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Molecular biology for cancer therapy: Review articles

Bahiru Tenaw Goshu

Department of Anatomy, School of Medicine, College of Medicine and Health Sciences, University of Gondar, P.box,196, Gondar, Ethiopia.

Institutional email address: Bahiru.tenaw@uog.edu.et

Publication used email address: haikutena@gmail.com



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## ABSTRACT

**Introduction**: Cancer, as clusters of diseases, uncontrolled cell proliferation due to tumor suppressor genes inactivation, oncogenes activation, and external factors.

**Methods**: To review data, electronic databases such as Nature, PubMed/PMC, Science Direct/Elsevier, EMBASE, and Google Scholar were used.

**Results**: Derestricted forms of proto-oncogenes are oncogenes, which had vital roles in various paths of cell cycle modulation. Translocations and chromosomal rearrangement and/or mutations in genes are the major factors for the transformation of proto-oncogene to oncogenes. Herein, to prevent the proliferation of cancerous cells, oncogenes are targeted molecules. From a cancer therapeutic target point of view, oncogene silencing and deletion, mutation of tumor suppressor genes, and retroviral therapy molecular techniques were developed.

**Conclusion**: To establish a cancer-free world, the most commonly used techniques are: Ribose Nucleic Acid interferences, zinc finger nucleases, and CRISPR.


**Keywords**: Cancer, Oncogenes, Proto-oncogenes, molecular technique

## Background

Cancer is defined as a disease that resulted from the uncontrolled division of cells without following the normal cell division regulatory mechanisms. Tumor suppressor genes inactivation, oncogenes activation, and external factors are the causative pathophysiologic processes for the uncontrolled division of cells. Oncogenes expression is an imperative occurrence in the early stages of tumor formation. The tumor-driven viruses that infect other cells, and change in the proto-oncogenes are the two physiologic processes to oncogenes activation. Although the oncogenic revolution of a single cell is the main source for much tumor development, tumor cells also adopt the potential to outflow their novel site of uncontrolled proliferation to the leftover body parts via various roots of metastasis mechanisms(1).

## Methods

The data were collected from published research articles focused on molecular biology techniques for cancer therapy. Electronic databases such as PubMed, Nature, EMBASE, Science Direct, Google scholar used, and then "Cancer therapy", 'Oncogenes", "Proto-oncogenes", "Viral infection tumor", "molecular techniques and/or CRISPR" key terms were used as search options. Research papers published until 2017 included in this review.

## Results and discussion

To appreciate the correlation between carcinogens and mutagens, and then several carcinogens are reflected as mutagens, the change in the normal functional genes might cause too carcinogenic. In cancer research, the application of molecular biology tools supports the relation between carcinogens and mutagens (2). As causative factors, in addition to the over-triggering of oncogenes, Cancer maybe comes across as a result of any miffed of tumor suppressor genes (3).

### Cancer development: oncogenes role

As tumor-causing agents, oncogenes had roles in cancer development. To change normal gene exploit a solitary oncogenic trait is desirable. The host cells and viruses are the core sources of oncogenes (3). Gene alterations through various mechanisms or chromosomal translocation promote the normal proto-oncogenes conversion to oncogenes which clues to tumor development (4).

**Classification of oncogenes**

According to the protein products from the deregulation of proto-oncogenes, Oncogenes can be classified as Growth factor receptors, Growth Factors (GF), threonine kinases, and transcription factors (TF). Of these, For instance, the changes in the main oncogenes class, Growth Factors, promote cancer progression in the diverse region of the body as in bone (osteosarcoma, in the eye (glioblastoma), etc. (5, 6).

**Oncogenes for cancer therapy**

As oncogenes are targets for cancer therapy, gene therapy, and several drugs regulate and arrest their genes for cancer progression. The drugs/agents like Gleevec, Tarceva, bevacizumab, and Sorafenib are the commonly used agents that obstruct the activities of the BCR-ABL, EGFR, VEGF oncogenes, and B-Raf oncogene, respectively. Furthermore, the combination of these drugs also used as a chemotherapy agent to prevent the spread of oncogenes, then hinder signaling pathways to cancer (7).

**Tumor suppressor genes in cancer**

Tumor suppressors constrain cellular uncontrolled proliferation and progression of tumor development. As a target of cancer therapy, the Inactivation of the tumor suppressor genes prevents its regulation of cell proliferation that caused abnormal cell division. Thus, Tumor suppressor genes altered their functions. To prevent tumor spread and progression, both duplicates of the tumor suppressor genes should be deactivated as one copy is adequate for directing cell division (8).

**Roles of Tumor Suppressor Genes**

As for end products, Proteins formed from the activation of tumor-suppressing genes, have been intricate in DNA repair, enhance apoptosis, and act as receptors in cell proliferation hang-up or regulation, and chromosome abnormality control (9).

A repressor protein product, Wilms tumor 1, provides the clampdown effect on the transcription of GFs that persuade genes. This outcome verified that tumor-suppressor genes have been involved to act as transcription controlling products. Furthermore, Wilms tumor 1 gene overexpression as a

consequence of target for insulin-like GF is the causative for the uncontrolled cellular production (10).

**P53 Tumor Suppressor Gene**

P53 regulates various events occurred in different stages cell cycle. Thus, any tuning in the p53 modulating role leads to a cell division unwarranted. Therefore, it may speculate that the alteration of P53 is one of the foremost factors for tumor development (11).

**Molecular pathology: Diagnosis of cancer**

Pathologically correct investigations of cancer cases are the main strategies in the patients' decent prognosis. Thus, different technologies have emerged, and routinely engaged to diagnose cancer at the molecular level. These methods include immunohistochemistry, immune fluorescence, and in situ hybridization. Sanger sequencing (chain termination method), pyro sequencing, cancer genotyping, and next-generation sequencing were used to perform cancer subtypes. The next-generation sequencing is serving to uncover the true diversity of cancers as well as to define recurring mutations targeted with new therapies. Such genomic level analyses will continue to have an impact for many years (12, 13).

**Time trends of Cancer treatment**

In addition to the medical and surgical treatments of cancer cases, there were varied emerging techniques that have been applied timely till the state-of-the-art Clustered regularly interspaced palindromic sequences application (14). Moreover, gene substitution, viruses-based chemotherapy, and oncogenes down-regulation also conducted to terminate cancer cells perpetually (15).

**Molecular biology techniques for cancer treatment**

1. **Homologous recombination**

To inactivate the target gene, homologous recombination techniques were implemented to describe gene action. As of its early strategy, it is not that fruitful to be competent on the target protein site. It was a very lengthy, laborious process, and also it has a mutagenic effect (16).

2. **RNA Interference**

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As the name indicates, the RNA interference (RNAi) method prevents the translation process of protein production while binding non-coding RNA to a messenger RNA molecule. As a result of this interference, the function of the gene might vanish. For cancer therapy, Therefore, RNA Interference applied to abolish genes that promote cancer development (17-19).

As compared with the homologous recombination method, the RNA interference is well-timed, inexpensive, and has an extraordinary value. Although it is better than homologous recombination, this method had its own drawbacks such as wears knockdown completion, momentary gene inhibition, and leads to an unexpected impact on the target site. To resolve these drawbacks, the different scholars twitch to invent more advanced methods (20).

### 3. **Zinc finger proteins**

As to genome editing technology application, Zink Finger Proteins (ZFPs) are the first nucleases applied. As a protein structure, ZFNs) are synthetic restriction enzymes engendered from the binding of a zinc finger DNA-binding domain to a DNA-cleavage domain. Zinc finger domains may be plotted to target specific preferred DNA sequences and this permits zinc-finger nucleases to target exclusive sequences in genomes (21-28). These arrays bind to adjacent DNA sequences to get a DNA break. Substitution, deletion, and insertion were used to repair. Therefore, this method recognizes base pairs in clear-cut loci of DNA (25, 29, 30 ).

### 4. **Transcription activator-like effector nucleases**

As of is a genomic edition technique, the Transcription activator-like Effector Nuclease (TALENs) use DNA binding motifs and the nuclease. The TALENs domain recognizes single-nucleotide while ZNFs recognizes triplets. Moreover, TALEN has a humble design process and resilient interactions of domain targets (31, 32). Transcription activator-like effector nucleases detect the double-stranded DNA sequences of specific genes effectively (33-35). The DNA break would be repaired by non – homologous end-joining pathways. What is more, TALENs eliminate the previously encountered genetic changes? As it is a gene-editing technique, it is vital to treat the cancer cells proficiently in the genome (34).

### 5. **CRISPR/CAS9 system**

Clustered regularly interspaced short palindromic repeats strategy consists of nucleotide bases tailed by short fragments of double-stranded DNA from a formerly conquering organism that affords immunity to the most prokaryotic organisms. The most significant rewards of CRISPR/Cas9 over other genome editing technologies are its simplicity and efficiency. This ground-breaking technique licenses scholars' committed successes in genomic sequencing, accordingly serving to explain the functional arrangement of the genome and detecting the casual genetic variations. CRISPR mainly institutes two working groups of guide RNA and Cas9 system that identify the complementary genomic sequences in specific sites (35, 36).

## Comparison of CRISPR/Cas9 system with traditional methods

As compared with other molecular biology techniques, The CRISPR/Cas9 system is an ideal method that depends upon the RNA complex. Hence, CRISPR/Cas9 system is with no trouble, resourceful, no need of varied proteins, and less laborious steps than nuclease-driven methods. Over and above, as compared with the traditional method, it takes a short period, and with less laborious. The CRISPR method, therefore, can announce multifarious changes in several genes altered instantaneously to guide RNAs (gRNAs) (12, 34).

## Conclusion and future direction

In the recent decades, Molecular biology techniques have been promptly advanced as to a cancer therapy systems developing, and later the expansion of advanced methods as of Clustered regularly interspaced palindromic sequences, Transcription activator-like effector nucleases, and Zinc finger proteins. Nowadays, scholars can effortlessly advance their exploration of the target genome sequence. This review, therefore, will offer a huge advantage for cancer therapy, ducking the hazards encountered by the aforementioned molecular biology techniques. Further research on more advanced molecular biology techniques' mechanisms of functions for cancer therapy should be conducted that may be helpful to provide clear and correct diagnosis and establish better clinical management of cancer.

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