Cancer Therapy & Oncology
International Journal
ISSN: 2473-554X

Juniper Publishers
key to the Researchers

Mini Review
Volume 25 Issue 3 - November 2023
DOI: 10.19080/CTOIJ.2023.25.556165

Cancer Ther Oncol Int J

Cancer Cell Attains Functional Malignancy at 360° Circle

K Ramalingam[1]* and Babu K[2]

[1]*Mediclone Biotech Research Centre, Chennai-48, Tamil Nadu, India & Dr. Rai Memorial Medical (Cancer Hospital) Centre, (Ethical Committee), Chennai, Tamil Nadu, India*

[2]*Arignar Anna Government Arts College, Namakkal-637002, Tamil Nadu, India*

Submission: September 27, 2023; **Published:** November 13, 2023

***Corresponding author:** K Ramalingam, Mediclone Biotech Research Centre, Chennai-48, Tamil Nadu, India

Keywords: Carcinogenesis risk; Mesodermal; Philadelphia chromosomes; anti- apoptotic signals; Full-fledged Malignancy

Abbreviations: PK: Protein Kinase; PGF: Polypeptide Growth Factors; EGF: Epidermal Growth Factor; IGF: Insulin-like Growth Factor; ER: Estrogen; PR: Progesterone

Introduction

The transformation of a normal cell into a malignant cancer cell needs multifarious inducing risk factors. Cancer is a multifactorial disease and depends upon the nature of the environment, ethnicity of a population and their genomic profiles etc. The initiation of carcinogenesis risk involves the interactions of two or more prognostic factors viz., carcinogenic chemicals present in the cigarette smoke, alcohol, industrial pollutants, the dietary abnormalities, exposure to radiations, oncogenic virus as well as chronic infections by bacteria, viruses and internal parasites, mechanical injury or thermal trauma, genetic predisposition, aging debility, immune suppression, or onset of immune surveillance debility etc. Recent investigations have attributed the hormonal induction as a cause to reproductive or gynecologic cancers. Cancer can arise in any organ of the body, irrespective of their differentiation from ectodermal, mesodermal, and endodermal origin.

In the normal development of an individual after birth, billions of cells undergo division to attain growth. These normal divisions are subjected to a feedback regulation by which the tissues receive signals and stop growing after differentiation. When the tissues undergo any injury through either mechanical or biological by infections, they undergo dedifferentiation and redifferentiation and thus regenerate the damaged part of the tissue [1]. In this context, all tissues have stem cells (10%-20%) which are endowed with the capacity for proliferation as well as for differentiation. In this way development also attains a predetermined size. The metabolic machinery of these vital organs turns the wheels of life by synthesizing different kinds of proteins in their cells. According to the details of Human Genome project about 30000 fundamental genes are involved to synthesize about 60000 proteins [2]. In the earlier periods the differentiation or origin of cancer has been less well understood and remained as an enigmatic phenomenon.

In this era, the incidence of cancer and its death rate was found to be more in all European countries, USA and in all developing countries. Cancer was found a leading cause of death in Western societies. In USA cancer represented the second leading killer diseases and it cause 215 cancer deaths per 100,000 people in 1991 and following four – lung, colorectal, breast, and prostate have caused the maximum deaths among them. Moreover 16.9 million alive Americans were with lethal invasive cancer as documented in 2019 and 1.9 million new cancer cases are expected to be diagnosed in 2021 [3]. Consequent to the declaration in 1970s of war on cancer the various causative / factors agents have been investigated and the research on epidemiology has revealed that 85 percent of all cancers are caused predominantly by environmental factors. The demographic studies strengthened the above inference which revealed that some ethnic populations which are free from cancer in their natives and vulnerable to develop the cancer when they immigrated to United States. Thus, it is tenable to agree that the incidence of cancer could be due to the residential environment than that of the country/ environment of the ancestry of the same population.

The various environmental agents that are carcinogenic include different categories. Viz.,

The various pesticides.

i. Fertilizer chemicals.

ii. Hormonal preparations to enhance agricultural and livestock productivity.

iii. Exposure to harmful radiations such as radon's, X- rays

iv. Industrial pollutants in water and soil.

v. Chemicals released to air from industries.

vi. Prevalence of oncogenic viruses in the environment.

vii. Exposure to pathogenic parasitic infections and subjecting to chronic inflammation (Schistosoma haematobium).

viii. Oxidative stress and subjecting chronically to the stress and free radicals (ROS & RNA) injury of the tissue.

ix. Continuous traumatic stress.

x. Inappropriate drugs and their intake.

xi. Excessive use of antibiotics.

xii. Excessive and abnormal stresses like Hypertensions, sleeplessness, workaholic behaviour, depression etc.

xiii. Chronic and perennial diseases and

xiv. Aging of body cells.

Ramalingam [4] has categorized the various exogenous and endogenous risk factors for cancer origin (Figure 1). In the light of the observations in different geographical regions and their genomic profiles, the molecular basis of the disease has been elucidated for the malignant transformation. In the modern perception of environmental rigours, and the lifestyle changes in individuals the sequence of cellular changes and events delineate the concept that the malignant cell transformation in both structure and function undergo 360° circle to accomplish the above with sequel changes both in-vivo and ex-vivo of the cell. In the process of carcinogenesis, the basic molecular event which remains as the bottom line is the mutational changes in the orderly sequences of nuclear genome. Recent studies [5] have also brought to light the role of mutational changes in the mitochondrial genome and added more insights to the understanding of cancer biology and cancer disease. In the transformation of normal cell into a malignant one, the initial events accumulation of the mutation and / or the changes in the cells in- vivo regarding the transcripts and the translatory proteins, enzymes, growth hormones which trigger the anti-apoptosis in these cells represent the half circle of 180°.

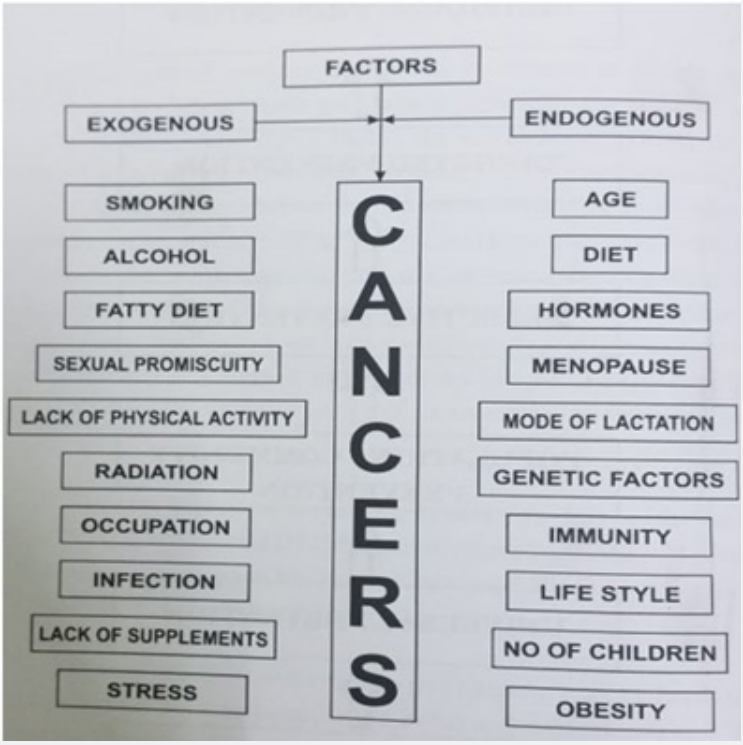

Figure 1: The exogenous and endogenous factors responsible for cancer.

How to cite this article: K Ramalingam, Babu K. Cancer Cell Attains Functional Malignancy at 360° Circle. Canc Therapy & Oncol Int J. 2023; 25(3): 556165. DOI: 10.19080/CTOIJ.2023.25.556165

The main phenotypic derangements in the malignant cancer cells include basically.

i. Alterations in the cellular membranes [6]

ii. Alterations in the levels of enzymes especially the enzymes involved in nucleic acid synthesis and metabolism.

iii. At the genetic level the appearance of inappropriate gene products e.g., Placental hormones and foetal antigens are not present in normal cells.

iv. Expression of abnormal genetic information

v. Gain or loss of chromosomal materials e.g., Philadelphia chromosomes, (non-Hodgkins's lymphoma, ALL and cML)

vi. Derepression of oncofoetal genes which are present but remain silent in normal cells.

vii. Alterations in the post transcriptional processing of critical cellular macromolecules.

viii. The functional malignancy of a cancer cell necessitates the following changes in ex-vivo.

ix. The expression of tumour specific surface antigens

x. The formation of stroma around the cancer cells groups with several matrix proteins

xi. Formation of absorptive areas viz., the "caveolae" for the efficient intake of extraneous metabolites like sugar, glutathione, glutamine, free fatty acids of n6 category etc.

xii. Expression of hormone binding external surface receptors. e.g., Estrogen (ER), Progesterone (PR), Her 2neu etc.,

Most of the characteristic oncoproteins are synthesized by the cancer cell itself. Accomplishment of all the above-mentioned cancer characteristics confer the malignant status of a cancer cell. There are six alterations that are essential for the malignancy transformation from benign condition.

i. Self-sufficiency in growth signals,

ii. Insensitivity to antigrowth signals,

iii. Limitless replicative potential,

iv. Ability to evade apoptosis,

v. Angiogenesis, and

vi. Ability to invade the tissues and metastasize.

All the above-mentioned diagnostic characteristics of structural and functional phenotypes of malignant cancer cells have been delineated in the reviews of Hanagan and Weinberg [7]. However, the proliferation and growth of these cancer cells needs several other mechanisms at their primary site. Viz.

i. Various growth factors for the continuous growth of cancer mass include polypeptide growth factors (PGF), epidermal growth factor (EGF), insulin-like growth factor (IGF), platelet derived growth factor (PDGF) etc.,

ii. For cancer cell energetics anaerobic fermentation provides the synthesis of lactic acid and the acidic milieu for cell survival. In this context Wiesenthal and Ruddon [8] have reported that human leukemic cells and Burkitt's lymphoma cells synthesize acidic nuclear proteins is of interest to mention.

iii. The aerobic respiration in cancer cells which is taking place alongside anaerobic respiration is involved in the synthesis of macromolecules and such organelle as centrosomes for favouring the cell divisions.

iv. When the cancer cell (tumour) mass reaches the maximum threshold size, their migration from the primary site to distant sites (i.e., in the third stage) to the axillary lymph nodes and contiguous regions is favoured by matrix degradation enzymes (Proteinases, MMPases).

v. The invasion of malignant cancer cells from their site of origin represents the critical stage of metastasis. It also prompts the development/ process of Neo- Angiogenesis. Several angiogenic factors are synthesized by the primary cancer cells to pave way for the intravasation of the metastatic cells and to the invasion to distant organs for the establishment of secondary cancer mass are VEGF, Thrombospondin. The malignancy in the cancer cells also evade the growth suppression by the host immuno-surveillance by suppressing such genes as Rb, TP53 and TGF beta etc. The mutations in the e-cadherin genes in cancer cells promote the contact-guidance and loss of contact inhibition mechanisms in cell membrane. Thus, the malignant cancer cells resist cell death via increased anti- apoptotic signals and decreased pro-apoptotic pathways.

The replicative immortality of malignant cancer cells becomes possible by increased telomerase activity and c-Myc and Max gene functions. Tumour microenvironment characterized with acidosis due to Warburg effect. Though acidosis is cytotoxic and reduces cancer proliferation, acidosis facilitates cancer cell invasion by the degradation of extra cellular matrix. Towards this the excess bile acids deoxycholic and chemo deoxy cholic acid upregulate the c-Myx gene c-Myc prtoteins are of interest to note [9]. Tumour has obligatorily evolved to adopt in acidosis environment as Darwinian concept [10]. The genomic mutations that initiate carcinogenesis involve an inductive interaction mechanism viz, signal transduction in which a molecular signal is perceived by the cancer cell. The molecular signals act as a ligand for the transmembrane receptor of the same. The extra cellular ligand binding domain causes a conformational change in the cytoplasmic domain and stimulates the activity of an enzyme cascade viz, protein kinase (PK). Signal transducing biomolecules include hormones, growth factors,

How to cite this article: K Ramalingam, Babu K. Cancer Cell Attains Functional Malignancy at 360° Circle. Canc Therapy & Oncol Int J. 2023; 25(3): 556165. DOI: 10.19080/CTOIJ.2023.25.556165

second messengers, Phospholipids, and protein kinase cascade etc., For the uncontrolled divisions and growth of the mutated cancer cells operated by the oncogenes, the signal transduction is awfully crucial and paramount [11]. The cancer cell thus attains its full-fledged malignancy both in structure and functions through various infrastructures and takes a circuitous route at 360° both at in-vivo and ex-vivo ambience (Figure 2).

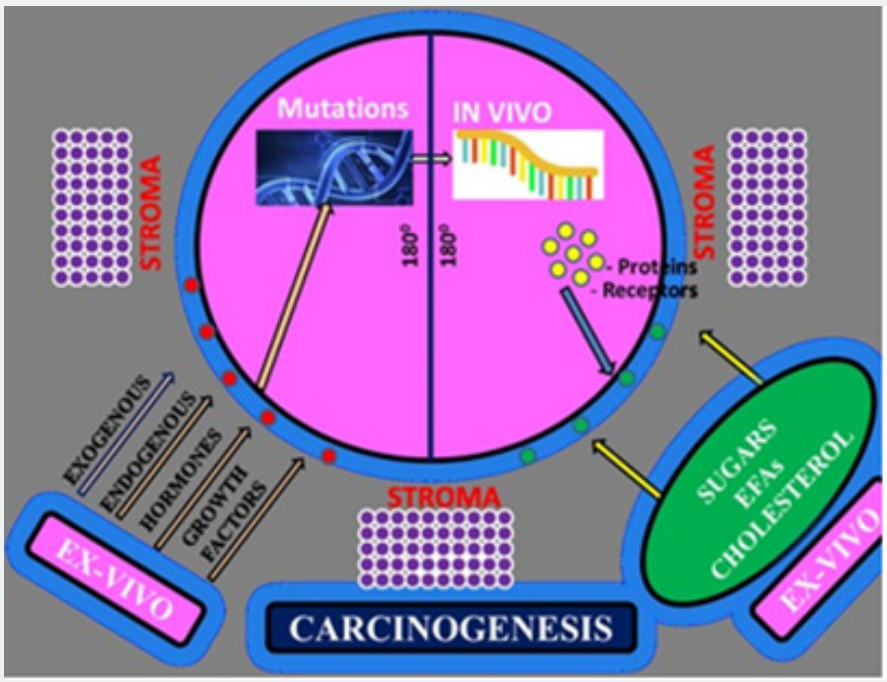

Figure 2: 360° of both at in-vivo and ex-vivo ambience to attain the malignancy in cells.

References

1. Guo Y, Wu W, Yang X, Fu X (2022) Dedifferentiation and in vivo reprogramming of committed cells in wound repair (Review). Molecular Medicine Reports 26(6): 369.
2. (2001) The International Human Genome Mapping Consortium. A physical map of the human genome. Nature 409: 934-941.
3. (2021) Cancer facts and figures, 2021 American Cancer Society.
4. Ramlingam K (2018 & 2019) Prudent proxies to prevent cancer, Natural elixirs- wise alternatives 2(5).
5. Zong WX, Rabinowitz JD, White E (2016) Mitochondria and Cancer. Molecular cell 61(5): 667-676.
6. Mitchison JM (1961) Biological Units: The Cell, Biochemistry, physiology, morphology. vol. 4 and vol. 5, Specialized Cells. Jean Brachet and Alfred E. Mirsky, Eds. Academic Press, New York. vol. 4, 1960. xv + 511 pp. vol. 5, 1961. xv + 597 pp. $20.Science 134: 324-324.
7. Hanahan D, Weinberg RA (2000) The hallmarks of cancer. Cell 100(1): 57-70.
8. Weisenthal LM, Ruddon RW (1972) Characterization of human leukemia and Burkitt lymphoma cells by their acidic nuclear protein profiles. Cancer Res 32(5): 1009-1017.
9. Wang X, Sun L, Wang X, Kang H, Ma X, et al. (2017) Acidified bile acids enhance tumor progression and telomerase activity of gastric cancer in mice dependent on c-Myc expression. Cancer Med 6(4): 788-797.
10. Bourguignon LY, Singleton PA, Diedrich F, Stern R, Gilad E (2004) CD44 interaction with Na+-H+ exchanger (NHE1) creates acidic microenvironments leading to hyaluronidase-2 and cathepsin B activation and breast tumor cell invasion. J Biol Chem 279(26): 26991-27007.
11. Balinsky BI (1970) An Introduction to Embryology. Third (3rd Edition), WB Saunders Company.

How to cite this article: K Ramalingam, Babu K. Cancer Cell Attains Functional Malignancy at 360° Circle. Canc Therapy & Oncol Int J. 2023; 25(3): 556165. DOI: 10.19080/CTOIJ.2023.25.556165

DOI: 10.19080/CTOIJ.2023.25.556165

How to cite this article: K Ramalingam, Babu K. Cancer Cell Attains Functional Malignancy at 360° Circle. Canc Therapy & Oncol Int J. 2023; 25(3): 556165. DOI: 10.19080/CTOIJ.2023.25.556165