

Oscillatory release cycles of permissive dimensions in carcinogenesis

Abstract

Multiple proteomic pathways synergize systems and lead to the de-stabilization of the genome. Dimensions for permissive modulation and plasticity of release of gene mutagenicity are accompanying parameters that allow for potential involvement in carcinogenesis and spread. Indeed, genesis of the malignant tumor is further exemplified by confirmatory profiles of receptivity and response. The combinatory systems of gene mutability include the capacity for quantitative complementarity and for further characterization of permissiveness, as further dictated by the multi-profile genomic performance of cyclic oscillations. Increased parametric response in growth and spread of individual neoplasms is a generalized response in the targeting of cells of mature and less mature type. System profile inclusion is the realization of phenotypic traits in consequence to dimensional inclusion and of instability of inclusion of multiple lesions in the cellular genome.

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Introduction

Circadian rhythms modulate cell division and metabolism in cancer and may potentiate a tumor-suppressive role in lung tumorigenesis.¹ Circadian rhythms are oscillations of multiple biologic processes directed by endogenous clocks and may be functionally disrupted in various cancers such as breast, ovarian, endometrial, prostate and hematologic malignancies.² Silencing expression of the Clock gene in glioma cells down regulates c-Myc and Cyclin B1 and up regulates p53 and may play a significant role in inhibiting apoptosis by attenuating pro-apoptotic signaling.³ O6-Methylguanine transferase constitutes a mechanism of transfer of alkyl groups to the acceptor cysteine in a manner that exemplifies the epigenesis of a series of protective mechanisms toward the repair of DNA-adduct lesions in carcinogenesis. The mechanistic removal of methyl groups interacts with the methylation of the promoter of O6-methylguanine transferase that renders the transferase inactive. The spectrum of activation of ethyl guanine is included within oscillatory cycles of activation and de-activation that affirms epigenesis of profile mechanisms even in the absence of self-progressing lesions in the cellular DNA.

Oscillatory regimes result from competition for shared glucose resources between cancer cells and immune cells; this may account for much of the dynamics of the immune system in response to malignant cells.⁴ Complex integration in a micro-environment emphasizes the dynamics of alkyl insertion in terms of binding and also potential enzymatic potentiation in patients treated with anti-cancer chemotherapy resistance. Duplex mechanisms in DNA lesion repair is an essential transfer within the further de-construction of methyl guanine transferase activity. Histone deacetylase inhibitor phenyl butyrate improves radiation-induced injury by modulating DNA repair and wound healing genes.⁵

Dimensions of conformation

Conformation is inclusive in systems that link chemoresistance to various phases of ongoing carcinogenesis. Oscillations can arise in a model of competition between normal and genetically damaged abnormal stem cells as suggested in chronic myelogenous leukemia.⁶ Cell cycle dependent oscillatory expression of estrogen receptor-

alpha implicates Pol II elongation with malignant tumor genesis.⁷ The dynamics of transformation in carcinogenesis are analogous to the emergence of chemotherapeutic agent resistance and within the frameworks of ongoing progression for transformation. It is hypothesized that at least 50% of breast cancer risk is associated with germ cell damage by cosmic radiation as a priming event leading to a higher risk for breast carcinogenesis.⁸ Aging involves progressive decline in the stability, continuity and synchronization of multi-frequency oscillations with the potential promotion of temporally disorganized states and carcinogenesis.⁹

Microenvironments and carcinogenesis

A strict concept of molecular transfer is profile system of regulation within various pathways as found in terms of ongoing biochemical events within cells. Simple models of mutations in carcinogenesis may include time delay and diffusion with consequent destabilization in cases of increasing delay.¹⁰ The control of shifts of molecules as carried out by biochemical activity is illustrated by methyl guanine transfer of alkyl groups that allow a permissive microenvironment to evolve in molecular pathologic processes.

Molecular lesions

Inclusive phenomena as molecular lesions are direct precursors for progression of pathways in carcinogenesis and also as putative repair mechanics as further exemplified by chronic pathology. Over-expression of translation initiation factor eIF4E within context of stem/progenitor cell population expansion may initiate malignant transformation in terms of evasion of DNA damage checkpoints activated by oncogenic stimuli.¹¹

Ion channels and oscillatory mechanisms

Ca²⁺ signaling pathways are altered in cancer cells and may be modulated to decrease cancer cell proliferation and to promote apoptosis.¹² Oscillatory currents may be generated by influxes of divalent cations to maintain Ca²⁺ oscillations in ras-transformed NIH/3T3 cells.¹³ Cellular calcium entry triggers oscillatory calcium-induced calcium release from intracellular sources and cytoskeletal remodeling by actin stress fiber depolymerisation and active Na

(+)/H (+) exchanger with consequent intracellular alkalosis and cell swelling.¹⁴ Oscillations initiated randomly from single cells spread over neighboring cells and may implicate an advancing Ca^{2+} wave.¹⁵ Spontaneously oscillating K^+ channel activity develops in malignant transforming cells in alkali-transformed Madin-Darby canine kidney cells.¹⁶

End-pathway

The end-pathway influence of accumulating oxygen free radicals is characterized by further confirmation of template biology as indeed projected in diverse disease products of potential self-amplifying nature. Coordinate transcriptional control of replication-dependent human H4, H3 and H1 histone multi-gene families may be involved in dysregulation leading to heterogeneous aberrations in cell growth during carcinogenesis.¹⁷ The inclusive dimensions are extended and projected within a permissive release in mutagenesis and as further identifiable within the mechanisms controlling tumor growth and spread. Malignancy is a direct consequence of mitochondrial dysfunction, impaired microtubule polar oscillations and the generated electromagnetic field; mitochondria form boundary elements between biochemical-genetic and physical processes, with excitation of the coherent state far from thermodynamic equilibrium.¹⁸ Oscillatory degrees of tumorigenic attributes of release are a specific series of permissive transmutation that are well-exemplified by the dimensions of de-control and of transformation of pathway or network activities. Epidermal stem cells are functionally modulated by circadian oscillations and with successive clock wave these may regulate their proliferation or differentiation.¹⁹ Definition of the serial events as constitutive indices for further change includes the characterization of dual sets of parameters as indeed arising from dysfunctionality of DNA mutations.

Performance parameters

Performance characters of activity are indeed self-expression of the mutability of inherently synthetic dimensions of extending DNA and of repair mechanisms of genomic replication and distribution within daughter cells. The microtubular-microfilamentous structure conveys growth-regulatory input from the cell membrane to the nucleus and is implicated in carcinogenesis.²⁰ Proportion template inclusion in pathways of carcinogenesis mirrors closely the self-confirming processivity as viewed within the framework for further mutability. The Warburg effect may arise from convective disturbance in the cell and provide a biophysical defect in cancer initiation.²¹ Tumor recurrence is reflecting end-product of carcinogenesis as further promoted by the inclusive and quantifying doses of carcinogen release as increasingly conforming systems of template-induced replication of mutagenic systems for further progression.

Proportional identity confirmation is indeed a function of template replication and also of template genesis in the series of involved parameters of quantitative assimilation of endogenous carcinogens. Replacement of wild-type genes by mutated genes is further projected as an unstable genome and as the quantifying targets for carcinogenesis. Imperfect gene replication is supported by the transcription and translation machineries that allow the permissive establishment for further progressive change. The circadian clock controls cell proliferation and metabolism oxidative and genotoxic stress response, and DNA repair which are involved in carcinogenesis.²² A contrasting duality of DNA replication and of mutagenesis is profile modulation of the series of targeted mechanics as carcinogenesis and as dynamics of the pathologic growth and spread of the malignant cells. Malignant transformation is itself a strictly distinct attribute of mutagenesis in

a manner that conforms to the contrasting dimensions for further change. Fluctuations in the intracellular redox state during cell cycling could constitute a fundamental mechanism linking oxidative metabolic processes to cell cycle regulatory processes.²³

Non-immunogenicity is a cardinal promoter for increasing potentiality for genomic instability within cells undergoing carcinogenesis. Malignant transformation is inclusive dimension for a permissiveness that projects as further primer attributes for the bypass of lesions as carried out by polymerase activity. Circadian rhythms are oscillations of multiple biologic processes directed by endogenous clocks and may be functionally disrupted in various cancers such as breast, ovarian, endometrial, prostate and hematologic malignancies.² Repair as conforming quantitation is a potential mechanism in chemotherapeutic resistance as further evidenced by the proportion of growing malignant lesions that spread.

Variability in response and signaling

Variability of signaling and receptor response allows for dimensions of permissively complementing the establishment of genomic instability within specific parameters of quantitative and qualitative nature as dictated by systems of modulated phenotype. Dysfunction of mitochondria and disintegration of the cytoskeleton may have an impact in carcinogenesis and result in disturbed coherence of cellular electrically polar oscillations and in the generation of an electromagnetic field.²⁴ It is further to substantial increment in cellular metabolism and of degrees in modulated autonomy that carcinogenesis constitutes the release of prospective ligand binding and receptor dysfunctional response.^{25–28}

Concluding remarks

Considerable variability of incremental stimulation and of genomic instability includes the emergence of multifocal lesion creation that is included in the prospective characterization of indices of potential dual increment and response. Carcinogenesis is a system profile for directed genomic instability within defined terms of ongoing transformation as further complemented by the degree of quantifiable dimensions of receptivity and response to biologic agents such as growth factors, ligand binding and targeting, and a whole series of gene-defined responses. It is towards the creation of a plastic micro-environment that constitutive phenotype is modulated to implicate such genomic instability in terms of oscillatory performance of pathogenic delineation and characterization for multifocal lesion interactivity.

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Conflict of interest

Author declares that there is no conflict of interest.

References

1. Papagiannakopoulos T, Bauer MR, Davidson SM, et al. Circadian rhythm disruption promotes lung tumorigenesis. *Cell Metab.* 2016;24(2):324–331.
2. Rana S, Mahmood S. Circadian rhythm and its role in malignancy. *J Circadian Rhythms.* 2010;8:3.
3. Wang F, Li C, Yongluo, et al. The circadian gene clock plays an important role in cell apoptosis and the DNA damage response *in vitro*. *Techno Cancer Res Treat.* 2016;15(3):480–486.

4. Kareva I, Berezovskaya F. Cancer immunoediting: a process driven by metabolic competition as a predator-prey-shared resource type model. *J Theor Biol.* 2015;380:463–472.
5. Chung YL, Pui NN. Dynamics of wound healing signaling as a potential therapeutic target for radiation-induced tissue damage. *Wound Repair Regen.* 2015;23(2):278–286.
6. Drobnjak J, Fowler AC. A model of oscillatory blood cell counts in chronic myelogenous leukemia. *Bull Math Biol.* 2011;73(12):2983–3007.
7. Vantaggiato C, Tocchetti M, Cappelletti V, et al. Cell cycle dependent oscillatory expression of estrogen receptor-alpha links Pol II elongation to neoplastic transformation. *Proc Natl Acad Sci USA.* 2014;111(26):9561–9566.
8. Juckett DA, Rosenberg B. Time series analysis supporting the hypothesis that enhanced cosmic radiation during germ cell formation can increase breast cancer mortality in germ cell cohorts. *Int J Biometeorol.* 1997;40(4):206–211.
9. Belancio VP, Blask DE, Deininger P, et al. The aging clock and circadian control of metabolism and genome stability. *Front Genet.* 2015;5:455.
10. Piotrowska MJ, Forys U, Bodnar M, et al. A simple model of carcinogenic mutations with time delay and diffusion. *Math Biosci Eng.* 2013;10(3):861–872.
11. Avdulov S, Herrera J, Smith K, et al. eIF4E threshold levels differ in governing normal and neoplastic expansion of mammary stem and luminal progenitor cells. *Cancer Res.* 2015;75(4):687–697.
12. Parkash J, Asotra K. Calcium wave signaling in cancer cells. *Life Sci.* 2010;87(19–22):587–595.
13. Higashida H, Hoshi N, Hashii M, et al. Ba²⁺ current oscillation evoked by bradykinin in rad-transformed fibroblasts. *Biochem Biophys Res Commun.* 1991;178(2):713–717.
14. Furst J, Haller T, Chwatal S, et al. Simvastatin inhibits malignant transformation following expression of the Ha-ras oncogene in NIH 3T3 fibroblasts. *Cell Physiol Biochem.* 2002;12(1):19–30.
15. Wojnowski L, Hoyland J, Mason WT, et al. Cell transformation induces a cytoplasmic Ca²⁺ oscillator in Madin-Darby canine kidney cells. *Pflugers Arch.* 1994;426(1–2):89–94.
16. Schwab A, Westphale HJ, Woinowski L, et al. Spontaneously oscillating K⁺ channel activity in transformed Madin-Darby canine kidney cells. *J Clin Invest.* 1993;92(1):218–231.
17. Van Wijnen AJ, Owen TA, Holthuis J, et al. Coordination of protein-DNA interactions in the promoters of human H4, H3, and H1 histone genes during the cell cycle, tumorigenesis, and development. *J Cell Physiol.* 1991;148(1):174–89.
18. Pokorny J, Pokorny J, Kobilkova J. Postulates on electromagnetic activity in biological systems and cancer. *Integr Biol (Camb).* 2013;5(12):1439–1446.
19. Janice P, Toufighi K, Solanas G, et al. Human epidermal stem cell function is regulated by circadian oscillations. *Cell Stem Cell.* 2013;13(6):745–753.
20. Puck TT. Cyclic AMP, the microtubule-microfilament system, and cancer. *Proc Natl Acad Sci USA.* 1977;74(10):4491–4495.
21. Rietman EA, Friesen DE, Hahnfeldt P, et al. An integrated multidisciplinary model describing initiation of cancer and the Warburg hypothesis. *Theor Biol Med Model.* 2013;10:39.
22. Khapre RV, Samsa WE, Kondratov RV. Circadian regulation of cell cycle: molecular connections between raga and the circadian clock. *Ann Med.* 2010;42(6):404–415.
23. Menon SG, Goswami PC. A redox cycle within the cell cycle: ring in the old with the new. *Oncogene.* 2007;26(8):1101–1109.
24. Pokorny J. Biophysical cancer transformation pathway. *Electromagnet Biol Med.* 2009;28(2):105–123.
25. Rangarsjan N, Fox Z, Singh A, et al. Disorder, oscillatory dynamics and state switching: the role of c-Myc. *J Theor Biol.* 2016;386:105–114.
26. Lin LL, Huang HC, Juan HF. Circadian systems biology in Metazoa. *Brief Bioinform.* 2015;16(6):1008–1024.
27. Rana S, Munawar M, Shahid A, et al. Deregulated expression of circadian clock and clock-controlled cell cycle genes in chronic lymphocytic leukemia. *Mol Biol Rep.* 2014;41(1):95–103.
28. Becchetti A. Ion channels and transporters in cancer. 1. Ion channels and cell proliferation in cancer. *Am J Physiol Cell Physiol.* 2011;301(2):C255–C265.