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DEVELOPMENTS OF CARCINOGENESIS INDUCED BY ABNORMALITIES OF WNT GENES

Rajendran Prakash

VMKV Engineering College, Periyaseeragapadi, Salem - 636308, Tamil Nadu, India.

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Correspondence to Author:
R. Prakash

VMKV Engineering College, Periyaseeragapadi, Salem - 636308, Tamil Nadu, India.

E-mail: yokaprakash0007@gmail.com

ABSTRACT: In cancers, many signals were involved in self-renewal, differentiation and proliferation. Especially, Wnt signaling pathway plays crucial impact in stem cells and cancer development. Wnt genes were involved in the stimulation of Wt signaling pathway in stem cells development. Despite, mutation and overexpression of Wnt genes induced regulation of carcinogenesis. Out of 19 Wnt genes, each Wnt gene has a crucial role in the growth of stem cells and cancer stem cells. In cancer stem cells, aberrant expression of Wnt genes implicated a variety of cancer. Clinical studies, Inhibition of Wnt signaling pathway one of the expensive strategies of cancer therapy. Drugs were developed against cancer development based on inhibition of abnormality of Wnt signaling.

INTRODUCTION: Since 1982, the int-1 gene was originally identified as a proto-ongogene in mouse mammary tumor and finally called Wnt1 (Wingless int-1). Nowadays, Wnt genes involved in stem cells development and other human disorders [1, 2]. Most of the cancers, Wnt genes were expressed aberrantly. Abnormalities of Wnt signaling pathways regulated variety of cancers. Mutations and overexpression of Wnt genes stimulated cell growth, proliferation, and self-renewal of cancer stem cells.

Wnt Genes in Cancer Development: Wnt genes were mutated or highly expressed to the stimulated vast growth of cancer cells. These cells were lead to enormous death rate compare then other diseases. Many types of cancer were stimulated by mutation or overexpression of specific genes.

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Abnormalities of Wnt genes were regulated carcinogenesis, and 19 Wnt genes have been the specialized role in cancer development. Each Wnt gene plays a crucial impact in each cancer type [5].

Abnormalities of Wnt genes regulated vast cancer development such as breast cancer, endometrial carcinoma, pancreatic adenocarcinoma, prostate cancer, leukemia, melanoma, lung carcinogenesis, medulloblastoma, gastric carcinoma, colorectal adenocarcinoma, esophageal squamous cell carcinoma, Basal cell carcinoma, oral squamous cell carcinoma, head and neck squamous cell carcinoma, bladder cancer, teratocarcinoma, ovarian carcinogenesis and non-small cell lung cancer [3, 4].

Cancer Stem Cells in Breast: Nowadays, breast cancer plays a crucial role in human death, and it occurred mostly in the female. Most of the genes were involved in tumorigenesis and some Wnt genes highly expressed in breast cancer. Wnt1 gene was first identified as an ongogene in mouse mammary tumor [1]. Wnt1 gene highly expressed in breast cancer, and most of the case mutated Wnt1 gene promoted breast cancer. Normally Wnt1 gene

has important role in self-renewal and proliferation of stem cells, likewise abnormality of Wnt1 gene regulated self-renewal, differentiation and proliferation of cancer stem cells in the breast. Other all Wnt genes were also regulated breast tumor [6].

Cancer Stem Cells in Rectum: Wnt genes were involved in one part of cancer development such some colorectal or colon, or rectal cancer was caused by abnormalities of Wnt genes. Overexpression of Wnt genes such as Wnt1, Wnt2, Wnt3, Wnt6, Wnt9a, Wnt10A, and Wnt16 were induced specialized cancer of colorectal cancer [9]. Wnt2 gene was highly expressed in colon cancer.

Mutation of Wnt genes such as Wnt5a, Wnt7a, Wnt10B, and Wnt16 have also stimulated the regulation of cancer development in the colon. These Wnt genes were also involved in cancer stem cells self-renewal in rectum [8, 10].

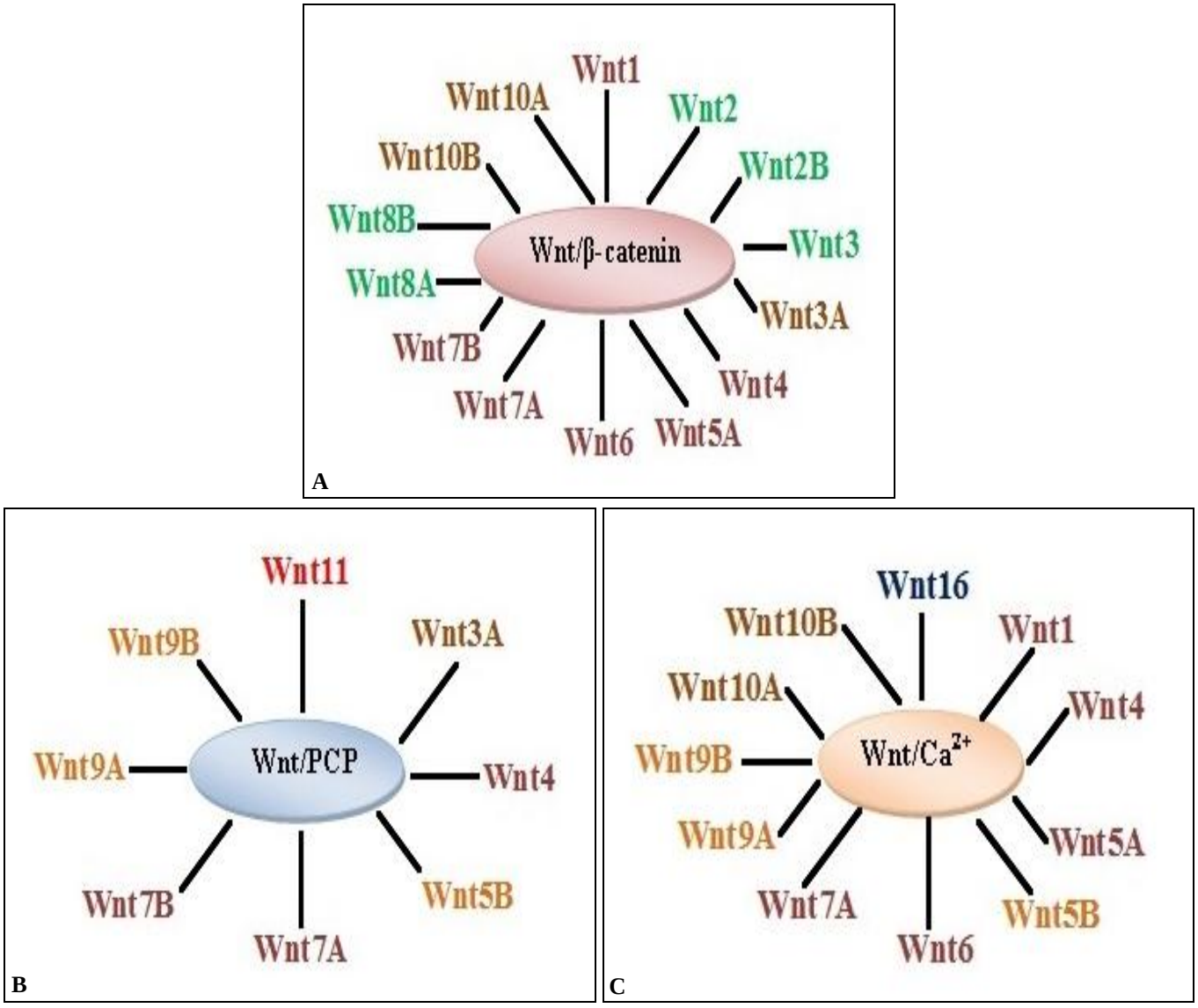

FIG. 1: STIMULATION OF Wnt SIGNALING BY SPECIFIC Wnt GENES. GREEN COLORS INDICATED ONLY Wnt /β-CATENIN SIGNALING GENES (CANONICAL PATHWAY). ORANGE COLORS INDICATED ONLY NON-CANONICAL PATHWAY GENES. RED ACCENT COLORS INDICATED BOTH CANONICAL AND NON-CANONICAL Wnt GENES. A: Diagram shown Wnt/β-catenin signal stimulated by Wnt genes; B: Diagram shown Wnt/PCP signal regulated by Wnt genes; C: Diagram shown Wnt/Ca^{2+} signal induced by Wnt genes.

Cancer Development in the Prostate Gland: In the prostate gland, aberrant expression of Wnt genes was regulated cancer development in male. Prostate cancer one of the critical cancer type because a lot of males died for this cancer [11].

TABLE 1: Wnt GENES IN CANCER DEVELOPMENTS

Wnt genes	Nature of miscues	Types of cancer	References
Wnt1	Overexpression	Mammary carcinogenesis, gastric cancer, melanoma, esophageal squamous cell carcinoma, neuroblastoma, non-small cell lung cancer, colorectal carcinomas and prostate cancer, hepatocellular carcinoma	3, 8, 15, 20-25
Wnt2	Overexpression	Esophageal squamous cell carcinoma, gastrointestinal and colorectal cancer, mesothelioma and lung Cancer, endometrial carcinoma, breast cancer	16, 26-28
Wnt2B	Overexpression	Breast cancer, teratocarcinoma, gastric cancer, basal cell carcinoma, gastric cancer, breast cancer, head and neck squamous cell carcinoma, cervical cancer and leukemia, ovarian cancer	29-31
Wnt3	Overexpression	Mammary carcinogenesis, endometrial carcinoma, non-small cell lung cancer, teratocarcinoma, gastric cancer, hepatocellular carcinoma, epithelial cancer	16, 32-34, 40, 48
Wnt3A	Overexpression and mutation	Teratocarcinoma, breast and gastric cancer, glioma tumorigenesis, prostate cancer, leukemia, multiple myeloma, oral squamous cell carcinoma	33-38, 64
Wnt4	Overexpression and mutation	Leukemia, breast and ovarian carcinogenesis, lung cancer	39, 41, 42
Wnt5A	Increased expression and mutation or loss of function	Endometrial carcinoma, pancreatic adenocarcinoma, prostate cancer, leukemia, melanoma, lung carcinogenesis, medulloblastoma, gastric carcinoma, colorectal adenocarcinoma, esophageal squamous cell carcinoma and breast cancer, Basal cell carcinoma, oral squamous cell carcinoma	16, 43-47, 64
Wnt5B	Overexpression	Epithelial cancer, Breast cancer, Uterine leiomyomas, gastric cancer, teratocarcinoma	48-51
Wnt6	Overexpression	Gastric cancer, colorectal adenoma, cervical cancer and breast cancer	52-54
Wnt7A	Overexpression and mutation	Endometrial carcinoma, renal cell and non-small cell lung carcinomas, ovarian carcinomas, colorectal, breast, pancreatic and gastric cancer	16, 55-57
Wnt7B	Overexpression	Endometrial carcinoma, breast cancer, and embryonal tumor, prostate cancer, lung, esophageal, gastric and pancreatic cancer, bladder cancer	16, 57-60
Wnt8A	Overexpression	Embryonal tumors and breast cancer, teratocarcinoma, germ cell tumors, basal cell carcinoma, oral squamous cell carcinoma	61-64
Wnt8B	Overexpression	Breast cancer, basal cell carcinoma, gastric cancer	54, 63, 66
Wnt9A	Overexpression	Breast cancer, basal cell carcinoma, gastric, colorectal and pancreatic cancer	54, 63, 66
Wnt9B	Overexpression and mutation	Oral squamous cell carcinoma, teratocarcinoma, breast, pancreatic and gastric cancer	7, 64, 67
Wnt10A	Overexpression	Colorectal cancer, promyelocytic leukemia, endometrial carcinoma, renal cell carcinoma, gastric, esophageal, teratocarcinoma and breast cancer	67-70
Wnt10B	Overexpression and mutation	Breast cancer, endometrial carcinoma, osteosarcoma, hepatocellular carcinoma and colon cancer, esophageal, gastric, cervical and pancreatic cancer	16, 54, 71-73
Wnt11	Overexpression and mutation	Oral squamous cell carcinoma, colon carcinoma, hepatocellular carcinoma, prostate and breast cancer, gastric, cervical and renal cell carcinoma	13, 64, 74-76
Wnt16	Overexpression	Prostate cancer, acute lymphoblastic leukemia, breast cancer, colorectal and basal cell carcinomas	54, 77, 78

Many characters were involved in prostate cancer development but most of the prostate cancer regulated by abnormalities of signals, especially Wnt signaling. Aberrant of expression of Wnt genes involved cancer development in prostate gland [12]. Mostly, Wnt1 highly expressed in prostate cancer and other genes such as Wnt3a, Wnt5a, Wnt7b, Wnt11, and Wnt16 were also induced

carcinogenesis in the prostate gland. Wnt3a gene was highly expressed in prostate cancer. Other Wnt genes expressions were not studied well in prostate cancer development [13].

Vast Cell Growth in Lung Organ: Wnt signals were involved in cell cycle and cell growth. Abnormality of the Wnt signaling pathway regulated enormous cell growth and differentiation. In the lung, Wnt genes were highly expressed and regulated enormous cell growth, and mutation of Wnt genes were expressed in non-small cell lung cancer [14]. Mutated Wnt1 was highly expressed in non-small cell lung cancer, and other types of Wnt genes were also regulated lung cancer such as

Wnt2, Wnt2b, Wnt3, Wnt5a, Wnt7a and Wnt7b. Wnt5a gene was highly expressed in lung cancer [15].

Other Types of Cancer: In cancer, Wnt genes have stimulated the regulation of a variety of cancer, and some genes were specialized to caused specific cancer type. Wnt1 Wnt2, Wnt5a, Wnt7b, Wnt10a, Wnt10b genes were expressed in esophageal squamous cell carcinoma. Wnt1 and Wnt5a were highly expressed in melanoma [22, 44].

Mutation of Wnt2b, Wnt4, Wnt5a, Wnt10a, and Wnt16 have induced the regulation of cell growth and differentiation in leukemia. In endometrial cancer, Wnt genes have a specialized role in self-renewal of cancer stem cells, and Wnt2, Wnt3, Wnt4, Wnt5a, Wnt7a, Wnt7b, and Wnt10b genes were expressed in endometrial cancer [16]. Wnt9a was reported in acute lymphoblastic leukemia. Epigenetic inactivation of Wnt7a and Wnt9a were recently reported in pancreatic cancer [5].

Cancer Treatment: Wnt signals activated in intestinal, prostate and mammary tumor and also implicated in skin cancer, lung cancer, bladder cancer, leukemia, and other cancers. Aberrant expression and mutation of Wnt genes highly stimulated the regulation of various cancers. Therefore inhibition of Wnt signals leads valuable strategies of cancer therapy [17]. Many important drugs were involved in Wnt signals inhibition and also these drugs synthesized as an antagonist of Wnt signals. Anti-cancer drugs such as Non-steroidal anti-inflammatory drugs (NSAIDs), vitamin D and their derivatives, small molecules inhibitors, and antibody-based treatment [18, 19].

NSAIDs has suppressed the activation of cancer reported in colon cancer. Vitamin D was also involved in colon cancer treatment, and it inhibited the activation of β-catenin. Other chemopreventive agents such as curcumin and lycopene also deactivated Wnt signaling pathway [19].

CONCLUSION: Cancers are one of the critical diseases in our animal kingdom. Many of the cancer was caused by physical, chemical, and biological factors. These all factors were affected the cellular level of function. These functions were stimulated *via* various signaling pathways.

In cell-cell interaction, signaling pathways were communicated one cell to other cells. Therefore, abnormalities of all signals were regulated a variety of cancer and other disorders.

Among these signals, Wnt signals were regulated both stem cells and cancer stem cells. Especially deregulation of Wnt signals were implicated carcinogenesis.

In cancer, inhibition of Wnt signals important strategies of cancer treatment. Many drugs were synthesized against the abnormalities of the Wnt signaling pathway. But these drugs were killed cancer cells, not cancer stem cells. So, a new herbal product of drugs will use to kill cancer stems cells without side effect.

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REFERENCES:

1. Nusse R, Brown A, Papkoff J, Scambler P, Shackleford G and McMahon A: A new nomenclature for int-1 and related genes: the Wnt gene family. Cell 1991; 64: 231.
2. Nusse R and Varmus HE: Many tumors induced by the mouse mammary tumor virus contain a provirus integrated into the same region of the host genome. Cell 1982; 31: 99-09.
3. Nusse R, Theunissen H, Wagenaar E, Rijsewijk F, Gennissen A and Otte A: The Wnt-1 (int-1) oncogene promoter and its mechanism of activation by insertion of proviral DNA of the mouse mammary tumor virus. Mol Cell Biol 1990; 10: 4170-9.

4. Nusse R and Varmus H.E: Wnt genes. Cell 1992; 69: 1073-87.
5. Ochoa-Hernandez AB, Juarez-Vazquez CI, Rosales-Reynoso MA and Barros-Nunez P: WNT-β-catenin signaling pathway and its relationship with cancer. Cir Cir 2012; 80: 389-98.
6. Brown AM: Wnt signaling in breast cancer: have we come full circle? Breast Cancer Res 2001; 3: 351-5.
7. Katoh Y and Katoh M: Comparative genomics on Wnt9a orthologs. Oncol Rep 2005; 13: 989-92.
8. Thorstensen L, Diep CB, Meling GI, Aagesen TH, Ahrens CH and Rognum TO: WNT1 inducible signaling pathway protein 3, WISP-3, a novel target gene in colorectal carcinomas with microsatellite instability. Gastroenterology 2001; 121: 1275-80.
9. Dimitriadis A, Vincan E, Mohammed IM, Roczo N, Phillips WA and Baindur-Hudson S: Expression of Wnt genes in human colon cancers. Cancer Lett 2001; 166: 185-91.
10. de Sousa EM, Vermeulen L, Richel D and Medema JP: Targeting Wnt Signaling in Colon Cancer Stem Cells. Clin Cancer Res 2011; 17: 647-53.
11. Majid S, Saini S and Dahiya R: Wnt signaling pathways in urological cancers: past decades and still growing. Mol Cancer 2012; 11: 7.
12. Yardy GW and Brewster SF: Wnt signaling and prostate cancer. Prostate Cancer Prostatic Dis 2005; 8: 119-26.
13. Uysal-Onganer P, Kawano Y, Caro M, Walker MM, Diez S and Darrington RS: Wnt-11 promotes neuroendocrine-like differentiation, survival and migration of prostate cancer cells. Mol Cancer 2010; 9: 55.
14. Stewart DJ: Wnt signaling pathway in non-small cell lung cancer. J Natl Cancer Inst 2014; 106: djt356.
15. Huang CL, Liu D, Ishikawa S, Nakashima T, Nakashima N and Yokomise H: Wnt1 overexpression promotes tumor progression in non-small cell lung cancer. Eur J Cancer 2008; 44: 2680-8.
16. Bui TD, Zhang L, Rees MC, Bicknell R and Harris AL: Expression and hormone regulation of Wnt2, 3, 4, 5a, 7a, 7b and 10b in normal human endometrium and endometrial carcinoma. Br J Cancer 1997; 75: 1131-6.
17. Paul S and Dey A: Wnt signaling and cancer development: therapeutic implication. Neoplasm 2008; 55: 165-76.
18. Herbst A and Kolligs FT: Wnt Signaling as a Therapeutic Target for Cancer. Methods Mol Biol 2007; 361: 63-91.
19. Valkenburg KC, Graveel CR, Zylstra-Diegel CR, Zhong Z and Williams BO: Wnt/β-catenin Signaling in Normal and Cancer Stem Cells. Cancers (Basel) 2011; 3: 2050-79.
20. Katoh M: Expression and regulation of WNT1 in human cancer: up-regulation of WNT1 by beta-estradiol in MCF-7 cells. Int J Oncol 2003; 22: 209-12.
21. Niederleithner H, Heinz M, Tauber S, Bilban M, Pehamberger H and Sonderegger S: Wnt1 is anti-lymphangiogenic in a melanoma mouse model. J Invest Dermatol 2012; 132: 2235-44.
22. Lv J, Cao XF, Ji L, Zhu B, Wang DD and Tao L: Association of β-catenin, Wnt1, Smad4, Hoxa9, and Bmi-1 with the prognosis of esophageal squamous cell carcinoma. Med Oncol 2012; 29: 151-60.
23. Zhang L, Li K, Lv Z, Xiao X and Zheng J: The effect on cell growth by Wnt1 RNAi in human neuroblastoma SH-SY5Y cell line. Pediatr Surg Int 2009; 25: 1065-71.
24. Fiorentino M, Zadra G, Palescandolo E, Fedele G, Bailey D and Fiore C: Overexpression of fatty acid synthase is associated with palmitoylation of Wnt1 and cytoplasmic stabilization of beta-catenin in prostate cancer. Lab Invest 2008; 88: 1340-8.
25. Wei W, Chua MS, Grepper S and So SK: Blockade of Wnt-1 signaling leads to anti-tumor effects in hepatocellular carcinoma cells. Mol Cancer 2009; 8: 76.
26. Zhang Z, Zhang L, Zhang L, Jia L, Wang P and Gao Y: Association of Wnt2 and sFRP4 expression in the third-trimester placenta in women with severe preeclampsia. Reprod Sci 2013; 20: 981-9.
27. Bravo DT, You L, Mazieres J, He B, Xu Z and Jablons DM: Targeting Wnt-2 in Mesothelioma and Lung Cancer. Clinical Lung Cancer 2008; 9: 289.
28. Guo B, Wu L, Wang X and Tu Z: Expression Wnt2 in breast cancer tissues and sera of the patients. Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi 2013; 29: 633-6.
29. Katoh M: Differential regulation of WNT2 and WNT2B expression in human cancer. Int J Mol Med 2001; 8: 657-60.
30. Katoh M and Katoh M: Transcriptional regulation of WNT2B based on the balance of Hedgehog, Notch, BMP and WNT signals. Int J Oncol 2009; 34: 1411-5.
31. Wang H, Fan L, Xia X, Rao Y, Ma Q and Yang J: Silencing Wnt2B by siRNA interference inhibits metastasis and enhances chemotherapy sensitivity in ovarian cancer. Int J Gynecol Cancer 2012; 22: 755-61.
32. Nakashima N, Liu D, Huang CL, Ueno M, Zhang X and Yokomise H: Wnt3 gene expression promotes tumor progression in non-small cell lung cancer. Lung Cancer 2012; 76: 228-34.
33. Katoh M: Regulation of WNT3 and WNT3A mRNAs in human cancer cell lines NT2, MCF-7, and MKN45. Int J Oncol 2002; 20: 373-7.
34. Kim M, Lee HC, Tsedensodnom O, Hartley R, Lim YS and Yu E: Functional interaction between Wnt3 and Frizzled-7 leads to activation of the Wnt/beta-catenin signaling pathway in hepatocellular carcinoma cells. J Hepatol 2008; 48: 780-91.
35. Kaur N, Chettiar S, Rathod S, Rath P, Muzumdar D and Shaikh ML: Wnt3a mediated activation of Wnt/β-catenin signaling promotes tumor progression in glioblastoma. Mol Cell Neurosci 2013; 54: 44-57.
36. Verras M, Brown J, Li X, Nusse R and Sun Z: Wnt3a growth factor induces androgen receptor-mediated transcription and enhances cell growth in human prostate cancer cells. Cancer Res 2004; 64: 8860-6.
37. Kawaguchi-Ihara N, Murohashi I, Nara N and Tohda S: Promotion of the self-renewal capacity of human acute leukemia cells by Wnt3A. Anticanc Res 2008; 28: 2701-4.
38. Qiang YW, Shaughnessy JD and Yaccoby S: Wnt3a signaling within bone inhibits multiple myeloma bone disease and tumor growth. Blood 2008; 112: 374-82.
39. Garcia-Castro B, Alvarez-Zavala M, Riveros-Magana AR, Ortiz-Lazareno PC, Ratkovich-Gonzalez S and Hernandez-Flores G: Restoration of WNT4 inhibits cell growth in leukemia-derived cell lines. BMC Cancer 2013; 13: 557.
40. Roelink H, Wagenaar E, Lopes da Silva S and Nusse R: Wnt-3, a gene activated by proviral insertion in mouse mammary tumors, is homologous to int-1/ Wnt-1 and is normally expressed in mouse embryos and adult brain. Proc Natl Acad Sci USA 1990; 87: 4519-23.
41. Peltoketo H, Allinen M, Vuosku J, Kujala S, Lundan T and Salminen A: Characterization and expression of the human WNT4; lack of associated germline mutations in high--to moderate--risk breast and ovarian cancer. Cancer Lett 2004; 213(1): 83-90.
42. Garnis C, Campbell J, Davies JJ, Macaulay C, Lam S and Lam WL: Involvement of multiple developmental genes on chromosome 1p in lung tumorigenesis. Hum Mol Genet 2005; 14: 475-82.

43. Lu W, Wei W, de Bock GH, Zhou H, Li Q and Shen X: The roles of Wnt5a, JNK and paxillin in the occurrence of metastasis of pancreatic adenocarcinoma. Int J Clin Oncol 2013 [Epub ahead of print]
44. Da Forno PD, Pringle JH, Hutchinson P, Osborn J, Huang Q and Potter L: WNT5A expression increases during melanoma progression and correlates with outcome. Clin Cancer Res 2008; 14: 5825-32.
45. Li J, Ying J, Fan Y, Wu L, Ying Y and Chan AT: WNT5A antagonizes WNT/β-catenin signaling and is frequently silenced by promoter CpG methylation in esophageal squamous cell carcinoma. Cancer Biol Ther 2010; 10: 617-24.
46. Leris AC, Roberts TR, Jiang WG, Newbold RF and Mokbel K: WNT5A expression in human breast cancer. Anticancer Res 2005; 25: 731-4.
47. Nitzki F, Zibat A, Konig S, Wijgerde M, Rosenberger A and Brembeck FH: Tumor stroma-derived Wnt5a induces differentiation of basal cell carcinoma of Ptch-mutant mice via CaMKII. Cancer Res 2010; 70: 2739-48.
48. Kato S, Hayakawa Y, Sakurai H, Saiki I and Yokoyama S: Mesenchymal-transitioned cancer cells instigate the invasion of epithelial cancer cells through secretion of WNT3 and WNT5B. Cancer Sci 2013 [Epub ahead of print]
49. Saitoh T and Katoh M: Expression and regulation of WNT5A and WNT5B in human cancer: up-regulation of WNT5A by TNFalpha in MKN45 cells and up-regulation of WNT5B by beta-estradiol in MCF-7 cells. Int J Mol Med 2002; 10: 345-9.
50. Mangioni S, Vigano P, Lattuada D, Abbiati A, Vignali M and Di Blasio AM: Overexpression of the Wnt5b gene in leiomyoma cells: implications for a role of the Wnt signaling pathway in the uterine benign tumor. J Clin Endocrinol Metab 2005; 90: 5349-55.
51. Saitoh T and Katoh M: Molecular cloning and characterization of human WNT5B on chromosome 12p13.3 region. Int J Oncol 2001; 19: 347-51.
52. Yuan G, Regel I, Lian F, Friedrich T, Hitkova I and Hofheinz RD: WNT6 is a novel target gene of caveolin-1 promoting chemoresistance to epirubicin in human gastric cancer cells. Oncogene 2013; 32: 375-87.
53. Kirikoshi H, Sekihara H and Katoh M: WNT10A and WNT6, clustered in human chromosome 2q35 region with head-to-tail manner, are strongly coexpressed in SW480 cells. Biochem Biophys Res Commun 2001; 283: 798-05.
54. Benhaj K, Akcali KC and Ozturk M: Redundant expression of canonical Wnt ligands in human breast cancer cell lines. Oncol Rep 2006; 15: 701-7.
55. Kondratov AG, Kvasha SM, Stoliar LA, Romanenko AM, Zgonnyk YM and Gordiyuk VV: Alterations of the WNT7A gene in clear cell renal cell carcinomas. PLoS One 2012; 7: e47012.
56. Yoshioka S, King ML, Ran S, Okuda H, MacLean JA and McAsey ME: WNT7A regulates tumor growth and progression in ovarian cancer through the WNT/β-catenin pathway. Mol Cancer Res 2012; 10(3): 469-82.
57. Kirikoshi H and Katoh M: Expression of WNT7A in human normal tissues and cancer, and regulation of WNT7A and WNT7B in human cancer. Int J Oncol 2002; 21: 895-00.
58. Zheng D, Decker KF, Zhou T, Chen J, Qi Z and Jacobs K: Role of WNT7B -induced noncanonical pathway in advanced prostate cancer. Mol Cancer Res 2013; 11: 482-93.
59. Kirikoshi H, Sekihara H and Katoh M: Molecular cloning and characterization of human WNT7B. Int J Oncol 2001; 19: 779-83.
60. Bui TD, O Brien T, Crew J, Cranston D and Harris AL: High expression of Wnt7b in human superficial bladder cancer *vs.* invasive bladder cancer. Br J Cancer 1998; 77: 319-24.
61. Saitoh T, Mine T and Katoh M: Expression and regulation of WNT8A and WNT8B mRNAs in human tumor cell lines: up-regulation of WNT8B mRNA by beta-estradiol in MCF-7 cells, and down-regulation of WNT8A and WNT8B mRNAs by retinoic acid in NT2 cells. Int J Oncol 2002; 20: 999-03.
62. Saitoh T and Katoh M: Molecular cloning and characterization of human WNT8A. Int J Oncol 2001; 19: 123-7.
63. Lee KH, Li M, Michalowski AM, Zhang X, Liao H, Chen L: A genomewide study identifies the Wnt signaling pathway as a major target of p53 in murine embryonic stem cells. Proc Natl Acad Sci U S A 2010; 107: 69-74.
64. Andrade Filho PA, Letra A, Cramer A, Prasad JL, Garlet GP and Vieira AR: Insights from studies with oral cleft genes suggest associations between WNT-pathway genes and risk of oral cancer. J Dent Res 2011; 90: 740-6.
65. Saitoh T, Mine T and Katoh M: Up-regulation of WNT8B mRNA in human gastric cancer. Int J Oncol 2002; 20: 343-8.
66. An CH, Kim SS, Kang MR, Kim YR, Kim HS and Yoo NJ: Frameshift mutations of ATBF1, WNT9A, CYLD and PARK2 in gastric and colorectal carcinomas with high microsatellite instability. Pathology 2010; 42: 583-5.
67. Kirikoshi H, Sekihara H and Katoh M: Molecular cloning and characterization of WNT14B, a novel member of the WNT gene family. Int J Oncol 2001; 19: 947-52.
68. Chen H, Wang Y and Xue F: Expression and the clinical significance of Wnt10a and Wnt10b in endometrial cancer are associated with the Wnt/β-catenin pathway. Oncol Rep 2013; 29: 507-14.
69. Hsu RJ, Ho JY, Cha TL, Yu DS, Wu CL and Huang WP: WNT10A plays an oncogenic role in renal cell carcinoma by activating WNT/β-catenin pathway. PLoS One 2012; 7: e47649.
70. Kirikoshi H, Inoue S, Sekihara H and Katoh M: Expression of WNT10A in human cancer. Int J Oncol 2001; 19: 997-01.
71. Modder UI, Oursler MJ, Khosla S and Monroe DG: Wnt10b activates the Wnt, notch, and NFκB pathways in U2OS osteosarcoma cells. J Cell Biochem 2011; 112: 1392-02.
72. Yoshikawa H, Matsubara K, Zhou X, Okamura S, Kubo T and Murase Y: WNT10B functional dualism: beta-catenin/Tcf-dependent growth promotion or independent suppression with deregulated expression in cancer. Mol Biol Cell 2007; 18: 4292-303.
73. Kirikoshi H and Katoh M: Expression and regulation of WNT10B in human cancer: up-regulation of WNT10B in MCF-7 cells by beta-estradiol and down-regulation of WNT10B in NT2 cells by retinoic acid. Int J Mol Med 2002; 10: 507-11.
74. Posviatenko AV, Kulikova KV, Gnuchev NV, Georgiev GP, Kibardin AV and Larin SS: Functional properties of the WNT11 new isoform, expressed in colon carcinoma cell line HT29. Mol Biol (Mosk) 2012; 46: 129-38.
75. Toyama T, Lee HC, Koga H, Wands JR and Kim M: Noncanonical Wnt11 inhibits hepatocellular carcinoma cell proliferation and migration. Mol Cancer Res 2010; 8: 254-65.
76. Kirikoshi H, Sekihara H and Katoh M: Molecular cloning and characterization of human WNT11. Int J Mol Med 2001; 8: 651-6.

77. Sun Y, Campisi J, Higano C, Beer TM, Porter P and Coleman I: Treatment-induced damage to the tumor microenvironment promotes prostate cancer therapy resistance through WNT16B. Nat Med 2012; 18: 1359-68.

78. Teh MT, Blaydon D, Ghali LR, Briggs V, Edmunds S and Pantazi E: Role for WNT16B in human epidermal keratinocyte proliferation and differentiation. J Cell Sci 2007; 120: 330-9.

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