



# Contrasting Dynamics of Apoptosis and of Cell Cycling in Carcinogenesis



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## Abstract

It is in terms of a cell cycle that potentially renders the dividing cell exquisitely sensitive to dynamics of an apoptosis program that the pre-set dimensions of acquisition of stem cell attributes further conform to dimensions of a potential malignant transformation step. The hallmark of carcinogenesis as genomic instability arises within a cyclic setting of whole susceptible and dividing cells that project as derived gene amplification and over-expression. Aurora kinases are central determinants in the contrast profiling of apoptosis and of cell cycling in specific dimensions of genomic instability. The further derived models of a malignant transformation are inductive and further realized in terms of the cell that inherently cycles and determines whole arrayed sets of susceptibility issues in evolving transformation.

## Introduction

The amplification and especially over-expression of the Aurora kinases effectively constitute an excellent model concept in the understanding of the malignant transformation of carcinogenesis in multiple organ oncogenesis. Multi-organ derivation of especially the metastasis phenomenon allow for the development of a spread process of establishment and progression of many tumor types. The inherent dimensions of metastatic neoplasms are paramount consideration in evolving tumor spread in a manner that allows for systemic dissemination of tumors as dictated by systems of attempted restitution of parameters in oncogenesis. CDKN2A drives carcinogenesis by inducing aneuploidy and cell cycle up-regulation [1].

## Aurora Kinases

The development of Aurora kinases as modeled systems of disruption of the cell cycle dynamics is exemplified by the inclusion of resistance to immune system action and for the emergence of parametric independence in tumor origin, establishment and progression. Bacillus Calmette-Guerin combined with Aurora-A inhibition may constitute a new intravesical modality treatment in preventing bladder carcinogenesis [2]. Aberrant cell cycle regulation of human embryonic stem cells is related to centrosome amplification with enhanced chromosomal instability [3]. SIX homeobox 3 acts as a tumor suppressor that directly represses the transcription of Aurora A and Aurora B and thus inhibits astrocytoma tumorigenesis [4].

The simple scheme for gene amplification and/or overexpression allows for permissive emergence of dynamic adaptation to such injury as aneuploidy, poly-polyploidy and

cell-cycle arrest, within the added inherent susceptibility of genomically unstable tumor cells to apoptotic cell death. Defects in resolving kinetochore-microtubule attachment errors during mitosis are linked to chromosome instability associated with carcinogenesis as well as resistance to cancer therapy [5]. The near-timed or consequent cascades in cell signaling realize significance in terms of the cell cycling check-points in further disrupting the integral dimensions of tumor cell evolution. It is further to the check-point disruptions that tumor cells evade apoptotic cascades of influence in attempted control/de-control of tumor cell turnover. Chromosome instability is due to a deficiency in cell division, including centrosomal amplification and cytokinesis failure and can result in aneuploidy [6]. The activity of Aurora A might be regulated by the ubiquitin-conjugating enzyme 2C that constitutes a key component in the ubiquitin proteasome system by partnering with the anaphase-promoting complex [7].

## Cell Turnover in Tumors

The significance of evolving turnover of tumor cells is characteristically a fundamental process for the evolutionary history of the genomic injury as the malignant transformation step progresses as established dys-homeostasis of the cell cycle dynamics. Translational up regulation of Aurora-A by hnRNP Q1 contributes to cell proliferation and carcinogenesis in colorectal cancer [8].

The clearly demarcated attributes of the dividing tumor cell are contradistinctive to the dimensions of homeostatically controlled parent cells that evolve as potentially projected

schemes for parametric modeling of whole populations and sub-populations of parenchymal or epithelial cells in multiple organs. Over expression of cyclin D2 in diploid cells strongly potentiates the ability to proliferate with increased DNA content despite the presence of functional p53; tetraploidization or genome doubling is prominent in tumorigenesis, primarily because cell division in polyploid cells is error-prone and produces aneuploid cells [9]. It is in terms of manipulative processing of contextual dimensions induced essentially by amplification and over-expression of Aurora kinases that the systemic cancerization of parent cells includes the acquisition of attributes central to stem cell evolution. Aurora B inhibition appears to have Janus face-like effects of antitumor mode of action versus induction of aneuploid progeny [10].

Translational modeling is a system reformulation of the cooperative dimensions of a neoplastic lesion that essentially competes for attributes of developmentally similar processes of evolution within the further systemic progression of lesion modulation by the malignant cells themselves. In realized inclusion phenomena of conditioned induction an essential parametric setting affords for neoplastic cells to integrally incorporate stem cell biologic traits.

The perusal for the emergence of biologic processes of induction arise as integral attributes of an amplified/overexpressing gene or genes within the resolving dimensions for further progression of the cell cycling in malignant transformation. The dysregulation of cell cycle kinases plays a crucial role in carcinogenesis and the expression of various kinases is attributable to aggressive tumor growth and an unfavorable prognosis in cancer patients [11].

### Patterns of Distribution

The distributional patterns of cell cycling are contrasting phenomena to the development of progressive apoptotic death arrays of behavior of systems of resolution as malignant transformation. In such manner, the cell cycle is indeed not only an integral single unit of behavior of dividing cells but also a system of inducing dysfunctionality in the potential series of arrayed evolution as stem cell dynamics. Aurora-A mediated histone H3 phosphorylation of threonine 118 controls condensin 1 and cohesion occupancy in mitosis and hence is essential for effective chromosome segregation [12]. The whole disruptive influence of a genomically instability is further evidence in the potential array for further progression as metastatic tumor cells that are inherently cycling forms of cell transformation.

### Potential Induction

Potential forms of abnormal induction include aneuploidy that is provoking stimulus in apoptosis of cells that are systems of inherent instability related specifically to pathologic cell cycling. Aurora kinases and cell cycle arrest or delay are characterized models for the incipient potential induction of a series of derived attributes in acquisition for system profile establishment as specifically projected by the malignant transformation step.

Over-expression of Aurora B may contribute to tumorigenesis not only by inducing chromosomal instability by also by suppressing the functioning cell cycle inhibitor p21[Cip1] [13]. Inclusive development of the G2/M phase is specialized and concurrent dimensions in a tumorigenesis that is inherently progressive. It is in terms of such inherent progressiveness of the cell cycling that malignant cells acquire systems of immortalization in contexts of the malignant transformation event. It is included cell cycling events and especially within the system profiles of susceptible biology of such cycling cells that malignant induction emerges as progression of the malignant transformation of cells [14].

### Re-Modeling

The cells that divide and undergo malignant change are cells that are re-modeled as systems of a progression reformulation that is in part or largely controlled by Aurora kinases. In such terms, Aurora kinases are targeted resolving parameters in the acquisition of an aberrant cell cycling within its own right and as further implicated in contexts of evolving dimensions of an abnormal cell cycling [15]. It is in terms of such progression of disrupted check-points in cell division that amplified Aurora kinase activity proves to be system projection of self-progression in a manner akin to positive-feedback non-resolution. Phosphorylation of multifunctional nucleolar protein nucleophosmin by aurora kinase B is crucial for mitotic progression [16].

### Apoptosis

Apoptosis attributes belie a close dynamic relation to the cell cycling process in the acquisition of abnormal attributes in cell transformation [17]. It is this realization that apoptosis is both parent and derivative dysfunctionality of cell cycling in mode preference for progression of the malignant transformation step.

Inclusive parameters arise directly from amplified gene expression as actively constituted by the phenomenon of contrasting signaling delivered to a susceptible and dividing cell that constitutes the attributed derivation of multi-potential and inducing formulas for biologic progression. It is in terms of apoptosis that the confined attributes of potential cell death include the acquisition of gene expression that is amplified and transforming.

Hence, in terms of the evolving inclusion of potential apoptosis that tumor cells both constitute and further evolve as cells that cycle and further provide the delivery of system pathways that evade immune systems and that are particularly transforming as aneuploidy and genomic instability. The negative interplay between Aurora A/B and BRCA1/2 controls cancer cell growth and tumorigenesis via distinct regulation of cell cycle progression, cytokinesis and tetraploidy [18].

### Concluding Remarks

The alternative pathways of apoptosis and cell cycling are re-characterizations of an integral phenomenon of transforming steps within contexts for transformation in terms of highly

inductive phenomena as well-demarcated by the emergence of genomic instability.

Genomic instability is a phenomenon of contractual re-programming that evolves in the context of such sharply contrasted dimensions of apoptosis and cell cycling. It is the further confirmatory development of pathway progression that cell cycling is abnormal model for a parent projection as determined by amplified gene expression and as system profile for schematic outlines in cell transformation. It is within the further determination of cell cycling that the origin of the malignant transformation step both constitutes and further evolves as system contrast with a highly conserved evolutionary model of apoptosis arising directly from abnormal dynamics of the susceptible cycling cells.

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