Commentary

iMedPub Journals
www.imedpub.com

Journal of Clinical Epigenetics
ISSN 2472-1158

2017
Vol.3 No. S1:13

DOI: 10.21767/2472-1158.100047

Role of Epigenetic Regulation of Growth Arrest States in Normal and Cancer Cells

John J Wille

Bioplast Medical LLC, Chesterfield, NJ 08515, USA

Received: March 20, 2017; **Accepted:** March 28, 2017; **Published:** March 31, 2017

Corresponding author: John J Wille

jjwille@aol.com

Bioplast Medical LLC, 9 Georgetown Chesterfield Rd., Chesterfield, NJ 08515, USA.

Tel: (609) 656-0784

Citation: Wille JJ. Role of Epigenetic Regulation of Growth Arrest States in Normal and Cancer Cells. J Clin Epigenet. 2017, 3:S1.

Clinical epigenetics is the application of molecular biological techniques for detecting changes in DNA methylation or histone modification in order to diagnose or study disorders characterized by heritable defects in gene expression, e.g., transcription control by ENL YEATS domain in yeast [1] or the effect of depletion of *SmarcB1* on myc network signaling on the development of Kras-independent pancreatic cancer cells [2].

Similarly, cancer epigenetics is the study of somatically heritable changes to molecular processes that influence the information flow between DNA of cancer cells and their gene expression which involves comparison between normal cells and cancers in DNA methylation, histone modifications in genes encoding epigenetic regulators as exemplified by recent report of chemical probe for dissecting the cancer epigenome [3]. Shorter telomeres have also been implicated in genomic instability and oncogenesis [4]. DNA damage is assumed to be the primary underlying cause of cancer and deficient DNA repair and epigenetic reduction in DNA repair. Cancer epigenetics can occur through a numbers of gene modification mechanisms including: DNA methylation (hyper- and hypomethylation) [5,6], decreased histone acetylation of nucleosomic octomers (H1-H2a/H3-H4)and by microRNA gene silencing, as miRNAs control about 60% of the transcriptional activity of protein encoding genes. Epigenetic control of chromosomal translocations product occurs in the Philadelphia (Ph) chromosome, in patient with Chronic Myelogenous Leukemia (CML). The subsequent 9q2 translocation results in the Abl oncogene activation. Finally, a number of compounds are considered epigenetic carcinogens and teratogens such as second-generation effects of diethylstilbestrol, arsenite, hexachlorobenzene and nickel compounds [7]. Further studies on mechanisms of cancer epigenetics are detailed in the following citations [8-15].

Little is known about the epigenetic events associated with exit of normal somatic cell from neither the proliferative state nor how it may differ in cancer cells. However, there is extensive literature concerning the epigenetic involvement of chromatin structure and remodeling, nuclease chromatic sensitivities, and chromatic histone protein modifications during the G1/S transition of normal somatic cells and the transition from the pluripotency cell cycle to the somatic cell proliferative state [16]. Are there epigenetic processes involved in states of cell cycle arrest?

Bacteria can enter a state of dormancy or spore formation of as yet there are no reports as such [17]. By contrast, there is a vast literature on the epigenetic control of mammalian cell senescence in both normal and cancer cells by cell cycle dependent histone deacetylase inhibitors in fibroblast cells [18]. Many reports involve the role of p53 tumor suppressor gene activation and high levels of p16 as mediated thru MEK/MAPK mitogenic signaling [19-23] Other epigenetic mechanism involve the over expression of ectopic RAS [24], telomere shortening [25], and finally, the role of WNT16B in human epidermal keratinocyte proliferation control [26]. What about reversible G_1 cell cycle arrest?

Recently, a single report [27] examined the patterns of global DNA methylation following G_1 growth arrest in normal and several different epidermoid cancer cell lines. They report that the 5-methylcytosine content of mouse embryonic fibroblast arrested by nutrient deficiency, serum deprivation, confluency arrest, and arrest at a novel cell differentiation restriction point were all hypermethylated relative to proliferating cultures. In addition, four different proliferating cultures of epidermoid cancer cell were hypomethylated relative to normal proliferating human epidermal keratinocytes, while two different squamous carcinoma cell lines were further hypomethylated by suspension-induced growth arrest. These findings strongly support a role of epigenetic events in regulating switching states between proliferation and growth arrest.

References

1 Erb MA, Scott TG, Li BE, Xie H, Paulk J, et al. (2017).Transcriptional control by the ENL YEATS domain in acute leukemia. Nature 543: 270-274.

2 Genovese G, Carugo A, Tepper J, Robinson FS, Li L, et al. (2017) Synthetic vulnerabilities of mesenchymal subpopulations in pancreatic cancer. Nature 542: 362-366.

3 Shortt J, Ott CJ, Johnstone RW, Bradner JE (2017) A chemical probe toolbox for dissecting the cancer epigenome. Nat Rev Cancer 17: 160-183.

4 Shammas MA (2011) Telomeres, lifestyle, cancer, and aging. Curr Opin Clin Nutr Metab Care 14: 28-34.

5 Baylin SB, Esteller M, Rountree MR, Bachman KE, Schuebel K, et al. (2001) Aberant patterns of DNA methylation, chromatin formation, and gene expression in cancer. Human Mol Genet 10: 687-692.

6 Baylin SB (2005) DNA methylation and gene silencing in cancer. Nat Clin Pract Oncol 2: S4-S11.

7 Newbold RR (2006) Adverse effects of the model environmental estrogen diethylstilbestrol are transmitted to subsequent generation. Endocrinology 147: S11-S17.

8 Weinberg RA (2007) The Biology of Cancer. Garland Science, Taylor & Francis Group, LLC: NY, USA.

9 Jones PA, Baylin SB (2002) The fundamental role of epigenetic events in cancer. Nat Rev Genet 3: 415-428.

10 Jaenisc R, Bird A (2003) Epigenetic regulation of gene expression: how the genome integrates intrinsic and environmental signals. Nat Genet 33: 245-254.

11 Clark SJ, Melki J (2002) DNA methylation and gene silencing in cancer, which is the guilty party. Oncogene 21: 5380-5387.

12 Das PM, Singai R (2004) DNA methylation and cancer. J Clin Oncol 22: 4632-4642.

13 Stirzaker C, Song JZ, Davidson B, Clark SJ (2004) Transcriptional gene silencing promotes DNA hypermethylation through a sequential change in chromatin modification in cancer cells. Cancer Res 64: 3871-3877.

14 Mutskov V, Felsenfeld G (2004) Silencing of transgene transcription precedes methylation of promoter DNA and histone H3 lysine 9. EMBO J 23: 138-149.

15 Patra SK (2008) Ras regulation of DNA methylation. Expert Cell Res 314: 1193-1201.

16 Medina R, Ghule PN, Cruzat F, Barutcu AR, Montecino M, et al. (2012) Epigenetic control of cell cycle-dependent histone gene expression is a principal component of the abbreviated pluripotent cell cycle. Mol Cell Biol 32: 3860-3871.

17 Casadesus J, Low D (2006) Epigenetic gene regulation in the bacterial world. Microbiol Mol Biol Rev 70: 830-856.

18 Ogryzko VV, Hirai TH, Russanova VR, Barbie DA, Howard BH, et al. (1996) Human fibroblast commitment to a senescence-like state is response to histone deacetylase inhibitors is cell cycle dependent. Mol Cell Biol 16: 5210-5218.

19 Lin AW, Barradas M, Stone JC, van Aelst L, Serrano M, et al. (1998) Premature senescence involving p53 and p16 is activated in response to constitutive MEK/MAPK mitogenic signaling. Genes Dev 12: 3008-3019.

20 Campisi J, d'Adda di Fagagna F (2007) Cellular senescence: when bad things happen to good cells. Nature Rev Mol Cell Biol 8: 729-740.

21 Levine AJ (2016) The role of the p53 protein in stem-cell biology and epigenetic regulation. Cold spring Harb Perspect Med.

22 Chen J (2016) The Cell-cycle arrest and apoptotic functions of p53 in tumor initiation and progression. Cold spring Harb Perspect Med.

23 Tonnessen-Murray CA, Lozano G, Jackson JG (2016) The regulation of cellular functions by the p53 protein: cellular senescence. Cold spring Harb Perspect Med.

24 Maurelli R, Tinaburri L, Gangi F, Bondanza S, Severi AL, et al. (2016) The role of oncogenic Ras in human skin tumorigenesis depends on the clonogenic potential of the founding keratinocytes. J Cell Sci 129: 1003-1017.

25 Bermardes de Jesus B, Blasco MA (2012) Assessing cell and organ senescence biomarkers. Circulation Res 111: 97-109.

26 Teh MT, Blaydon D, Ghali LR, Briggs V, Edmunds S, et al. (2007) Role of WNT16B in human epidermal keratinocyte proliferation and differentiation. J Cell Sci 120: 330-339.

27 Wille JJ, Park JY (2013) Cell cycle arrest mediates global DNA methylation patterns in normal human keratinocytes, epidermoid carcinoma cells and murine embryoinic fibroblasts. J Cancer Ther 4: 199-207.