e-ISSN:2319-9865
p-ISSN:2322-0104

Research & Reviews: Journal of Medical and Health Sciences

# Cancer-Related Reprogramming of Human by Tumor Suppressor Gene

**Nisha Dhama[1]*, Abhishek Babu[2], Nitika Sharma[1]**

[1]Department of Biotechnology, Meerut Institute of Engineering Technology, Meerut, India
[2]Banaras Hindu University, Varanasi, India

## Review Article

Received date: 10/08/2016
Accepted date: 11/08/2016
Published date: 17/08/2016

***For Correspondence**

Nisha Dhama, Department of Biotechnology, Meerut Institute of Engineering Technology, Meerut, Tel: 8897465898.

**E-mail:** nishadhama1@gmail.com

**Keywords:** Stem cells, Tumor cells, Pluripotent stem cells, Tumor suppressor genes.

**ABSTRACT**

Due to their pluripotent qualities, human impelled pluripotent stem cells (iPSCs) have awesome potential for restorative application and for the investigation of degenerative diseases. These cells are produced from typical substantial cells, multipotent undifferentiated cells, or cancer cells. They express embryonic immature microorganism markers, for example, OCT4, SOX2, NANOG, SSEA-3, SSEA-4 and REX1, and can separate into all grown-up tissue sorts, both *in vitro* and *in vivo*. In any case, a portion of the pluripotency-advancing elements have been involved in tumor genesis. Here, we depict the benefits of tumor suppresser qualities as reinventing elements for the era of iPSCs without tumorigenic action. The underlying stride of reconstructing is actuation of the exogenous pluripotent components to create the oxidative anxiety that prompts senescence by DNA harm and metabolic anxieties, along these lines instigating the statement of tumor silencer qualities, for example, p21CIP1 and p16INK4a through the initiation of p53 to be the pre-affected pluripotent undeveloped cells (pre-iPSCs). The receptive oxygen species (ROS) created by oxidative anxiety may be basic for the actuation of endogenous reconstructing component qualities by means of epigenetic changes or cancer prevention agent responses

## INTRODUCTION

Undifferentiated organisms with the ability to separate into all grown-up tissue sorts can be gotten from the inward cell mass of the mouse blastocyst [1]. These embryonic immature microorganisms (ESCs) are one of kind assets for the exploration of cell improvement and separation, with a definitive point of repairing harmed tissues and organs in people. The reinventing of separated mammalian substantial cells into an undifferentiated pluripotent state was initially exhibited by the introduction of feasible youthful sheep after atomic exchange of grown-up physical cells into unfertilized enucleated oocytes [2]. Nonetheless, the methodologies used to get pluripotency in people, for example, the atomic exchange of substantial cells or the combination of physical cells with ESCs, have dependably been connected with moral worries that meddle with the utilization of these sorts of cells in fundamental examination and clinical treatment.

The center ESC administrative hardware includes OCT4, SOX2, and NANOG, which control their own particular expression and the expression or concealment of different variables required in self-restoration, pluripotency, and dedifferentiation [3-10]. As of late, two reports demonstrated that TFCP2L1 is another basic element for atomic reconstructing [11,12]. A few studies have demonstrated that the actuation of the Wnt pathway can make ESCs remain pluripotent [13-17]. Conversely, different studies showed that the Wnt pathway controls the separation of ESCs and the terminal separation of post mitotic cells [18-25]. The viability of the atomic reinventing of malignancy cells with transformed p53 or erased p53 is expanded to produce iPSCs; be that as it may, the recurrence of tumor genesis is likewise unmistakably expanded in these reconstructing disease immature microorganisms [26]. Therefore, none of the conventional models fuses the likelihood of tumor-related cell reinventing and the pliancy connected with the loss of p53 capacity. Hence, the tumorigenicity hazard connected with these immature microorganisms must be expelled before the accomplishments saw in fundamental exploration can be securely deciphered into clinical applications.

In this audit, we abridge the association between tumor silencer qualities (to keep away from the development of tumor cells) and full reinventing to iPSCs. We address the topic of whether disease cell-particular iPSCs are proportional to different sorts of foundational microorganisms, for example, completely dedicated iPSCs (full-iPSCs), from the perspective of beating their tumorigenic properties.

## ROLE OF TUMOR SUPPRESSORS

Immature microorganism genomes must be thoroughly "watched" all through each formative stage on the grounds that such cells extend intermittently to empower tissue repair and substitution. In this manner, as dedicated genomic duplication over a lifetime is limited to minimize the amassing of oncogenic injuries amid such developments, lacking genomic dependability control would be particularly injurious in ESCs in light of the fact that they are the forebears of all grown-up organ frameworks. Gatekeeping tumor silencers, for example, p16INK4a, p14ARF and p53, contrarily manage cell expansion and survival [27]. These quality items were initially found by prudence of their part in tumor, yet most likely advanced to control homeostasis in ordinary tissues by managing the expansion and survival of typical cells. Gatekeeping tumor silencers tend to adversely direct undifferentiated organism capacity [28] and manage foundational microorganism maturing in light of the fact that their look and/or capacity increment with age [29-31]. Raised p53 expression or constitutive p53 initiation can exhaust undifferentiated cells [32], bringing on untimely maturing, and abbreviate life-range in spite of diminishing disease rate [33-35]. These impacts in mice additionally seem to reflect comparative capacities in people in light of the fact that a polymorphism in p53 that lessens p53 capacity expands malignancy rate and life-range in people [36]. This recommends expanded p53 movement ensures against disease however can advance maturing and abbreviate life range, in any event when a specific limit of action is come to. The elements of the p16INK4a, p14ARF, and p53 tumor silencers rely on upon expression level and connection, consequently advancing the upkeep of mitotically dynamic cells in a few settings, while advancing cell passing or senescence in different settings. For instance, p53 advances the support of genome uprightness [37] and advances tissue era in ATR mutant mice by advancing DNA repair and/or by advancing the passing of cells with DNA harm [38]; in any case, in light of oncogenic boosts or telomere weakening, p53 drains foundational microorganisms [32,39].

### Deficiency of p53

Despite the fact that p53 transformation and pathway inactivation are found in the greater part of tumors, they give off an impression of being particularly thought among tumors that display pliancy and loss of separation qualities [40-42]. Choice for p53 utilitarian inactivation amid growth movement has ordinarily been ascribed to the survival formal that outcome from lessened apoptosis, cell cycle capture, and expanded open doors for cell advancement managed by genomic flimsiness. In light of the above examination, in any case, it is additionally conceivable that p53 misfortune destabilizes the separated state and empowers inversion to a more stem-like state.

### Stemness Characteristics

It is surely understood that the hindrance of the p53 pathway expands the clear productivity of iPSC era significantly [43-47]. The down regulation of qualities that add to cell-cycle capture or apoptosis likewise increments reconstructing. For instance, in spite of the fact that a transformation in MDMX diminished p53 movement by just two-fold at benchmark, it expanded reconstructing proficiency significantly [45]. These outcomes have a few imperative ramifications. To begin with, unpretentious changes in p53 movement are all that is required to build the likelihood of reinventing. Second, reinventing is restricted by an assortment of p53-affected defensive pathways, including, however not constrained to, those included in cell-cycle capture, senescence, and apoptosis. Third, through its capacity to restrain cell-cycle movement, p53 gives an intense boundary to the procurement of the dedifferentiation required in iPSC development.

### Roles of Oxygen Species and Tumor Suppressor Gene

The cell harm created by free radicals may produce ROS as an outcome of oxidative phosphorylation in the mitochondrial electron transport chain [48]. ROS, for example, superoxide and hydroxyl radical, are exceedingly receptive and can harm mitochondrial and atomic DNA, and proteins and lipids, by adjusting them artificially. Atomic reconstructing prompted by Yamanaka variables includes broad chromatin rebuilding and resets the epigenetic system to create iPSCs [49]. This ordinary iPSC strategy utilizing infection interceded quality exchange is currently a typical technique to convey reconstructing variables [50]. Elective reconstructing techniques without infection disease may be valuable to build the survival rate of iPSCs because of less ROS creation. Undeveloped cells give off an impression of being especially touchy to raised ROS levels. Expanded ROS levels coming about because of metabolic changes in iPSCs may impede the survival of reconstructed cells, as recommended by perceptions of iPSC-era under hypoxic conditions [51-54]. Likewise, mitochondrial capacities are additionally stifled in iPSCs or human ESCs [55], proposing that ROS era by reconstructing variables is unfavorable to the era of iPSCs. Vitamin C has been accounted for to be a viable compound to help iPSC era. Treatment with vitamin C diminished p53/p21 levels, which are the primary obstruction to fruitful reinventing [56]. Wang et al. [57] found that the histone demethylases Jhdm1a/1b are the direct downstream effectors of vitamin C, notwithstanding cancer prevention agent movement. Jhdm1b advances cell-cycle movement and stifles senescence by subduing the INK4a/ARF locus amid reconstructing. Besides, hindrance of the mammalian focus of rapamycin (mTOR) pathway

by rapamycin, PP242 or the insulin/insulin development variable 1 (IGF-1) flagging pathway eminently improves the effectiveness of reconstructing [58]. In light of the idea that reinventing is a distressing procedure that actuates apoptosis and cell senescence, it was demonstrated that focusing on the mTOR pathway reduces the senescence forced by the DNA harm reaction [59].

Furthermore, it was accounted for that senescence disables the reconstructing to iPSCs and that reinventing triggers an anxiety reaction of senescence at the underlying stage [60].

The presentation of Yamanaka variables at first triggers stress reactions with attributes of oxidative anxiety like increments in the oxidized 8-oxoguanine and reinventing prompted senescence (RIS) by upregulating p53, p16INK4a, and p21CIP1 at the underlying stage (pre-affected pluripotent undifferentiated organisms (pre-iPSCs)). This upregulation of p16INK4a and p21CIP1 was seen in heterokaryon-based reconstructing [61,62], proposing the presence of an innate connection amongst senescence and reinventing. Hence, the raised levels of p16INK4a and p21CIP1 that were distinguished in pre-iPSCs were diminished at a later stage in mouse embryonic fibroblasts, and expanded levels of p53 and p21CIP1 in IMR90 cells were likewise diminished at a later stage [60,63,64]. The hindrance of senescence utilizing knockdown develops of p53, p21CIP1, and p16INK4a at the late stage at long last enhanced the effectiveness of the reinventing of physical cells or essential malignancy cells, and the subsequent iPSCs showed qualities of pluripotent undifferentiated cells (full-iPSCs) [60,65-69]. Different reports have affirmed the inclusion of these two stages in reinventing to full-iPSCs. Pre-iPSCs that neglected to reconstruct completely are caught in a late stride of reinventing [63]. Hindrance of DNA methylation, knockdown of genealogy particular qualities, or treatment with two inhibitors [66] can either change over some of these pre-iPSCs to full-iPSCs, or expansion the extent of completely reinvented iPSCs versus pre-iPSCs. The restraint or the lightening of senescence can build the quantity of cells that surpass the early boundary forced by RIS, bringing about a higher number of both pre-iPSCs and completely reconstructed iPSCs. A mix of both techniques might be utilized synergistically to improve reinventing productivity.

The tumor silencer p53 has been concentrated most broadly as a significant sign that proselytes different upstream burdens into downstream reactions, including cell-cycle capture, senescence, DNA repair, reconstructing, and customized cell passing [70]. p53 has been involved as a master of separation by uprightness of its capacity to restrain the immature microorganism normal for self-restoration in a few frameworks [65,71]. Together with the exhibit by Yamanaka that separated cells can be reconstructed to a dedifferentiated state [67], and the show that p53 is a powerful reinventing obstruction [43-47,53,68], this has prompted a resurgence of enthusiasm for the possibility that loss of separation [72] might be connected to p53 pathway disturbance in tumors. Late studies have given extra proof of the connection amongst p53 and the development of dedifferentiated, stem-like phenotypes [72,73].

The viability of reinventing is in reality expanded by a few fold, however these iPSCs reconstructed from malignancy cells once in a while keep up or deliver p53 transformations, bringing about tumor arrangement. A few qualities in the first Yamanaka iPSC mixed drink, for example, c-MYC, produce oncogenic stresses that actuate the p53 pathway to instigate cell-cycle capture or passing [74]. Subsequently, c-MYC expression, together with general tissue society burdens, would be relied upon to initiate p53 amid the era of iPSCs, to lessen reinventing recurrence or rate. These outcomes have a few imperative ramifications. To start with, unpretentious changes in p53 action are all that is expected to build the likelihood of reinventing. At introductory stages, the reinventing elements prompt ROS generation by DNA harm and repair capacity and, at a later stage, these ROS ought to be stifled by the autoxidation arrangement of cells or other epigenetic changes [75].

## ADVANTAGES OF REPROGRAMMED CANCER CELLS

These reconstructed disease cells from growth patients may on the other hand be utilized to discover hereditary and epigenetic hints with respect to how the atomic reinventing was blocked while producing completely skillful iPSCs or undifferentiated organisms [76-88]. Undoubtedly, reconstructed malignancy cells produced from patients for the instigation of pluripotent cells gave a potential cell-based treatment model to reestablish tissues or organs crushed by chemotherapy, despite the fact that these cells are not completely pluripotent cells [89]. Amassing proof demonstrates that the epigenetic system influences the properties of reinvented iPSCs and seems to hold epigenetic engraving connected with their tissue kind of birthplace [90-94]. Along these lines, epigenetic components have been perceived to assume vital parts in disease improvement and cell separation. In view of these outcomes, the reinvented disease cells can serve as the perfect model framework to ponder the atomic components of tumorigenesis and the properties of malignancy undeveloped cells to build up basic methodologies for growth and regenerative prescription.

## CONCLUSION

Here we have assessed the tumorigenicity dangers connected with iPSCs. As of late, hereditary changes, including duplicate number varieties and protein-coding point transformations, were seen amid the reconstructing procedure by utilizing high-determination hereditary methodologies [95-100]. Point changes were enhanced in disease related qualities [95]. These concentrates firmly recommend iPSCs have a high tumorigenicity potential. Along these lines, particularly, to accomplish the remedial use of growth cells by means of the reconstructing strategy, transfection of tumor silencer qualities, such asp16INK4a/RB, p21CIP1, p14ARF and p53, joined with pluripotent components, for example, OCT4 or SOX2 may be best contrasted and viral transduction of powerful oncogenes. Vitally, reconstructing and senescence are connected procedures, as appeared by studies exhibiting that

the reinventing of cells is additionally testing in cells that are nearer to the onset of senescence [69]. The outflow of reconstructing components triggers RIS by initiating a few tumor-suppressive instruments. What's more, quality expression profiling concentrates on have uncovered that mark qualities that are initiated amid reinventing are regular to these antiproliferative reactions [69]. The little number of reports on the reconstructing of human essential malignancy cells restrains our capacity to interpret the organic or specialized obstructions that keep the reinventing of tumor cells. Nonetheless, we underscore that human pluripotent undifferentiated organisms ought to be checked to dispose of the likelihood of any transformations in tumor silencer qualities, as they may prompt tumorigenesis after exchange to patients.

## REFERENCES

1. Nottegar A, et al. Tumor suppressor gene ARID1A in cancer: Recent advances and future perspective. J Carinog Mutagene. 2016;7:255.
2. Kanungo J. Tumor suppressors and endodermal differentiation of P19 embryonic stem cells. Cell Dev Biol. 2015;4;e138.
3. Reisman D, et al. The bi-directional nature of the promoter of the p53 tumor suppressor gene. J Leuk. 2015;
4. Zhao G, et al. miR-203 Functions as a tumor suppressor by inhibiting epithelial to mesenchymal Transition in ovarian cancer. J Cancer Sci Ther. 2015;7;034-043.
5. Gaal Z, et al. Decreased expression levels of tumor suppressor microRNAs in hairy cell leukemia. J Leuk. 2015.
6. Sun W, et al. Tumor suppressor RIZ1 in carcinogenesis. J Carcinog Mutagen. 2014;5:160.
7. Liu DZ, et al. Mutations in tumor suppressor genes: Links between cancers and autism spectrum disorders? J Cytol Histol 5: e109. 2013
8. Yan B, et al. Signaling networks of activated oncogenic and altered tumor suppressor genes in head and neck cancer. J Carcinogene Mutagenes. 2013;7:004.
9. Pivetta E, et al. A rare bird among major extracellular matrix proteins: EMILIN1 and the tumor suppressor function. J Carcinogene Mutagene S. 2013;13:009.
10. Reisman D, et al. Transcriptional activation of the p53 tumor suppressor gene provides a rapid protective mechanism against DNA damage during S-phase of the cell cycle. J Leuk. 2013.
11. Kisiel JB, et al. Methylated bone morphogenetic protein 3. 2013.
12. Majeed R, et al. Therapeutic targeting of cancer cell metabolism: Role of metabolic enzymes, oncogenes and tumor suppressor genes. J Cancer Sci Ther. 2012;4:281-291.
13. Yochum GS , et al. AXIN2: Tumor suppressor, oncogene or both in colorectal cancer? J Cancer Sci Ther 4. 2012.
14. Zandi R, et al. Overexpression of the novel tumor suppressor gene FUS1 suppresses the growth of small cell lung cancer cells. J Clinic Experiment Pathol S. 2011;5:001.
15. Naga Deepthi CH, et al. Role of tumor suppressor protein p53 in apoptosis and cancer therapy. J Cancer Sci Ther S. 2011;17:001.
16. Dingwall S, et al. Expression of histocompatibility 2 blastocyst. 2015.
17. Jerez Puebla LE, et al. Frequency of blastocystosis and its association with clinical symptoms in 2 years of surveillance at "Pedro Kourí" institute. Clin Microbiol. 2014;3:178.
18. Gustin SLF, et al. Frozen blastocyst transfer has similar success rates in Asian and Caucasian patients. J Preg Child Health. 2014;1:122.
19. Roberts T, et al. Update on the molecular epidemiology and diagnostic tools for Blastocystis sp. J Med Microb Diagn. 2014;3:131.
20. Günther K, et al. Rapid monolayer neural induction of induced pluripotent stem cells yields stably proliferating neural stem cells. J Stem Cell Res Ther. 2016;6:341.
21. Kaur KK, et al. Induced Pluripotent stem cells-emphasis on transcriptomics and recent advances in therapeutic potential. Transcriptomics. 2016;4:134.
22. Abu-Hassan DW, et al. Induced pluripotent stem cells restore function in a human cell loss model of open-angle glaucoma. J Clin Exp Ophthalmol. 2016;7:535.
23. Brooks PT, et al. Structural analysis of three dimensional human neural tissues derived from induced pluripotent stem cells. J Stem Cell Res Ther. 2016;6:337.
24. Sahito RGA, et al. Gelatine microspheres support direct intramyocardial delivery of induced pluripotent stem cell-derived cardiomyocytes. J Stem Cell Res Ther. 2015;5:306.

25. Tandle A, et al. Mitotic protein kinase 1: Role in spindle assembly checkpoint revisited. J Cancer Clin Trials. 2016;1:111.

26. Parandhaman DK, et al. Multifaced pknE: Apoptosis inhibition, HIV co-infection, host signaling cross-talk and in orchestrating the physiology of *Mycobacterium tuberculosis*. J Microb Biochem Technol. 2016;8:231-235.

27. Zhang J, et al. ClC-3 is Involved in NPPB-induced apoptosis in DU145 prostate cancer cells. J Mol Biomark Diagn S. 2016;2:018.

28. Giacoppo S, et al. Role of Wnt/B-catenin signaling in regulating the balance between oxidative stress and apoptosis in peripheral blood mononuclear cells from patients with facioscapulohumeral muscular dystrophy. J Mol Genet Med. 2016;10:213.

29. Prayitno A, et al. *Jatropha Curcas* Linn can reduce the expression of Hsp70 that will result in reduced errors in protein folding and promotion of normal protein function in proliferation and apoptosis. Immunome Res. 2016;12:114.

30. Burlaka I, et al. Beyond proteinuria: Apoptosis and vitamin D3 state in children with diabetic nephropathy. J Clin Exp Pathol. 2016;6:266.

31. Luo S, et al. Two novel curcumin analogues induced reactive oxygen species generation and mitochondrial-related apoptosis in human breast cancer MCF - 7 cells. J App Pharm. 2016;8:215.

32. Xu D, et al. High-expressed CXCR7 contributes to CXCL12-mediated protection from apoptosis in lymphoma cells. J Mol Genet Med. 2016;10:208.

33. Lee JR, et al. Effects of HERV-R env knockdown in combination with ionizing radiation on apoptosis- related gene expression in A549 lung cancer cells. Biochem Physiol. 2016;5:200.

34. Jia Z, et al. Histone deacetylase inhibitors can repress proliferation and induce apoptosis in gingiva progenitor cells from idiopathic gingival fibromatosis. J Stem Cell Res Ther. 2016;6:327.

35. Wei H, et al. Anti-oxidative stress and anti-apoptosis effects of He Ying An Xin-formula. J Pharmacogn Nat Prod. 2016;2:115.

36. Oh MH, et al. Protective effect of S-Adenosyl-LMethionine on oxidative stress-induced apoptosis regulates Nrf2 via IGF-I in rat bone marrow mesenchymal stem cells. J Stem Cell Res Ther. 2016;6:323.

37. Etetor Eshiet R, et al. The biologic potential of lyophilized extracts of *Brickellia cavanillesii*. 2015.

38. Jiang N, et al. Gas6/Axl inhibits osteosarcoma apoptosis through regulation of apoptosis-related protein Bcl-2. J Bioanal Biomed. 2016;8:001-008.

39. Levy I, et al. Tumor necrosis factor related apoptosis inducing ligand-conjugated near IR fluorescent iron oxide/human serum albumin core-shell nanoparticles of narrow size distribution for cancer targeting and therapy. J Nanomed Nanotechnol. 2015;6:333.

40. Mito F, et al. Significance of plasma apoptosis inhibitor of macrophage concentrations in patients with obstructive sleep apnea syndrome: A new biological indicator of severity and treatment responses. J Sleep Disord Ther. 2015;4:219.

41. Fatani SH, et al. Correlation between serum anti-apoptotic Bcl-2 level and its immunohistochemical expression in relation to apoptosis in gastric cancer. J Mol Biomark Diagn. 2015;6:248.

42. Sanyal SN, et al. Activation of mitochondrial apoptosis and regulation of ceramide signalling by COX-2 inhibitors in colon cancer. Transl Med. 2015;5:159.

43. Malemud CJ, et al. Chondrocyte apoptosis in rheumatoid arthritis: Is preventive therapy possible? Immunother open acccess. 2015;1:102.

44. Atienza EM, et al. Probiotic modulation of intestinal cell apoptosis in inflammatory bowel disease and colon cancer. Immunother open acccess. 2015;1:101.

45. Salahuddin M, et al. Potential drug targets in the death pathway: Therapeutic approaches in apoptosis. Biochem Physiol. 2015;4:e141.

46. Rocha KKHR, et al. Lithium toxicity effects on oxidative stress, dyslipidemia and apoptosis in the aged rats. Biochem Pharmacol. 2015.

47. Guo H, et al. Neuroprotection of sesamin against cerebral ischemia *in vivo* and N-Methyl-D-Aspartate-induced apoptosis *in vitro*. Biochem Pharmacol. 2015.

48. Meng X, et al. Effects of limb remote post conditioning on apoptosis and long-term neurological outcomes of focal cerebral ischemia/reperfusion injury in rats. J Diabetes Metab. 2015;6:596

49. Rasmussen TK, et al. MicroRNA-21 can regulate apoptosis of CD4+ T cells in systemic lupus erythematosus. Rheumatology. 2015.

50. Chai S, et al. Mechanistic progress of estrogen-induced apoptosis in estrogen-deprived breast cancer cells. J Cell Sci Ther. 2015;6:218.

51. Zhang XD, et al. Mechanism of DRAM1's regulation of autophagy and apoptosis. J Pharmacogenomics Pharmacoproteomics. 2015;6:e147.

52. Navalta JW, et al. The current state of exercise- induced lymphocyte apoptosis. Single Cell Biol. 2015;4:113

53. Rossi T, et al. Effect of a purified extract of olive mill waste water on endothelial cell proliferation, apoptosis, migration and capillary-like structure *in vitro* and *in vivo*. J Bioanal Biomed S. 2015;12:006

54. Khasawneh MA, et al. *Leptadenia pyrotechnica* induces P53-dependent apoptosis in colon cancer cells. Nat Prod Chem Res. 2015;3;177.

55. Hennequart SC, et al. G2/M arrest sensitises erythroid leukemia cells to Trail induced apoptosis. J Leuk. 2015;3:174.

56. Heiler S, et al. Pancreatic cancer stem cell markers and exosomes -the incentive push. World J Gastroenterol. 2016.

57. Schulz A, et al. Neuron-specific deletion of the Nf2 tumor suppressor impairs functional nerve regeneration. PLoS One. 11:e0159718.

58. Pal D, et al. Regulation of cell proliferation and migration by miR-203 via GAS41/miR-10b axis in human glioblastoma cells. PLoS One. 2016;11:e0159092.

59. Dal J, et al. Growth hormone and insulin signaling in acromegaly: Impact of surgery versus somatostatin analog treatment. J Clin Endocrinol Metab. 2016.

60. Sahli N, et al. Impact of brachytherapy in the treatment of locally advanced cervical cancer: Results from a single institution. Gynecol Obstet. 2016;6:386.

61. Sarwar R, et al. Association of promoter polymorphisms in Xrcc2 gene involved in DNA double strand break repair and increased susceptibility to thyroid cancer risk in Pakistani population. J Carcinog Mutagen. 20.

62. Manzo C. Cancerogenesis and polymyalgia rheumatica. J Carcinog Mutagen. 2016;7:268.

63. Ichihara H, et al. Negatively charged cell membranes-targeted highly selective chemotherapy with cationic hybrid liposomes against colorectal cancer *in vitro* and *in vivo*. J Carcinog Mutagen. 2016;7:267.

64. Khan MA. 4-Aminobiphenyl and nitric oxide synergistically modified human DNA: ItÃ¢Â€Â™s implication in bladder cancer. Biochem Anal Biochem. 2016;5:279.

65. Kahouli I, et al.Characterization of *L. reuteri* NCIMB 701359 probiotic features for potential use as a colorectal cancer biotherapeutic by identifying fatty acid.

66. Lay FD and Liang G. Rethinking demethylating agents in epigenetic cancer therapy. J Mol Pharm Org Process Res. 4:133.

67. Bisen PS. Nutritional therapy as a potent alternate to chemotherapy against cancer. J Cancer Sci Ther. 8:168.

68. Langdon SP and Sims AH. HER2-targeted antibody treatment for ovarian cancer Ã¢Â€Â“ future opportunities. J Mol Pharm Org Process Res. 4:1.

69. Mathioudakis A and Hardavella G. From lung cancer screening to targeted therapies: The endless race against lung cancer morbidity and mortality. J Lung Cancer Diagn Treat. 1:e101.

70. Naeini EE, et al. The effectiveness of stress management training on hardiness in patients with breast cancer. Abnorm Behav Psychol. 2016;2:115.

71. Hauptman N and GlavaÃ„Â D. Long non-coding RNAs in cancer: Diagnostic and prognostic value. Med Chem (Los Angeles). 6:422.

72. Shabani A. A review of anticancer properties of herbal medicines. J Pharma Care Health Sys. 3:160.

73. Akcay S, et al. Smoking cessation in lung cancer. J Lung Cancer Diagn Treat. 1:105.

74. Pezzella F. Cancer and blood vessels: A complex relationship. J Lung Cancer Diagn Treat. 1:104.

75. Purkayastha K, et al. To determine the role of procalcitonin in febrile neutropenic episodes of children undergoing treatment for childhood cancers. J Clin Case Rep. 2016;6:805.

76. Sinakosa ZM and Geromichalosb GD. The effect of saffron (*Crocus sativus*) carotenoids on hemostasis and atherosclerosis. Next Generat Sequenc & Applic. 2016;3:127.

77. Patel BD, et al. Quantification of newer anti-cancer drug clofarabine in their bulk and pharmaceutical dosage form. J Chromatogr Sep Tech. 2016;7:328.

78. Newman MA. Health as expanding consciousness. St. Louis: The C. V. Mosby Company.

79. Newman MA, et al. The focus of the discipline of nursing. Adv Nurs Sci. 14:1-6.

80. Ferrell BR and Winn R. Medical and nursing education and training opportunities to improve survivorship care. J Clin Oncol. 24:5142-5148.

81. Grant M, et al. Oncology nurse participation in survivorship care. Clin J Oncol Nurs. 14:709-715.

82. Irwin M, et al. Oncology nurses' perspectives on the state of cancer survivorship care: Current practice and barriers to implementation. Oncol Nurs Forum. 38:E11-E19.

83. Klemp JR, et al. Improving cancer survivorship care: Oncology nurses' educational needs and preferred methods of learning. J Cancer Educ. 26:234-242.

84. Shearer D and Adams J. Evaluating an advanced nursing practice course: Student perceptions. Nurs Stand. 26:35-41.

85. White KR and Coyne PJ. Nurses' perceptions of educational gaps in delivering end-of-life care. Oncol Nurs Forum. 38:711-717.

86. Newman MA. Caring in the human health experience. International Journal for Human Caring. 6:8-12.

87. Endo E, et al. Pattern recognition as a caring partnership in families with cancer. J Adv Nurs. 32:603-610.

88. Yuan and Changrong. Rethinking M-health in cancer care: From the perspective of patient participation. Cancer Nursing. 39:253-254,

89. Paterson CL, et al. Body image in younger breast cancer survivors: A systematic review. Cancer Nursing. 39:E39-E58.

90. Kelly DL et al. The microbiome and cancer: Implications for oncology nursing science. Cancer Nursing. 39:E56-E62.

91. Sterba KR, et al. Quality of life in head and neck cancer patient-caregiver dyads: A systematic review. Cancer Nursing. 39:238-250

92. Chow KM, et al. A review of psychoeducational interventions to improve sexual functioning, quality of life and psychological outcomes in gynecological cancer patients. Cancer Nursing. 39:20-31.

93. Davis LL, et al. State of the science: Taxane-induced musculoskeletal pain. Cancer Nursing. 39:187-196.

94. Chan and Raymond J. Evidence-based cancer nursing: cancer nursing and the Cochrane collaboration. Cancer Nursing. 36:1-2.

95. Miyashita M, et al. unmet information needs and quality of life in young breast cancer survivors in Japan. Cancer Nursing. 38:E1-E11.

96. Hinds, et al. The global champion for end-of-life care: Who are you? What is keeping you? Cancer Nursing. 39:1-2.

97. Gilbar and Peter. Intrathecal chemotherapy: Potential for medication error. Cancer Nursing. 37:299-309.

98. Moorhouse P. Treatment of hypertension in frail older adults in nursing homes: Evaluation of an educational intervention for physicians. J Gerontol Geriatr Res. 2015;S3:005.

99. Feghali A, et al. Utilization of intravascular ultrasound to assess vascular invasion in pancreatic cancer post chemoradiation therapy. J Vasc Med Surg. 2016;4:275.

100. Yuldasheva GA, et al. The mechanism of anti-cancer activity of complexes of molecular iodine with ÃŽÂ±-dextrins and polypeptides and lithium halogenides. J Antivir Antiretrovir. 2016;8:072.