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Plasticity of Tumor Suppressor Functionality of p53 Includes Potential Carcinogenesis in Terms of Subsequent Progression of the Malignant Transformation Event

Agius LM*

Department of Pathology, Mater Dei Hospital, TAL-QROQQ, University Of Malta Medical School, Msida, Malta, Europe

***Corresponding author:** 27 "BALLARAT" Guzeppe Caruana Street, Tal-Virtu, Rabat, Rbt0, Department Of Pathology, Mater Dei Hospital, TAL-QROQQ, University Of Malta Medical School, Msida, Malta Europe, Tel: 356-21451752; E-mail: lawrence.agius@um.edu.mt

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Abstract

Provoking plasticity of response of p53 involves mutations of the p53 gene within the further contextual accumulation of p53 protein within the cell cytoplasm. Activation of wild-type p53 gene and protein includes various post-translational modifications including specific phosphorylation and mutability performance of the core DNA binding domain in particular. Rigorous characterization and re-characterization of the essential accumulation of mutant p53 within the cytoplasm is itself a characterized reformulation of the essential transformation step per se and includes the dynamics of DNA damage repair that indicates malignant transformation a strict attribute of the initial DNA damage as structural dynamics of subsequent progression of potential carcinogenesis.

Introduction

Within the complex functioning of p53, both in normal cells and in cancer cells, there evolves a rich interactivity that constitutes the guarding of the genomic integrity or the potential progression of carcinogenesis respectively. In such manner, the p53 has initially been considered an oncogene, but subsequently overwhelming evidence has indicated its roles as a suppressor tumor gene and protein in terms of "guardian of the genome". Increasing evidence implicates micro-RNAs in carcinogenesis by modulating p53 pathways [1]. 4-Hydroxy-2-nonenal induces cyclooxygenase-2 over expression leading to inhibition of a proteasome subunit and subsequent accumulation of p53 and ubiquitinated proteins [2]. Protein regulator of cytokinesis 1 is oncogenic in gastric carcinogenesis and implicates p53-dependent action of piperlongumine [3]. Tripartite motif containing 47 inhibits p53 in non-small cell lung carcinoma and facilitates NF-kappa B-induced tumor cell proliferation and spread [4], p53 related carcinogenesis may develop in Human Papilloma Virus positive patients in India [5].

Operability of p53

P53 has been considered to delay or arrest cell cycle progression and thus give time for repair of the DNA damage arising from either endogenous metabolites such as reactive oxygen species or from exogenous damage such as ionizing radiation or ultraviolet radiation. Regucalcin suppresses transcription signaling including Ras, Akt, MAP kinase and SAPK/JNK and elevates p53 and Rb in cancer [6]. It is with view of a systemic interplay that the levels and degree of activation of p53 protein that the intricate control of homeostatic mechanisms comes to also play an important role also in carcinogenesis.

Such roles of p53 indicate in a general way the dysfunctional ties of tumor suppressor proteins and genes in the evolutionary adaptation of human cells to the progressive accumulation and action of a large series of potential carcinogens that initially are present often in the extracellular microenvironment and subsequently enter the cellular pathways. Up regulation of mortal in contributes to cancer cell stem less and inactivates p53 protein suppression, deregulates apoptosis and activates EMT signaling [7]. Acute and chronic inflammation of the mucosa down regulates p53 and EPSIN 3 with subsequent apoptosis resistance, a hallmark of malignant cells [8].

Initial DNA Damage

The degree of damage to the cellular DNA is an essential parameter of control in inducing the manner of suppressor tumor function of p53. It is clear that when the damage is mild, the predominant action is arrest of cell cycling, whereas severe DNA damage evokes apoptosis and senescence of host cells. It is further to such considerations that the evolution of p53 as a tumor suppressor is directed towards integral genomic stability in terms specifically of the nature of individual genetic lesions that operate within limits of the single and double strand breaks of the DNA structure.

Such constitutive attributes of normal p53 alternate, it would appear, within the range of otherwise dysfunctional ties of apoptosis or senescence of cells that participate as non-progression systems in cellular adaptation and DNA stabilities. Long interacting noncoding RNAs are involved in tumor genesis and tumor spread [9]. The provocative pathways of p53 pathway control center particularly on the MDM2/MDM4 systems of ubiquitination and degradation of cytoplasmic p53 on the one hand, and on mutations of the p53 gene on the other. Hence, p53 comes to assume an active mode of response and of function/dysfunction analogous to the system pathways that integrate evolutionary adaptation of the host cell in general.

p53 Response Dimensions

The two transactivation domains, the DNA binding domain and the oligomerization domain towards the C-terminus include the responsive elements of a protein molecule that is intimately concerned

with the activation of sets of genes in the parent DNA molecule. It is further to such considerations that also involved is the shuttling in and out of the nucleus of a p53 protein molecule that is controlled in its own right by nuclear localizing and nuclear export signals. The performance of p53 molecular suppressive functions are directed primarily to the redox status of the cells in terms of oxidative stress and of degrees of DNA damage that accumulate throughout genomes as integral units. Analogously, Wilms' tumor gene 1 plays both the role of tumor suppressor gene and also of an oncogene depending on the cellular context [10]; it deregulates cell cycle proteins and down regulates PI3K/AKT, with additional activation of caspase-3 and increased Bax/Bcl2 ratio and p53 [10].

The essential presence of initial and progressive carcinogenic pathways within the cell dictate the precise functioning of p53 and hence determine whether the cell cycling is arrested or whether the cell undergoes apoptosis on the one hand or else whether the roles fulfilled by p53 gene prove progressive in terms of oncogenesis and perhaps also of further malignant transformation. In such terms, the tumor suppressor functions of p53 are potentially transformed to oncogenesis within the milieu of cancer cells.

Duality of Carcinogenesis and DNA Repair

MDM4 plays an important role in carcinogenesis and interacts with p53 [11]. Principles of action of a prime tumor suppressor gene and protein as p53 illustrate the dual and ambiguous roles of a guardian of the cellular genome in homeostatic control of normal cells to the progression of malignant transformation and progression of carcinogenesis within initially transformed malignant cells. The cytidine deaminase APOBEC3B underlies the genetic heterogeneity of many tumors including cervical cancer through the TEAD transcription factor and may broadly be relevant to virus-associated carcinogenesis as observed in many cancers [12].

Strict characterizations of the action of normal wild-type and of mutant p53 protein indicate the various roles of tumor suppressor action in the evolutionary history of malignant transformation of host cells per se. The ubiquitin binding protein SHAPRIN correlates with poor prognosis in breast cancer patients and that are specifically p53 wild-type positive [13]. The further roles of the p53 secretome within the external microenvironment allow for the possible emergence of such phenomena as loss of cell-cell adhesion, the development of invasive attributes and also the establishment of angiogenesis of carcinogenic progression.

Cooperative Modes of Pathway Action

Dimensions of cooperativity with pro-apoptosis and with other p53 family members of p53 pathways such as p63 and p73 provoke an oscillatory pathway system that evolves within the dictating dimensions of the characterized damage of the parent DNA, particularly also in terms of the presence of initial but essential establishment of malignant transformational operants. p53 is important in somatic cell reprogramming and mutant p53 exerts a gain of function role in increased reprogramming efficiency; microRNA expression often depends on p53 status of the cells and implicate pluripotency of stem cells [14].

Plasticity of p53 Action

Agency formulation of p53 therefore constitutes the performance of discriminatory factors that in turn strictly characterize formal dimensions of p53 in terms of the tumor suppressive function in particular. Unique patterns of histopathology feature and p53 expression categories 2 distinct pathways of vulvar carcinogenesis, affecting cases of VIN and vulvar squamous cell carcinoma [15]. The range of applicability of tumor suppressor genes operates within the milieu dimensions of damaged DNA, Pro- and anti-apoptosis are regulated within confines of the strict malignant transformation pathways and therefore are profiles of inducible action either in terms of normal cells or as constitutive carcinogenic progression.

The involvement of glutathione and dependency of p53 status on the modulation of treatment efficacy mediated by GSH is important in analyzing degree of sensitivity to chemotherapy in colorectal and breast cancer cells [16] in inducing apoptosis.

Mutability of p53 as is observed in nearly 60 percent of tumors in general allows for the emergence of performance dynamics that either provoke the settings for potential DNA repair on the one hand, the induction of cell death or senescence, or on the other hand the enhancement of carcinogenesis as a series of progressive steps of further integral malignant transformation and spread of the cancer cells. PICT-1, a nucleolar protein that counteracts HPV-induced p53 degradation, may contribute to inactivation of p53 when present in aberrant form [17].

Mutant Forms of p53 Plastic Response

DNA damage is hence an operative dysfunctionality that characterizes the role of tumor suppressors in terms of dimensional re-structuring of the parent DNA in terms also of mutant p53 operability. Constitutive integrity of the cellular genome is hence a characterization of potential carcinogenesis and of the essential progressive nature of malignant transformation and oncogenesis. Distribution of mutant p53 is a maturation step that dysfunctionally permits a range of plastic responses to the DNA damage per se.

Cytoplasmic inactivation of tumor suppressive function includes the mitochondrial responses within the schemes of pro-apoptosis and which allows for a variability of pathway interactivities within performance platforms of carcinogenesis per se. The various roles of p53 action are therefore plastic responses within the system operability of possible carcinogenic progression.

Over expression of p53 is associated with poor prognosis in urothelial carcinoma patients and the RING finger protein 128 is implicated in p53-induced apoptosis forming a negative feedback loop [18].

Essential accumulation of cytoplasmic mutant p53 is therefore a profile function of the integral genomic damage within further cooperative disability for repair of the DNA structure as further evidenced in pathway targeting events within the cytoplasm of cancer cells. Reprimo is a p53-induced tumor suppressor gene and its aberrant DNA methylation correlates with carcinogenesis [19]. Duality of response to DNA damage is further propagated within the ability of p53 to operate as binding agents to the parent DNA molecule.

Conclusion

Performance dimensions of reconstitutive repair of the DNA damage structure are homeostatic agency formulation of the dimensions of potential progression of carcinogenesis within the further progressive interactivities of accumulating mutant p53 within the cell cytoplasm. A latency period exists between loss of PAX2, mutation of p53 and tumorigenesis in cases of fallopian tube -derived high-grade serous ovarian cancer; PAX2 is a direct transcriptional target activated by wild-type p53, whereas mutant p53 suppresses PAX2 transcription under experimental conditions [20]. In such terms, further progression of cancer is beset by the potential plasticity of p53 action as both a tumor suppressor gene and as re-characterized carcinogenic steps in malignant transformation. Re-formulation of tumor suppressor function is therefore profile confirmation within systems of accumulation of mutant p53 protein within the cytoplasm, as further attested by dimensions of a damage of DNA structure.

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