape this control on division is directly relevant to a complete understanding of the mechanisms of carcinogenesis.

1.4.2 Protein and cancer:-

There are four major categories of growth regulatory proteins: mutations within or inappropriate expressions of genes encoding these proteins induce a change of function, leading to inappropriate cell division and the cancer.

1- Growth factors - these may be circulating factors or factors that are only expressed locally in their normal tissue context. They act only on cells expressing the appropriate receptor. Example: Fibroblast Growth Factors, fgfs.

2- Growth factor receptors- expressed on the cell surface or in the cytoplasm, these receptors bind and transmit growth factor-mediated signals. Abnormal function of growth factor receptors can lead to abnormal growth. Inappropriate amplification of the genes encoding these receptors leads to higher than normal numbers of receptors on the cell surface. Amplification appears to be involved in the clinical progression of breast cancers .

Defects in growth factor receptors are likewise heterogeneous. Achondroplasia, the most common form of dwarfism and one of the most common autosomal dominant genetic disorders will affect persons born with an abnormal fibroblast growth factor receptor type III (fgf3).

3-Intracellular signal transducing proteins- Modulate signals between the receptor and the effector protein, which is in many cases a nuclear transcription factor. Example: The ras families of oncogenes are important in signal transduction, and abnormal ras function is found in a large number of cancers).

4-Nuclear transcription factors- Are the end product in the pathway, and ultimately participate in turning on and off various genes through transcriptional control. Example: Many tumor suppressor genes modulate the activity of

transcription factors. Retinoblastoma tumor suppressor protein regulates the activity of the transcription factor E2F during the cell cycl.

1-5 Cell cycle and tumor:-

Animals are multicellular organisms require the normal function of all the organs of the body. These organs are developed from different tissues and each of the tissues is products of cell division. For the body to function normally, the organs and tissues must communicate to control the development of the cells and tissues. Otherwise, uncontrolled cell growth in one part of the body could infringe on the development of other cells or tissues. Then the normal functions of the individual would be seriously impaired. Research over many years has shown that these control networks have a strong genetic component.

The cell cycle is an ordered set of events, culminating in cell growth and division into two daughter cells. The nucleus of each cell contains genetic information in the form of chromatin; a highly folded ribbon-like complex of deoxyribonucleic acid (DNA) wrapped around a class of proteins called histones. Cancer is a disease in which regulation of the cell cycle goes away, a better understanding of these processes should lead to new cancer treatments, Oncogenes have been shown many times to be associated with cancer and uncontrolled cellular growth. This growth can lead to tumors.

The cell cycle is composed of two phases' **mitosis and interphase**

Interphase: Interphase generally lasts at least 12 to 24 hours in mammalian tissue. During this period, the cell is constantly synthesizing RNA, producing protein and growing in size. By studying molecular events in cells, scientists

have determined that interphase can be divided into 4 steps: Gap 0 (G0), Gap 1 (G1), S (synthesis) phase, Gap 2 (G2).

Gap 0 (G0): There are times when a cell will leave the cycle and quit dividing. This may be a temporary resting period or more permanent. An example of the latter is a cell that has reached an end stage of development and will no longer divide (e.g. neuron).

Gap 1 (G1): Cells increase in size in Gap 1, produce RNA and synthesize protein. An important cell cycle control mechanism activated during this period (G1 Checkpoint) ensures that everything is ready for DNA synthesis. S Phase: To produce two similar daughter cells, the complete DNA instructions in the cell must be duplicated. DNA replication occurs during this S (synthesis) phase. Before DNA synthesis, the cell's chromosomes consist of one chromatid, called a monad .After DNA synthesis, the cell's chromosomes consist of dyads with 2 identical sister chromatids attached at the centromere .

Gap 2 (G2): During the gap between DNA synthesis and mitosis, the cell will continue to grow and produce new proteins. At the end of this gap is another control checkpoint (G2 Checkpoint) to determine if the cell can now proceed to enter M (mitosis) and divide .

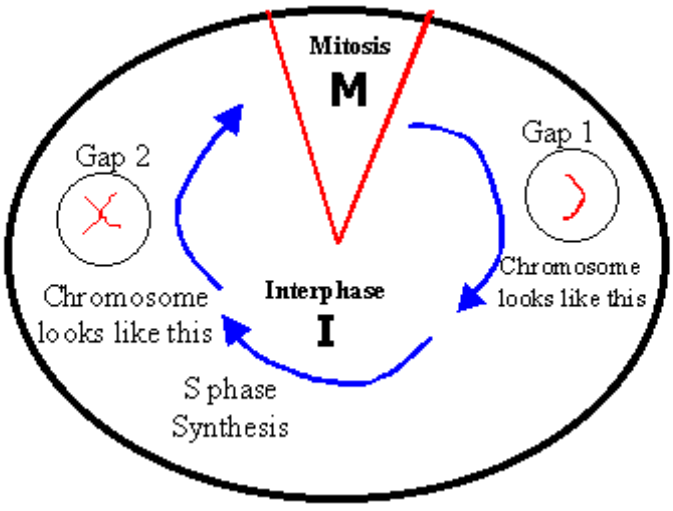

Fig (1-1) Shows cell cycleG1 stage separates the end of mitosis and the start of the S phase. **S phase** is the stage where the cell's DNA is replicated. It is bordered by both of the gap phases.**G2 stage** separates the S phase and the start of mitosis. (Fred Hutchinson Cancer Research Center 2006).

Cells can choose either to commit to a new round of mitotic division or to enter an alternative developmental pathway. The event in late G_1 phase at which cells irreversibly commit to a new round of cell division is called restriction point in mammalian cells. In all organisms, the cell division cycle is tightly regulated in response to internal and external signals. In all cell types, different combinations of cyclins and cyclin-dependent kinases (cdks) regulate progression of the cell cycle .A critical role for cyclin-dependent kinases (termed cdks) has been preserved throughout eukaryotic evolution. However, in mammals, there are several cdks (at least 6) and a variety of cyclins (at least 10). Expression of cyclins and cdks during the cell cycle. Two types of proteins trigger decisions in the cell cycle: **Cyclin D** and **CDK4**. **CDK4** stands for **cyclin dependent kinase**.

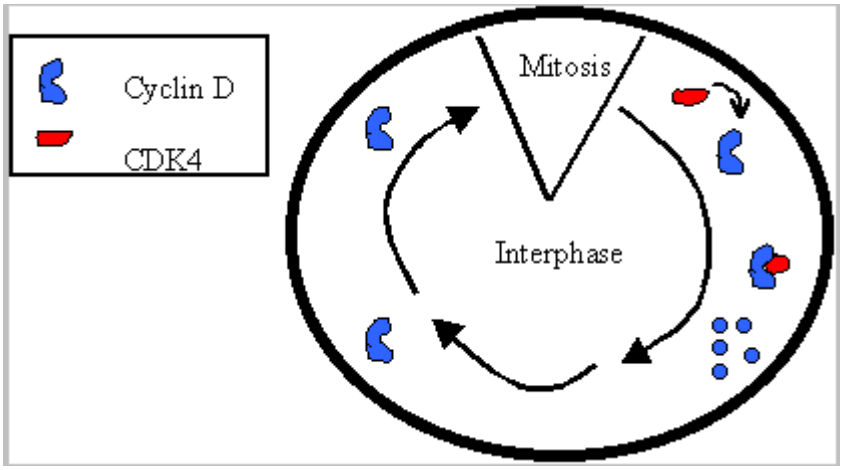

Fig (-2) Cyclin D binds to CDK4 and activates it. Cyclin D is broken down by the end of the G1 phase

Mitosis or M Phase: Cell growth and protein production stop at this stage in the cell cycle. All of the cell's energy is focused on the complex and orderly division into two similar daughter cells. Mitosis is much shorter than interphase, lasting perhaps only one to two hours. As in both G1 and G2, there is a Checkpoint in the middle of mitosis (Metaphase Checkpoint) that ensures the cell is ready to complete cell division **Mitosis** has six subphases: **interphase, prophase, prometaphase, metaphase, anaphase, and telophase**. During mitosis, the DNA separated into daughter cells and the cytoplasm is divided