



# Dimensions of A Distinct Phase of Pre-Carcinogenesis That Promote Subsequent Progression of the Epithelial-Mesenchymal Transition



Lawrence M Agius\*

Department of Pathology, Mater Dei Hospital, Malta

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\*Correspondence Address: Lawrence M Agius, Department of Pathology, Mater Dei Hospital, TAL-QROQQ, University of Malta medical school, Msida, Malta, Europe, Tel: 356-21451752; Email: lawrence.agius@um.edu.mt

## Abstract

Dimensions of protein-protein interactivity are identity profiles for the inclusion of a distinct pre-carcinogenesis that strictly proposes the contextual reproducibility of ongoing dimensions for further change leading to malignant transformation. Indeed, context dimensionality is the proponent system formulation of incremental stabilization of indices of progression from pre-carcinogenesis to carcinogenesis. The epithelial-mesenchymal transition is model system identification of a series of isoforms within both the canonical and non-canonical WNT pathways that conform to the progression of proliferation and of cell-cycling as indicated by the emergence of embryogenic dimensions of malignant transformation.

## Introduction

The duality of the contrasting systems of canonical and non-canonical WNT pathways allows for a system-based regulatory complex controlling in particular the onset and progression of carcinogenesis. The natural product Jatrophone inhibits Wnt/beta-catenin signaling and suppresses proliferation and the epithelial-mesenchymal transition in human triple-negative breast carcinoma [1]. Aberrant activation of the Hedgehog and wntless-Int1 (Wnt) pathways contributes to the genesis and progression of severe categories of cancer, and also epigenetic regulation of these pathways impacts tumor formation [2]. The WNT ligands are complexed entities that are further antagonized by secretory forms of the WNT components. E-cadherin expression dysregulation leads mainly to invasiveness reduction, growth inhibition, apoptosis, cell cycle arrest and differentiation; it sequesters beta-catenin from its binding to Lymphoid enhancer factor/T cell factor and thus inhibits proliferation genes by the Wnt signaling pathway [3]. Indeed, negative-feedback regulation of the WNT canonical signaling pathway by the non-canonical pathways allows for the representational reconstitution of mechanistic pathway control with an important series of implications for carcinogenetic predisposition.

Factors derived from conditioned medium of adipose-derived mesenchymal cells and secreted frizzled-related protein 4 significantly suppressed tumor cell viability and enhanced apoptosis through inhibition of canonical Wnt signaling [4]. Substantial scaffold support for the Frizzled receptors allows for interactivities involving in particular direct protein-protein moieties. The system structural dynamics include the Dishevelled subunit within system profile involvement of beta-catenin pathways. The Armadillo sequences of Dishevelled promote protein-protein interactions in a manner that allows or promotes both direct and indirect series of interactivities.

## Beta-Catenin

Hence, there emerges a canonical WNT pathway involving beta-catenin leading to intra-nuclear accumulation of beta-catenin in a specific mode of subsequent stabilization of this chemical intermediate. Within such system there is subsequent targeting of susceptible genes in specific conformational representation of system pathways in potential carcinogenesis. Promotional reconstitution of the canonical and non-canonical series of pathways thus constitutes a built-in series of pathway effects that stimulate cyclin-dependent D1 and the involvement

of Cyclin-dependent kinases CDK4 and CDK6. It is with reference to progression of the cell-cycle through the G1 phase that there is subsequent promotion of invasive attributes and the epithelial-mesenchymal transition of cells. Aberrant activation of the guanine nucleotide exchange factor Tiam1 leads to induced metastasis and epithelial-mesenchymal transition mediated by the Wnt/beta-catenin pathway as seen in thyroid carcinoma [5].

### System Pathways

System pathways are largely conserved in the evolution of species beyond the *Drosophila* in a manner that is revealed especially in terms of cell polarity dynamics and in the acquisition of the epithelial-mesenchymal transition in carcinogenesis. The first oncogene pathway identified inducing immune exclusion of tumors is the Wnt/beta-catenin pathway [6]. Knockout and transgenic mouse models allow for a dissection of the WNT pathways in terms of ongoing systems of pre-carcinogenesis. Wnt signaling is critical for determining tumor grade in adenoid cystic carcinoma since it regulates invasion and migration [7]. The WNT canonical pathway in particular is preferential setting in contextual reference to carcinogenesis that invokes direct and indirect protein-protein interactivities. Long non-coding RNAs are being recognized as key factors in cancer progression, as in the case of CCAL in hepatocellular carcinoma [8]. Collin 4B enhances metastasis and proliferation in pancreatic cancer cells by inducing epithelial-mesenchymal transition via the Wnt-beta-catenin signaling pathway [9].

Scaffold functionalities and in particular the Armadillo repeat sequences are paramount organizers in attribute functionality and dysfunctionality that help to define the contrasting roles of components of the WNT pathways in a potentially enhancing system of pre-carcinogenesis. miR-616 functions as a tumor promoter in glioma involving regulation of SOX7 and Wnt-beta-catenin signaling [10]. Indeed, defining roles of a strictly consequentially evolving pathway formulation implicate the real status of phase determination as a strictly valid pre-carcinogenesis. miR-638 may serve as a tumor suppressor as in human cervical cancer through the Wnt-beta-catenin signaling pathway and correlates with prognosis of cervical cancer patients [11].

### Pre-carcinogenesis

A distinct and viable phase of specific precarcinogenesis is recognizably a system interactivity between the canonical and non-canonical WNT system that contextually promotes dynamics of progression to neoplasia. Sex-determining region Y-box 7 (SOX7) suppresses beta-catenin-mediated transcription by disrupting the beta-catenin/BCL9 interaction and acts as a tumor suppressor [12]. As such, the incremental dimensions of carcinogenesis as a distinct biologic variability is permissive dimension to the inclusion of such potentially significant pathways as endocytosis, secretion into the extra-

cellular environment and the ubiquitination in the proteasomal subcompartment.

The localization and compartmentalization of WNT pathway components contrast with the intra-nuclear stabilization of trafficked beta-catenin. It is in terms of such dynamics that there evolves contextual referential systems in the globally cellular modifications of the WNT pathways. The serine protease High-Temperature Requirement A1 forms a complex with beta-catenin and reduces proliferation and may function as a suppressor of the canonical Wnt signaling pathway [13]. It is further to such considerations that contextual constitution allows for permissive and dynamic structuring of biologic attributes in pre-carcinogenesis. The leucine-rich repeat-containing GPCR family (LGR4) modulates breast cancer initiation, metastasis and cancer stem cells and it regulates the epithelial-mesenchymal transition by stimulating the canonical Wnt signaling [14].

### Negative-Feedback Control

Negative feedback regulation of the canonical WNT pathway is primal component system that represents multiple models of pre-carcinogenesis that permits formulation of distinct paradigms of orthologs and isoforms of WNT component pathways. The dynamics of pathway progression appear particularly conformational and system dynamics in a series of direct and indirect protein-protein interactivity. Cyclin-dependent Kinase 8 is a key oncogenic driver in several cancers in a context-specific manner as in breast, colorectal and hematologic malignancies; it activates oncogenic Wnt-beta-catenin signaling, transcription of oestrogen-inducible genes, and suppression of super enhancer-associated genes [15].

The intra-nuclear dimensions of accumulated beta-catenin thus invoke a series of trafficking systems in the context of further progression of cell-cycling and of the creation of the epithelial-mesenchymal transition in carcinogenesis. The great variability of isoforms of the WNT ligands, and of the Frizzled receptor accords with the dimensions of an embryogenic series of structural/functional moieties that include cell polarity dynamics. It is further to such contextual conditioning and re-conditioning that there evolves the dysregulatory progression of a WNT series of pathways that constitutively compound the potentiality for pre-carcinogenesis. Since miRNAs are often dysregulated in breast cancer, individual or combinations of circulating miRNAs may potentially serve as diagnostic, predictive or prognostic biomarkers as well as therapeutic targets [16].

### Incremental Induction

Incremental inductions of the WNT pathways are stem-cell attributes that implicate embryogenesis within the conditioned settings of a status formulation in pre-carcinogenesis. Senescence-associated stemness is a cell-autonomous feature exerting highly aggressive growth potential upon escape from

cell-cycle blockade and is enhanced in relapse tumors [17]. It is significant to consider contextual re-formulation as parameter identification within the further stages of progression of the epithelial-mesenchymal transition in carcinogenesis. The overall global status for further progression is inherent attribute of a series of embryogenic pathways beyond further contextual dimensions of the negative-feedback control of the canonical WNT as exerted by components of the non-canonical WNT pathway components. Mesenchymal markers on the surface of epithelial-mesenchymal-transition circulating tumour cells are associated with metastasis and can serve as potential biomarkers for metastasis [18].

## System Profiles

System proliferative dynamics are index phenomena in the constitution of the contextual re-conditioning of a distinct pre-carcinogenesis that is potential for further progression as malignant transformation. Micro-RNA-138 is an invasion and migration regulator in prostate cancer and is down-regulated in aggressive prostate cancer cell lines; miRNA-138 negatively regulates the Wnt/beta-catenin pathway activation in prostate cancer [19]. Complexity formulation is a chemical compound identity in the subsequent recognition of a pre-carcinogenesis step in outlining the distinct emergence of carcinogenic contexts.

Delivery systems in terms of intra-cellular trafficking of beta-catenin are further amplified by the Armadillo repeats that collectively re-define the protein-protein interactivities within systems of potential progression of both pre-carcinogenesis and of carcinogenesis per se. Incremental dimensions are themselves responsible for the progressiveness of dynamic modulations as portrayed by potential carcinogenesis. The large multifunctional protein "OBSCURIN" is encoded by OBSCN gene and interacts with many cancer-associated genes in breast carcinogenesis; prognostic molecular signatures such as copy number changes and gene expression of OBSCN gene may prove a useful marker for breast tumorigenesis and metastasis [20].

## Conclusion

Dimensions of inclusion and exclusion of dynamics of protein interactivity is borne out by the contextual reproduction of system pathways that permit the molecular modulation of contextual dysregulation. Such molecular dysregulation is parameter consequence of scaffolding systems of support in the trafficking of beta-catenin moieties to the nucleus. Further to such trafficking, the promotional stabilization of the intra-nuclear catenin invokes multiple parameters of gene targeting within the system formulation of dynamics of transfer and of isoform participation as protein-protein interactivities. Performance of structural-functional attributes is best considered as parameter adjustment and re-adjustment in the modulation of contextual conditioning of a distinct pre-carcinogenesis phase of progressive potential

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