*Review Article*

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# Indispensable Role of Protein in Cancer

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**Abstract**

Proteins are one of the most dynamic and versatile biomolecules which present in all the organisms. Protein plays a pivotal role in cell growth, cell motility, and biosignalling, provide immunity as well as cell recognition and many more biological processes like replication, transcription and repair. Transcription factors are also protein which present in vicinity of various DNA sequences and by binding to these sequences they can upregulate or downregulate the expression of the particular gene. Some protein performs more than one function in body and some are specific for a particular function in the biological system. Cancer is one of the deadly diseases of present century. Cancer is abnormal growth of cells which can be generated by multiple unlimited cell divisions and form a lump or tumor which can be benign or malignant. At present era the role of protein in cancer is very much skeptical that weather it enhance metastasis or suppress the effect of cancer. Cancer is the second most deadly disease of century after the heart disease. This mini review is an effort to give a glimpse of indispensable role of protein in cancer.

**Keywords:** Protein; Cancer; F-Box Protein; Cell Proliferation; Apoptosis; Metastasis.

## Introduction

Protein is a very versatile macromolecule which is essential to the entire organism. Protein plays crucial role in growth, regeneration, differentiation of cell, cell signaling, transmission of nerve impulse, in cell cycle, storage and various biological processes [1]. Besides these function proteins can also participate in various biological processes like replication, transcription, recombination and repair. Various transcription factors present in promoter and other genomic locations of a gene recognize specific DNA sequences and after binding to these they upregulate or downregulate a gene expression [2,3]. When normal gene expression of cells takes place it might contribute to the regular growth and normal functioning of the cell whereas its overexpression or down expression or expression of a defected protein, in neoplastic cells may cause abnormal tumor growth [4]. Many protein-encoding genes which regulate cell division and differentiation may undergo mutation and results into the abnormal behavior of neoplastic cells. With course of time more genes undergo mutation because the genes which produce proteins that usually repair DNA damage are themselves not functioning normally due to the mutation. Successively mutations begin to spread in the cell which leads to abnormalities in cell and daughter cells. Out of the whole genome only a small number of genes have been categorized under cancer causing genes. These malfunctioning genes can be classified as proto-oncogenes (which generate protein product for enhancing cell division and inhibit apoptosis),

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oncogenes (the genes which undergo mutation) and tumor suppressor (which synthesize proteins inhibit cell division and cause apoptosis) [5]. In normal cells controlled cell growth is regulated by maintenance of proto-oncogenes as well as tumor suppressor because proto-oncogenes enhance cell growth while later one slow down the cell growth. In normal cells, nucleus receives a signal for stimulation of cell division by a protein that is encoded by proto-oncogenes. These proteins are known as signaling proteins [6]. There are various proteins which are involved in signaling process and many other biological events. The substantial roles proteins play in other biological events are discussed in further section.

*Role of Protein in Augmentation and Suppression of Cancer*

Proteins are the main artist of the theater which is cell of the organism. It carries out various biological processes by interacting with other molecules such as DNA, RNA, small molecules, drugs as well as other proteins via binding sites present as binding pocket in proteins. Earlier it was discussed that protein take part in cell signaling and various other proteins play substantial role in signal transduction pathways. Cell growth is regulated by various cell signal transduction pathways, so their inhibition might be a factor of tumor pathogenesis. Activity of protein in signaling pathways can be hampered by phosphorylation which is achieved by the action of protein kinase [7]. Imanitib was reported as first anticancer agents targeted on a protein kinase for inhibition of the oncogenic kinase BCR-Abl and it is also participated actively in chronic myelogenous leukemia [8]. Protein Kinase A (PKA) is belongs to the serine-threonine protein kinase superfamily, which is recognize as cAMP-dependent protein kinase which perform signal transduction by binding to the cAMP. cAMP is found in almost all cells and it is produced from ATP by adenylate cyclases. It was used by a number of harmones, signal substances and neurotransmitters for sending messeage to intracelleular environment and this is the reason that rate of cAMP production is dependent on extracellular as well as intracellular signals. In cell it might play a pivotal role in activity of different proteins. In eukaryotes cAMP play a major role in activation of PKA.

Stork et al [9] and Insel et al [10] has been reported role of cAMP/PKA pathway in stimulation of cell growth in many cells as well as inhibiting in some other cells. Regulation of cell proliferation was intimidated by involvement of PKA action on transcription factors [11]. It was established by various group that dysregulation of PKA signaling might cause various types of cancer such as lung cancer, endocrine tumors as well as prostate cancer [12]. So, it was suggested that abnormal PKA should be investigated for diagnosis and treatment of cancer in patients. Lin et al has reported that another protein Ki67 by interacting with other nuclear protein NIFK play an important role in tumor formation in various organs such as breast, lung, brain and prostate gland [13]. But the exact mechanism by which cancer cells proliferate by involvement of this protein has become a riddle for scientists. In another report PIWI protein which is a subfamily of Argonaute protein family was proposed to be involved in tumor formation and its proliferation in breast. PIWI proteins are specifically play role in stem cell regeneration and germline development in various organisms [14].

Chen et al has reported earlier that S100 gene family protein is also play a substantial role in cancer formation and its progression. This family is specifically involved in calcium binding, calcium homeostasis, cell growth and migration, cell cycle and regulation of transcription factors [15]. By involvement of various biological functions this protein has a close relation with metastasis and cancer proliferation. Cells use its cytoskeleton for cell motility, polarization and division and the most important cytoskeleton protein is known as Actin-filament-bundling protein. The actin cytoskeleton represents an important mess of proteins that encroach on invasion, motility, polarity, survival and growth of normal cells, and as such is often sabotaged by cancer cells. Abnormal cancer cells use this actin protein to invade through the surrounding tissue and travel in lymphatic and vascular system and via this spread cancer in other tissues and organs [16]. Various proteins which participated in cancer formation or suppression is demonstrated by (Figure 1).

Inspite of protein which involve progression of cancer some proteins are found to be tumor suppressing. Insulin-like growth factors (IGFs) are a group of peptides which are involved in various cell processes like cell differentiation, proliferation and apoptosis; make it a strong contestant for the tumorigenesis. Two important peptides of this family are IGF-I and IGFBP-3, both are specifically dependent on growth hormone but also influenced by age, nutrition and sex of the organism. It was established by various group that high circulating concentration of IGF-I is associated with enhancement of cancer formation whereas IGFBP-3 showed contrasting results. Its high concentration involved in the reduced chance of cancer [17, 18].

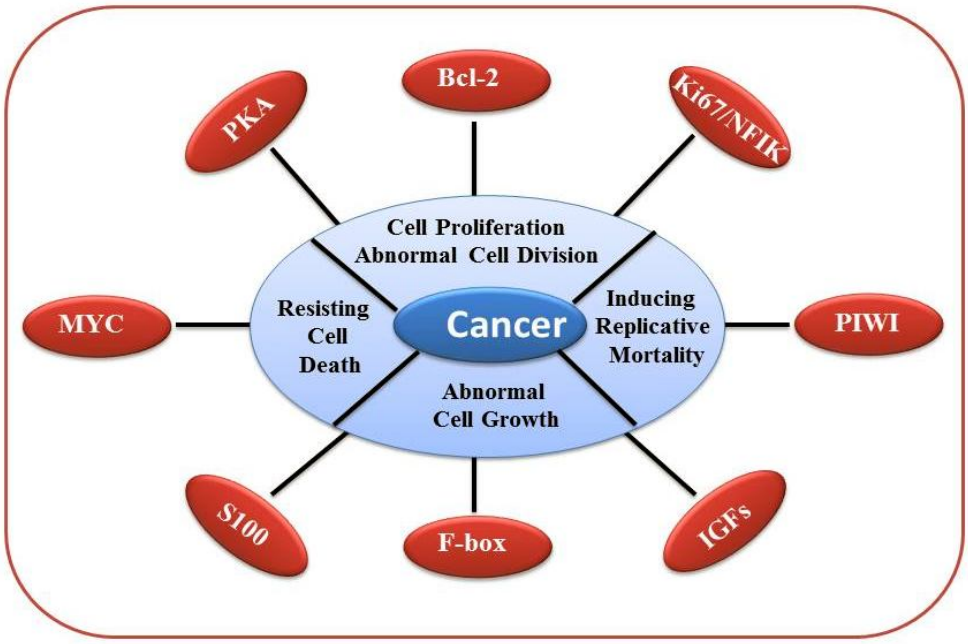


**Fig. 1:** Schematic representation of various proteins involve in cancer proliferation and suppression

IGF-I is considered to be antiapoptotic and mitogenic while IGFBP-3 as tumor growth inhibitor. Renhen et al has suggested that nutrition and life style also affects the circulation and function of these peptide growth hormones [19]. Wang et al has reported that human malignancies are expanded by proteolysis intervened by F-box proteins. These proteins play a pivotal role in cell cycle regulation. FBXW7 one of the F-box protein has already well-studied tumor suppressor that act and degrade various oncogenic proteins [20]. Sreedhar et al has also established in his report that heat shock proteins (Hsps) play as significant pharmacological target to encounter cancer. The important function played by Hsps in immune signaling and its innate quality make them potential target for tumor suppressant study [21]. There are many more proteins such as Bcl-2 family [22], LARP family protein [23], MYC family of protein [24], NEET protein [25] and Dynamin-related Protein 1 (Drp 1) [26] all are related with one or more than one type of cancer. These proteins plays substantial role in cancer proliferation as well as cancer progression of various tissues and organs such as lung, breast etc. Specifically Bcl-2 and MYC are the major class of proteins which regulate the cell proliferation and apoptosis.

## Conclusion

The role of protein is indispensable in a number of biological processes such as transcription, cell differentiation, cell growth, storage, cell division and cell signaling. Various proteins play a pivotal role in tumor progression and proliferation whereas some protein acts as dysregulation of cancer and tumor suppressant. Cancer has become the most deadly and serious disease at present era due to instant mutation in gene and abnormal growth of cells. It is need of the hour to identify the proteins which involve directly or indirectly in the cancer formation. Other factors like environment, life-style, tobacco and some steroids also play major role in causing cancer and metastasis. Individual with history of cancer in family should be tested for cancer on regular basis. Early diagnosis can increase the survival rate of patient and as we all are aware about prevention is better than cure we should change our life-style and say no to all the steroids and tobacco. This review is a small effort to shed light on role of protein on the cancer proliferation and progression which might give an insight to investigate other proteins for regulation and deregulation of genes and via targeting and alteration of these proteins cancer formations can be hampered.

*Conflict of Interest*

Author is confirming that there is no conflict of Interest in this article.

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