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Role of Biotechnology in Cancer Control

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ABSTRACT

Cancer control including predictive diagnosis, differential diagnosis, early detection, cancer progression control and proper treatment with biotechnology techniques has assumed a central emphasis in cancer research and treatment. Biotechnology as a modern science with high accuracy ,more efficiency power and analysis ability at bimolecular level provided researchers with detailed information about causes , biomarkers, related pathways, genes, factors , targets and anticancer ligands for control of different types of cancers to provide individualized therapy for compensation of disadvantages, incomplete ability of treatment and side effects of conventional methods of cancer therapy such as chemotherapy and radiotherapy. In this paper we have focused on biotechnology techniques for cancer control and discussed the role of each technique with example and the importance of each technique during control stages of cancer. The techniques are discussed here are such as Gene profiling, Genome analysis and Cell Culture, We hope this review will be helpful for researcher to understand the need and importance of biotechnology in conduction of cancer research programs, also This basic information provides opportunities for the researchers to expand and support the research area with their suggestive, feasible ideas and development of applicable new techniques for better cancer control with biotechnology.
Keywords: Biotechnology, Cancer Control, Gene profiling, Genome analysis, Cell Culture.

I. INTRODUCTION

Even with recent development and progression in diagnosis and treatment, cancer has remained a major cause of death. It is reported that cancer is the second main cause of death after heart disease. .Every year over 10 million people in the world detected with cancer and high percentage of this report die as a result of unsuccessful treatment of the disease. [1,2] Success percentage in cancer therapy is restricted due to difficulties in detection, late appearance of cancer and unavailability of differential therapy [3] Biotechnology contribution in cancer research has widely broken such restrictions and played significant role in developing new ways of cancer control and prevention . Cancer is a disease characterized by variation of the genome and the proteome. These alternations allow the cancerous cells to avoid normal cellular control mechanisms and to initiate growing unregulated. The major aim of cancer research programs conducted with biotechnology methods is to determine these molecular errors and use this observation to develop appropriate differential diagnostic, proper treatment and prevention diets .[4,5]

Biotechnology has helped researchers to understand cancer in different ways such as Gene profiling, Genome analysis, cell culture, culturing transgenic cell lines and specially identification of new biomarkers for detection of risk and progression of cancer. Available technologies in biotechnology help scientists to understand cause of cancer and the behavioral way of cancerous tissue in different environments. They also provide information about the factors increasing the growth rate of the cancers and the growth reducing factors as well .[4] Here we reviewed helpful technologies in biotechnology for cancer research to understand significance and need of the biotechnology in cancer therapy.

II. METHODS AND MATERIAL

Gene expression Profiling: It is a technique for measuring the expression level of large number of genes simultaneously ,used for classification of tumors and identification of specific alleles that increase the risk of developing cancer due to carrying genetic defect via inheritance in individuals which gives them a susceptibility to develop cancer over the lifetime. The most applicable gene expression profiling techniques are used by biotechnologists are, DNA sequencing, *In situ* hybridization, Real time PCR and gene mapping.[4,5]

DNA sequencing is a determination process of the proper order of nucleotides: adenine, guanine, cytosine, and thymine—within strand of DNA. This method is widely used in cancer research programs for detection of oncogenic DNA sequences. DNA sequencing of cancer –related genes is done for discovery of biomarkers. DNA sequences variants, single nucleotide change , small insertions and small deletions are detected using DNA sequencing .These DNA sequences variations are present in cancerous tissues while are absent in normal healthy tissues of the same individual. [5, 6]So detection of such oncogenic DNA sequence variants are key factors for development of new treatment .As the products of oncogenic DNA sequences are abnormal so they can serve as targets for pharmacologic prevention and the technique is continuously applicable for discovery of biomarkers until completion of observation of spectrum of DNA variation in cancerous tissues.[6] The use of DNA sequencing and its role in identification of mutations in cancer is discussed here in the form of an example: one requirement for tumor formation is somatic mutations in nuclear genome, but sequence of somatic mutations in mitochondrial genome are not well understood. Using sequencing methods: genomic and transcriptomic sequencing, scientists identified somatic mitochondrial mutations across 527 tumors and 14 cancer types. They have found that there is a particular strength against deleterious coding mutations, demonstrating requirement of functional mitochondria in tumor cells. They also observed a strong mutational strand bias as the major source of mutations .So using this method; they have showed mtDNA function in cancer. [7]

***In situ* hybridization** is another biotechnology technique widely used in cancer research programs. In this technique, localization of a specifics DNA, RNA sequence in a section of tissue (*in situ)* is done by using a labeled complementary DNA, RNA or probe. Using this method is helpful for the scientists to analysis expression of genes and their roles in development and progression of specific cancers.[4,6] For example, analysis of expression of AC3-33 gene which encodes a secretary protein that has inhibitory activity towards EIK1 transcriptional activity through ERK1/2 pathway by *in situ* RNA hybridization determined the role of AC3-33 gene in development and progression of some specific cancers. In this research, the result showed variation in expression level of AC3-33 across different tissues. Positive expression of the gene exhibited in squamous cell carcinoma of the esophagus, adenocarcinoma of the rectum, hepatocellular carcinoma, squamous cell carcinoma (SCC) of the lung, cancer-adjacent normal hepatic tissue, clear cell carcinoma of the kidney, invasive ductal carcinoma of the breast, SCC of the uterine cervix and cancer-adjacent normal kidney tissue while negative expression of the gene exhibited in adenocarcinoma of the stomach and colon, cancer-adjacent normal esophageal tissue, cancer-adjacent normal gastric tissue, cancer-adjacent normal colon tissue, cancer-adjacent normal rectal tissue, serous adenocarcinoma of the ovary and cancer-adjacent normal ovarian tissue.This technique helped in classification of tissues based on expression of AC3-33 gene into two groups positive and negative expression which lead in development of cancerous and normal cells respectively.[7]

Real time PCR is another profiling expression technique which has broad application in analysis and study of cancers. This technique is advanced form of polymerase chain reaction used for amplification and simultaneously detection or quantification a targeted DNA sequence .In this technique, general principle of PCR are applied and detection of amplified DNA is carried out while the reaction progress is in real time. Real time PCR is one of the central focus for cancer research programs .[5,6]For example, for expression of drug targets such as beta –tubulins which are targets for anticancer drugs in cancerous cells, scientists developed a method using RT-PCR for determination of mRNA expression of eight human beta tubulin isotypes which

encode class I, IIa, IIb, III, IVa, IVb, V, and VI and applied it to 21 healthy tissues and 79 tumor samples from seven cancer types. On the basis of expression pattern using RT-PCR they have found that non –tumoral tissues, TUBB (I), TUBB2C (IVb), and TUBB6 (V) were ubiquitous, TUBB1(VI) was hematopoietic cell-specific, and TUBB2A (IIa), TUBB2B (IIb), TUBB3 (III), and TUBB4 (IVa) showed high expression level in brain. In tumoral tissues, exhibition of most isotypes showed an alternation of expression pattern in specific tumor types. In overall expression of TUBB3 was increased while TUBB6 expression highly decreased in most tumors. Thus,non-tumoral tissues showed distribution of a complex tubulin isotypes which showed contribution to the toxicity profile of the drugs and significant alternations of specific isotypes in tumors stand for representation of markers for response to anticancer drugs.[9] Real –Time PCR assay also used for classification of tumours. For example scientists applied RT-PCR for classification of 30 main tumor types and 54 histological subtypes from 92 gene set.[10]

Gene mapping, is another biotechnology method for determination of location of genes, gap and related distances between gens on a chromosome. The main goal of gene mapping in cancer projects is positioning of genetic markers related to cancers onto their respective locus on the genome. Gene mapping aims to identify markers related to the specific cancer and individual so it provides personalized cancer therapy .Also it helps in early detection of cancer, identification of high-risk cancer patients and finding molecular markers that can predict therapy responses. [4, 5,6] For example scientists conducted a large scale analysis project of breast cancer in European ancestry population including 37954 patients with 2900 deaths from the cancer. This project genotyped 20000 to 90000 single nucleotide polymorphisms (SNPs) across the genome .Using genotyping method, they identified one new locus named rs2059614 at 11q24.2) associated with survival in ER-negative breast cancer cases and a second locus (rs148760487 at 2q24.2 was also identified in association with genome-wide statistical significance in initial analyses, this association was similar in ER-negative and ER-positive cancer cases.[11]

Genome analysis: includes determination, measurement and comparison genomic elements such as DNA sequences, Gene expression, regulatory and functional elements at genomic rate. [4,6]

Microarray analysis: The most applicable technique of genome analysis is microarray used for comparison level of expression of thousand genes simultaneously. This technique helps the scientists to understand which gene is turned on or off in presence or absence of cancer. The microarray analysis helps in identification of known genes playing role in cancer which in turn lead in identification of new target for cancer treatment. To understand the level of expression of genes in cancer cell line, Real time PCR is used which gives analytical information about quantify change of gene expression .[4,5,6]For example ,gene microarray analysis of lncRNA and mRNA expression profiles in patients with hypopharyngeal squamous cell carcinoma showed involvement of lncRNAs in development an progression of many types of cancers . In this method the researchers investigated differences in expression profiles of lncRNA and mRNA between three pairs of HSCC tissues and adjacent non-cancerous tissues by gene microarray analysis method. The result showed that In HSCC tissues significant upregulation of 669 lnRNAs and downregulation of 630 lnRNAs as compared to expression levels in adjacent non-cancerous tissues. Moreover, significant upregulation of 684 mRNAs and downregulationof 748 mRNAs in HSCC tissue observed. For confirmation of microarray results the scientists selected two differentially expressed lnRNAs (AB209630, AB019562) and 2 differentially expressed mRNAs (SPP1, TJP2) and applied qRT-PCR technique. The qRT-PCR results were the same as microarray analysis. The analysis showed distribution of the differentially expressed lncRNAs and mRNAs on each of the chromosomes (X and Y chromosomes) .based on the analysis, 71mRNAs involved in molecular functions were downregulated in cancerous cells. These results provide understanding the mechanism of underlying HSCC cancer genesis and also help in identification of new anticancer targets and detectable biomarkers for the disease. [12]

Cell culture: The process of growing the cells outside of their environment under controlled condition is called cell culture. Eukaryotic cells including human cancerous cells have potential to culture outside the human body under controlled condition in incubators. Identified gene

played role in cancer can be introduced to a cell line and subsequent changes and effects studied and analyzed by growing these cells in cell culture. In this technique, the gene first cloned and after insertion in plasmid vector, amplifies in bacteria. The vector is then transferred into mammalian cells using one of the cell transfection methods such as liposomes .Incubation of these cells is done at human body temperature and supplied with appropriate nutrients. By comparison the gene expression in these cells with controlled cells , researchers can identify the change appeared in the cells due to inserted gene.[6,13] For example secretion of autocrine hGH in the breast is essential for development of normal breast during puberty but increased levels of autocrine hGH observed in breast cancer. Scientists used tissue culture for analysis of this difference in levels of hGH in breast cancer development. Their finding has shown that secretion of hGH from breast cancer cells led in increasing growth rates and as a result the cells are more but hGH secreted from pituitary gland into the blood stream then to the tissue culture does not show increasing of cell growth. So this difference was helpful for them to find out causing molecules of breast cancer development .For further investigation, application of Microarray and PCR technologies together was used. [13, 14].

III. RESULT AND DISCUSSION

Biotechnology introduced as an important filed of research and study for cancer treatment as it develops targeted therapy. Analysis of cancer at molecular level is possible through biotechnology techniques. Cancer caused by variation of the genome and the proteome. These variations allows the cancerous cells to inhibit normal mechanism of control and to start growing uncontrolled .The major goal of biotechnology in study of cancer is to determine these molecular errors and using this knowledge , provide differential diagnostic and prevention diets. Biotechnology has assumed a significant place in cancer therapy and analysis. Using biotechnology techniques and combination of these techniques in different ways help scientists in identification of new markers , prediction of high risk cancer cases , detection of new targets and discovery of anticancer drugs which ultimately led in individualized therapy . Base on the objective of the cancer project, different methods in single or in combination are applied for investigation of cancer project's aim. In this paper we, reviewed main techniques of biotechnology which are categorized in three groups such as Gene profiling, Genome analysis, Cell Culture. Each of these analysis method group, include several techniques for example gene profiling has several techniques such as RT-PCR, gene mapping, DNA sequencing method, *in situ* hybridization etc. Genome analysis mainly applies Microarray techniques such as RNA microarray and DNA microarray techniques and cell culture using culturing cell lines of cancerous cells and normal cells for comparison and study of the cancer. These techniques are applied in combination forms for different research projects such as classification of tumors , identification new genetic markers, Identification of new oncogenic DNA sequence in cancer like mtDNA function in cancer ,classification of tissues based on expression of genes like expression of AC3-33 gene, classified tissues into two groups positive and negative expression tissue groups which lead in development of cancerous and normal cells respectively, Identification of drug targets by Real time PCR like identification of beta –tubulin as target for anticancer drugs, identification of new locus using genotyping methods like rs2059614 at 11q24.2) associated with survival in ER-negative breast cancer cases and locus (rs148760487 at 2q24.2 in association with genome-wide statistical significance , investigation of new down regulation class in cancer by RT-PCR like HLA class I down regulation in breast cancer [15].Identification of role of many sequences in cancer development using microarray technology like role of lncRNAs in development and progression of many types of cancers, identification of new targets for anti-cancer drugs like cyclin dependent kinases by combination of biotechnology methods [16] Determination of expression level of hormones and their role in cancer using tissue culture technology like determination of increased levels of autocrine hGH in breast cancer. Hence biotechnology provides different opportunities in research area for cancer study due to its broad area of research and availability of techniques. Using these techniques along with professional knowledge of biotechnology and it's principles could improve cancer therapy and overcome disadvantage of conventional methods of cancer therapy. We hope biotechnologists will develop more techniques and discovery items in order to decrease the cause of death and to limit

suffering percentage of cancerous patients .However cancer due to its complicated nature needs more time to completely analyzed but biotechnology provides a fast and promising way of therapy to reach the destination "complete therapy ".The biotechnology community encourages scientists to do their best in utilization of biotechnology's facilities in order to cover all aspects of cancer research such as treatment, prevention and prediction.

IV. CONCLUSION

By increasing new technologies in biotechnology such as PCR, Microarray technology, RFLP and so on and generation of several targets for drug such as CDKs, ion channels, GPCRs and aquaporins also Biomarkers , biotechnology can be broadly used in cancer treatment for targeted therapy which gives more efficiency and accuracy results than other conventional methods. In combination with bioinformatics method for investigation and detection of cancer materials, more efficiency and rapid result can be obtained. For example by detection of SNPs using bioinformatics methods or gene finding or detection of biochemical pathways related to cancer. Biotechnology can be utilized any animal models like mouse and zebrafish. So application of biotechnology in cancer control using developed methods and material can be achieved valuable results in short time.[16-25]

V. REFERENCES

[1] Anand P et al Cancer is a preventable disease that requires major lifestyle changes. Pharm Res. 2008 Sep; 25 (9):2097-116.

[2] Haggar FA, Boushey RP.Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. Clin Colon Rectal Surg. 2009 Nov;22(4):191-7.

[3] Ling CQ. Problems in cancer treatment and major research of integrative medicine. Zhong Xi Yi Jie He Xue Bao. 2003 Sep;1(3):168-70.

[4] Kewal K. Jain,Applications of Biotechnology in OncologySpringer, 2014. 885 p.

[5] Daniel H. Palmer,Lawrence S. Young, Vivien Mautner,Cancer gene-therapy: clinical trials . Trends in biotechnology 2006 24(2) p76–82,

[6] Farwell LM, Joshi VA.DNA sequencing of cancer-related genes for biomarker discovery. Methods Mol Biol. 2009;520:205-20.

[7] Stewart JB, et al .Simultaneous DNA and RNA Mapping of Somatic Mitochondrial Mutations across Diverse Human Cancers. PLoS Genet. 2015 Jun 30;11(6):e1005333.

[8] Hu F et al .Analysis of AC3-33 gene expression in multiple organ cancer and adjacent normal tissue by RNA in situ hybridization. Oncol Lett. 2015 Jun;9(6):2795-2798.

[9] Leandro-García LJ et al .Tumoral and tissue-specific expression of the major human beta-tubulin isotypes. Cytoskeleton (Hoboken). 2010 Apr;67(4):214-23.

[10] Erlander MG, Ma XJ, Kesty NC, Bao L, Salunga R, Schnabel CA.Performance and clinical evaluation of the 92-gene real-time PCR assay for tumor classification. J Mol Diagn. 2011 Sep; 13(5):493-503.

[11] Guo Q et al Identification of Novel Genetic Markers of Breast Cancer SurvivalJ Natl Cancer Inst. 2015 Apr 18;107(5).djv081

[12] Zhou J et al ,.Gene microarray analysis of lncRNA and mRNA expression profiles in patients with hypopharyngeal squamous cell carcinoma. Int J Clin Exp Med. 2015 Apr 15;8(4):4862-82.

[13] Cree IA. Principles of cancer cell culture. Methods Mol Biol. 2011;731:13-26

[14] Michael J. Waters* and Becky L. Conway-Campbel.The oncogenic potential of autocrine human growth hormone in breast cancer. Proc Natl Acad Sci U S A. 2004 Oct 19; 101(42):14992-3.

[15] Palmisano GL et al Investigation of HLA class I downregulation in breast cancer by RT-PCR. Hum Immunol. 2001 Feb;62(2):133-9.

[16] Ghorbani M, Karimi H, 'Role of Microarray Technology in Diagnosis and Classification of Malignant Tumours', International Journal of Scientific Research in Science and Technology(IJSRST), 1(3):117-121, July-August 2015

[17] Ghorbani M and Karimi H. Cyclin-Dependent Kinases as valid targets for cancer treatment. Journal of Pharmacy Research 2015,9(6),377-382

[18] Ghorbani M , Karimi H , 'Ion Channels Association with Diseases and their Role as

Therapeutic Targets in Drug Discovery', International Journal of Scientific Research in Science and Technology(IJSRST), 1(3):65-69,July-August 2015.

[19] Ghorbani M , Karimi H , 'Role of Aquaporins in Diseases and Drug Discovery', International Journal of Scientific Research in Science and Technology(IJSRST),1(3):60-64, July-August 2015

[20] 20Mahin Ghorbani, Hamed Karimi, 'Role of G-Protein Coupled Receptors in Cancer Research and Drug Discovery', International Journal of Scientific Research in Science and Technology (IJSRST),1(3), pp.122-126 , July-August 2015.

[21] Mahin Ghorbani, Hamed karimi, 'Role of Biomarkers in Cancer Research and Drug Development', International Journal of Scientific Research in Science and Technology(IJSRST),1(3), pp.127-132, July-August 2015

[22] Ghorbani M ,Karimi H ,Ten Bioinformatics Tools for Single Nucleotide Polymorphisms , American Journal of Bioinformatics ;2014:3(2):45-48

[23] Mahin Ghorbani, Hamed Karimi, 'Bioinformatics Approaches for Gene Finding ', International Journal of Scientific Research in Science and Technology (IJSRST),1(4),12-15, September-October 2015.

[24] Mahin Ghorbani, Hamed Karimi, 'Bioinformatics Methods for Biochemical Pathways and System Biology Analysis', International Journal of Scientific Research in Science and Technology (IJSRST),1(4) ,75-79, September-October 2015.

[25] Mahin Ghorbani ,Iranian traditional medicine for treatment of type II diabetes, anxiety and hypertension with introduction of zebrafish model system for their screening, International Journal of Herbal Medicine, ,2014, 2(5),13-19.