Review Article

Review on Cancer Cell Line Studies

S.Dhanalakshmi*, G. Sangeetha, K. Lokesh, U. Aleemasahada, Deng Arok deng
Department of Pharmacognosy, School of Pharmaceutical Sciences, Vels Institute of ScienceTechnology and Advanced Studies (VISTAS), Vels University, Old pallavaram, Chennai, India.
***Corresponding author's E-mail:** dhanadinesh2011@gmail.com

Accepted on: 12-10-2016; **Finalized on:** 30-11-2016.

ABSTRACT

Cancer cells that keep dividing and growing over time, under certain conditions in a laboratory. Cancer cell lines are used in research to study the biology of cancer and to test cancer treatments. Cancer cell lines have been widely used for research purposes and proved to be a useful tool in the genetic approach, and its characterization shows that they are, in fact, an excellent model for the study of the biological mechanisms involved in cancer [1.] The use of cancer cell lines allowed an increment of the information about the deregulated genes and signaling pathways in this disease. Cell lines (BEL-7402, NSCLC, NCI-H125, H157, etc.) which have been screened by Cell proliferation/cytotoxicity assay, MTT assay, Radioimmunoassay, TUNEL assay, Anchorage independent clonogenic assay, Ney fakh assay, Caspase-3/9 assay etc. After the in vitro screen, the most sensitive cancer cell lines can be selected for further tested in xeno graft or orthotopic tumor models in mice or rats (in vivo).

Keywords: Cancer cell line, Signalling pathway, Tumour.

INTRODUCTION

In the last few decades, human immortal rate due to cancer (Residents of cells from a multi cellular organism which would normally not proliferate indefinitely but, due to mutation, have evaded normal cellular senescence and instead can keep undergoing division [1]. Cancer is one of the most common cancers among women worldwide and disproportionately affects women in developing countries [2].Cancer is a multi factorial and multistep disease caused by the accumulation of multiple hits which involves genetic and epigenetic alterations leading to aberrant expression of genes involved in initiation, progression and promotion of carcinogenesis[3]. Endometrial cancer (EC) is one of the most common malignancies of the female reproductive system [4].

CANCER CELL LINES

Cell lines derived from tumours are the most frequently utilized models in cancer research and their use has advanced the understanding of cancer biology tremendously over the past decades. Genomic differences between cancer cell lines and tissue samples have been pointed out in several studies [5].

Cancer cell lines are frequently used as *in vitro* tumour models. Recent molecular profiles of hundreds of cell lines from The Cancer Cell Line Encyclopedia and thousands of tumour samples from the Cancer Genome Atlas now allow a systematic genomic comparison of cell lines and tumours. We identify several rarely used cell lines that more closely resemble cognate tumour profiles than commonly used cell lines, and we propose these lines as the most suitable models of ovarian cancer. Our results indicate that the gap between cell lines and tumours can be bridged by genomically informed choices of cell line models for all tumour types.8/

Lung Cancer

(MiTian, 2015) A549 human lung cancer cells were cultured *in vitro* and treated with oxycodone or morphine at various concentrations (10, 20 and 40 μg/ml). The levels of vascular endothelial growth factor (VEGF) and urokinase type plasminogen activator (uPA) were detected using enzyme linked immunosorbent assay. They concluded oxycodone was more effective in inhibiting the proliferation and migration of A549 lung cancer cells, as compared with morphine. These findings support the hypothesis that oxycodone may exert these effects on A549 tumor cells by modulating the expression levels of p53, Bax, Bcl-2, VEGF, ICAM-1 and uPA.

Breast Cancer

(S. Rezania, 2016) They conclude that GIRK1d acts as a dominant negative constituent of functional GIRK complexes present in the plasma membrane of MCF-7 cells, while over expression of GIRK1a and GIRK1c augmented their activity. The core component responsible for the cancerogenic action of GIRK1 is apparently presented by a segment comprising amino acids 235–402, that is present exclusively in GIRK1a and GIRK1c, but not GIRK1d (positions according to GIRK1a primary structure).

Prostate cancer

(Jinliang Liu, 2016) They investigated the role of lncRNA-THBS4-003 in the pathogensis of P Ca. The effects of forced THBS4 knockdown and lncRNA-THBS4-003

knockdown in the two PCa cell lines, DU145 and PC-3, were evaluated using cell migration and invasion assays, as well as using Western blot analysis. These findings suggested that the reciprocal regulation of lncRNA-THBS4-003 and THBS4 contributed to the pathogenesis of P Ca. Therefore silencing lncRNA-THBS4-003 or THBS4 may inhibit P Ca cell migration and invasion, and regulate the levels of MMP-9 through the mitogen activated protein kinase signaling pathway

Bladder Cancer

(Sunge Han Kim et al, 2016) The cisplatin sensitive human BC cell line (T24) and the cisplatin resistant BC cell line, T24R2, were used for microarray analysis to determine the differential expression of genes that are significant in cisplatin resistance. Candidate up regulated genes belonging to three well-known cancer-related KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways (p53 tumor suppressor, apoptosis, and cell cycle) were selected from the microarray data. These candidate genes, differentially expressed in T24 and T24R2, were then confirmed by quantitative RT-PCR and western blot.

Gastric cancer

(Youqing Xu, 2015**)** Gastric cancer tissues and cell lines BGC-823, SGC-7901, and HGC-27 were used to analyze miR-140 levels compared to normal tissues and cell line GES-1. In HGC-27 cells transfected with miR-140 mimic, we performed MTT, colony formation assay, and cell cycle assay by flow cytometry. SOX4, a predicted target of miR-140, was mutated to verify its regulation by miR-140, and was over expressed to analyze its function in cell proliferation. Doxorubicin treatment was performed to investigate the effect of miR-140 on drug resistance suggest that miR-140 directly inhibits *SOX4*, which might be one of its mechanisms in suppressing gastric cancer cell proliferation

Endometrial Cancer

(Stephen Charnock-Jones, 1993)Four species of VEGF were expressed by the endometrial carcinoma cell lines Ishikawa, HEC 1-A, and HEC 1-B. Estradiol increased steady-state levels of mRNA encoding VEGF in a dose- and time-dependent manner in HEC 1-A cells. Conditioned medium from these cells possessed angiogenic activity that was depleted by passage through a heparin affinity column. None of the cell lines demonstrated mRNA for acidic or basic fibroblast growth factor (FGF), despite previous reports of the identification of immune reactive basic FGF in HEC 1-A and HEC -B cells. These findings show that VEGFs, not FGFs, are the principal angiogenic growth factors secreted by these cells and that human endometrium expresses a secreted angiogenic growth factor whose site of expression changes during the menstrual cycle.

S.No	Cancer cell line	Cancerous Part	Reference
1.	HER2	Breast	1.
2.	The NSCLC cell line NCI-H3255 (Non – small-cell lung cancer)	Lung	2.
3.	MCF-7	Breast	
4.	MCF7, ZR75 and T47D	Breast	4.
5.	600MPE	Breast	5.
6.	BT483	Breast	5.
7.	BT549	Breast	5.
8.	PC-3	Prostate cancer	6.
9.	PC-93	Prostate cancer	7.
10	DU-145 , TSU-Pr1	Prostate cancer	8.
11.	LNCaP	Prostate cancer	9.
12.	C-4 LNCaP	Prostate cancer	10
13	MDA PCa 2a	Prostate cancer	11.
14	MDA PCa 2b	Prostate cancer	12.
15	ALVA-101	Prostate cancer	13.
16	22Rv1	Prostate cancer	14.
17	PPC-1	Prostate cancer	15
18	P69SV40T	Prostate cancer	16
19	RWPE-2	Prostate cancer	17
20	RT4	Bladder	18

21	UMUC3	Bladder	19
22	SWBC1	Bladder	20
23	TCC	Bladder	21
24	T24	Bladder	22
25	T24/83	Bladder	23
26	SW 1573 cell lines	Bladder	24
27	RT4, 647V, and 486P	Bladder	25
28	HT1376 and KoTCC-1,	Bladder	26
29	ErbB2, KRT7, KRT20, Muc5AC	Gastric Cancer	27
30	AGS, Hs746t and KATO-III, NCI-N87	Gastric Cancer	28
31	Ck 8, 18, 19, CEA and CA-19-9	Gastric Cancer	29
32	SNU-16	Gastric Cancer	30
33	HGT-1 cell	Gastric Cancer	31
34	SNU-182, sNU-423 , SNU-449, SNU-475	Liver Cancer	32
35	NCI-N87 [N87]	Stomace : Liver	33
36	SK-HEP-1	liver/ascites	34
37	MC/9	Liver	35
38	BEL-7402	Liver	36
39	KIM-1, KYN-1, KYN-2, KYN-3, HAK-1A, HAK-1B, HAK-2, HAK-3, HAK-4, HAK-5 and HAK-6	Liver	37
40	HT 29mdr Human	Human Colon cancer	38
41	PK1, CfPAC1, AsPC1	Human Pancreatic cancer	39
42	HL-60	Human Promyelocytic Leukemia	40
43	SNU, KATO III	Stomach cancer	41
44	A2780 and A1847	Ovarian cancer	42
45	A1847/CP6	Ovarian cancer	43
46	A2780/C	Ovarian cancer	44
47	A2780/cp70	Ovarian cancer	45
48	LL and H322	Ovarian : lung cancer	46
49	Ishikawa, HEC 1-A, and HEC 1-B.	Endometrial cancer	47
50	RER+, hMSH2	Endometrial cancer	48
51	HEC-1A and HEC-1B	Endometrial cancer	49
52	Hec-1A, KLE, and RL95-2	Endometrial cancer	50
53	RUCA-I cells, human Ishikawa and ECC-1 cells	Endometrial cancer	51
54	EN-1078D	Endometrial cancer	52

From this review it is concluded that cell lines are exceptionally versatile in the types of studies they may be used in. Immortalized cell lines are the *in vitro* equivalent of cancerous cells. Not only can they be build *in vitro* but can also be injected into mice to form xeno graft models of prostate cancer progression. They can be transformed and reviewed over time to disposes equential events that occur as a result of specific stimulus.

REFERENCES

1. Federico Cappu studied the, explain expression by using cancer cell line study, the Expression *of EGFR gene mutuation in Lung Cancer*, *Clin. Cancer Res.* Volume: 3, 2493–2500.
2. Soule H.D, reported the Human Cell Line from a Pleural Effusion Derived from a Breast Carcinoma *In VitroCell Dev. Biol. Anim.* 24, 423–431.
3. Bruce Westley *, A secreted glycoprotein induced by estrogen in human breast cancer cell lines *,J. Cancer,*Volume 20,Issue 2,June 1980, Pages 353-362.

4. Richard M. Neve, reported the collection of breast cancer cell lines for the study of functionally distinct cancer subtypes.*Clin.Cancer*, Vol: 5, 478-481.
5. Zaman, G. J. R., and Borst, P. MRP, mode of action and role in MDR. In: S. Gupta and T. Tsuruo (eds.), *Multidrug Resistance in CancerCells*, pp. 95"107.New York: John Wiley & Sons, 1996.
6. Claas, F. H. J. and van Steen brugge, G. J. (1983) Expression of HLA-like structures on a permanent human tumor line PC-93. *Tissue Antigens* 21, 227–232.
7. Kaighn, M. E., Narayan, K. S., Ohnuki, Y., Lechner, J. F., and Jones, L. W. (1979) Establishment and characterization of a human prostatic carcinoma cell line (PC-3). *Invest. Urol.* 17, 16–23.
8. Horoszewicz, J. S., Leong, S. S., Chu, T. M., Wajsman, Z. L., Friedman, M., Papsidero,et al. (1980) The LNCaP cell line: A new model for studies on human prostaticcarcinoma. *Prog.Clin. Biol. Res.* 37, 115–132.
9. 9. Wu, H.-C., Hsieh, J. T., Gleave, M. E., Brown, N. M., Pathak, S., and Chung, L. W.K. (1994) Derivation of androgen-independent LNCaP prostatic cancer cell sublines:Role of bone stromal cells. *Int. J. Cancer* 57, 406–412.
10. Navone, N. M., Olive, M., Ozen, M., Davis, R., Troncoso, P., Tu, S. M., et al. (1997) Establishment of two human prostate cancer cell lines derived from a singlebone metastasis. *Clin.Cancer Res.* 3, 2493–2500.
11. Navone, N. M., Rodriquez-Vargas, M. C., Benedict, W. F., Troncoso, P., Mc Donnell,T. J., Zhou, J. H., Luthra, R., et al. (2000) TabBO: A model reflecting common molecular features of androgen-independent prostate cancer. *Clin. Cancer Res.* 6, 1190–1197.
12. Plymate, S. R., Loop, S. M., Hoop, R. C.,Wiren, K. M., Ostenson, R., Hryb, D. J.,et al. (1991) Effects of sex hormone binding globulin (SHBG) on human prostaticcarcinoma. *J. Steroid Biochem. Mol. Biol.* 40, 833–839.
13. 13. Sramkoski, R. M., Pretlow, T. G. II, Giaconia, J. M., Pretlow, T. P., Schwartz, S.,Sy, M. S., et al. (1999) A new human prostate carcinoma cell line, 22Rv1. *In VitroCell Dev. Biol. Anim.* 35, 403–409.
14. Brothman, A. R., Lesho, L. J., Somers, K. D., Wright, G. L. Jr., and Merchant, D. J. (1989) Phenotypic and cytogenetic characterization of a cell line derived from primaryprostatic carcinoma. *Int. J. Cancer* 44, 898–903.
15. Bae,V. L., Jackson-Cook,Brothman C.K, Maygarden, S. J., and Ware, J. L.(1994) Tumorigenicity of SV40 T antigen immortalized human prostate epithelialcells: Association with decreased epidermal growth factor receptor expression. *Int.J. Cancer* 58, 721–729
16. 16. Bello, D., Webber, M. M., Kleinman, H. K., Wartinger, D. D., and Rhim, J. S. (1997) Androgen responsive adult human prostatic epithelial cell lines immortalized by human papilloma virus *Carcinogenesis* 18, 1215–1223.
17. Rhim, J. S., Webber, M. M., Bello, D., Lee, M. S., Arnstein, P., Chen, L. S.,(1994) Stepwise immortalization and transformation of adult human prostateepithelial cells by a combination of HPV-18 and v-Ki-ras.*Proc. Natl. Acad. Sci.USA* 91, 11874–11878.
18. Bergelson, J. M., Cunningham, Drouguett, G., Kurt-Jones, E. A., Krithivas, A., Hong, J. S., Horwitz, M. S., Crowell, R. L., and Finberg, R. W. Isolation of a common receptor for coxsackie B viruses , J.*Biotechnology*, 32-37.
19. Camps, J. L., Chang, S. M., Hsu, T. C., Freeman, M. R., Hong, S. J., Zhau, H. E., von Eschenbach, A. C., and Chung, L. W. K. Fibroblast-mediated acceleration of human epithelial tumor growth in vivo. Proc. Natl. Acad. Sci. USA, 81: 75–79, 1990.
20. Bai, M., Campisi, L., and Freimuth, P. Vitronectin receptor antibodies inhibit infection of Hela and A549 cells by adenovirus Type 12 but not by adenovirus Type 2. *J. Virol*., 68: 5925–5932, 1994.
21. 21. YingmingLi reported the Loss of Adenoviral Receptor Expression in Human Bladder Cancer Cells: A Potential Impact on the Efficacy of Gene Therapy, [*CANCER RESEARCH 59*, 325–330, January 15, 1999]
22. Julia Brown, Sarah J , Critical Evaluation of ECV304 as a Human Endothelial Cell Model Defined by Genetic Analysis and Functional Responses: A Comparison with the Human Bladder Cancer Derived Epithelial Cell Line T24/83 . LABORATORY INVESTIGATION, Vol. 80, No. 1, p. 37, 2000
23. Marcel Kool, Marcel de Haa.s .Analysis of Expression of cMOAT (MRP2), MRP3, MRP4, and MRP5, Homologues of the Multidrug Resistance-associated Protein Gene (MRP1), in Human Cancer Cell Lines.*CANCERRESEARCH*57, August 15, 19973537-3547.
24. Jan Lehmann , Antitumor Activity of the Antimicrobial Peptide Magainin II against Bladder Cancer Cell Lines, European *Urology*, Volume 50.Issue no. July 2006, Pages 141–147.
25. Taniguchi. K., Wada, M., Kohno, K., Nakamura.T., Kawabe, T., Kawakami, M., Kagotani, K., Okumura, K., Akiyama.S., and Kuwano, M. A human canalicularmultispecific organic anion transporter (cMOAT) gene is overexpressed in cisplatin resistant human cancer celllines with decreased drug accumulation, *Cancer Res*., 56: 129, 1996.
26. Hideaki Miyake, Koji Yoshimu.,Basic Fibroblast Growth Factor Regulates Matrix Metallo proteinases Production and In Vitro Invasiveness in Human Bladder Cancer Cell Lines., *Journal of Urology*, Volume 157,Issue 6, June 1997, Pages 2351–2355.
27. Jiafu Ji1,9, Xin Chen., Comprehensive analysis of the gene expression profiles in human gastric cancer cell lines., *Oncogene* (2002) 21, 6549 – 6556,
28. Basque JR, Chénard M, Gastric cancer cell lines as models to study human digestive functions .*Journal of Cell Biology*, 2001 Mar 26;81(2):241-51.
29. Peter Vollmers. H., Konrad Stulle., Characterization of four new gastric cancer cell lines. *Virchows Archiv B*December 1993, Volume 63, Issue 1, pp 335-343
30. Jae-GahbPark, Characteristics of Cell Lines Established from Human Gastric Carcinoma *CANCER RESEARCH* 50. 2773-2780. May I. I990.
31. Christian L. Laboisse, Characterization of a Newly Established Human Gastric Cancer Cell Line HGT-1 Bearing Histamine H2-Receptors1 Christian L. Laboisse, *CANCER RESEARCH* 42, 1541-1548, April 1982]
32. The Essentials of Life Science Research E Boven. *Int. J. Cancer* 1997, 70, 335–340.
33. N Ozturk et al. *PNAS* 2006, 103, 2178-2183.
34. A Ghosh; WD Heston. *J Cell Biochem*2004, 91, 528-39.
35. BS Taylor. *Mol Cell Proteomics* 2008, 7, 600-11.
36. PI Karakiewicz; GC Hutterer.*Nat ClinPractUrol*2008, 5, 82-92.

37. JW Liu et al. *Journal of Ehnopharmacology*2007, 113, 115–124.

38. H Yano et al. *Journal of Hepatology* 2004, 41, 782–789

39. U Valentiner .*Toxicology* 2002, 171, 187–199

40. M Miyazawa et al. *Cancer Letters* 2011, 305, 32–39

41. K Polkowski et al. *Cancer Letters* 2004, 203, 59–69.

42. Sachiko Okabe[1], Yumiko Ochia, Mechanistic Aspects of Green Tea as a Cancer Preventive: Effect of Components on Human Stomach Cancer Cell Lines, Japanese *Journal of Cancer Research,* Volume 90, Issue 7, pages 733–739, July 1999

43. Vincent, L., Pugh, T. D. & Goldfarb, S. (1979*) Cancer Res.* 39, 269-272.

44. Fiala, S., Fiala, A. E. & Dixon, B. (1972) *J. Natl. Cancer Inst*. 48, 1393-1401.

45. Neish, W. J. P. &Rylett, A. (1963) Biochem. Pharmacol. 12, 893-903. 44. Neish, W. J. P., Davies, H. N. & Reeve, P. M. (1964) Biochem. Pharmacol. 13, 1291-1303. 45. Fiala, S. &Fiala, E. S. (1973)

46. *J. Natl. CancerInst*. 51, 151-158. 46. Fiala, S. &Fiala, E. S. (1971) Naturwissensch aften 4, 330.

47. W Zhen, C J Link Jr, Increased gene-specific repair of cis platin inter strand cross-links in cisplatin-resistant human ovarian cancer cell lines. *Mol. Cell. Biol. S*eptember 1992vol. 12 no. 9 3689-3698

48. CJ, PinedoH M, Mechanisms of synergism between cisplatin and gemcitabine in ovarian and non-small-cell lung cancer cell lines, British journal of Cancer. 1999 Jun; 80(7): 981–990.

49. D. STEPHEN CHARNOCK-JONES, Identification and Localization of Alternately Spliced mRNAs for Vascular Endothelial Growth Factor in Human Uterus and Estrogen Regulation in Endometrial Carcinoma Cell Lines' BIOLOGY OF REPRODUCTION 48, 1120-1128 (1993)

50. Umar, Boyer Defective mismatch repair in extracts of colorectal and endometrial cancer cell lines exhibiting microsatellite instability. May 20, 1994 *The Journal of Biological Chemistry*269, 14367-14370.

51. Satya swaroop P.G. Human Endometrial Cancer Cell Cultures for Hormonal Studies, CANCER *RESEARCH* 38. 4367-4375, November 1978

52. Schneider CC., Inhibition of endometrial cancer cell lines by mifepristone (RU 486).*Journal society of Gynecology investigation,* 1998 Nov-Dec;5(6):334-8.

53. *G Vollmer, Endometrial* cancer: experimental models useful for studies on molecular aspects of endometrial cancer and carcinogenesis, Molecular Cell Physiology and Endocrinology, Institute of Zoology, Dresden University of Technology, Mommsenstr. 13, 01062 Dresden, Germany.

54. Marie-Claude Dery, Characterization of EN-1078D, a poorly differentiated human endometrial carcinoma cell line: a novel tool to study endometrial invasion *In vitro Reproductive Biology and Endocrinology* 20075, 38.

55. MiTian ,2016, Comparison Of Oxycodone And Morphine On The Proliferation, Apoptosis And Expression Of Related Molecules In The A549 Human Lung Adeno carcinoma Cell Line, Experimental And Therapeutic Medicine 12: 559-566, 2016.

56. S. Rezania, 2016 over expression of KCNJ3 gene splice variants affects vital parameters of the malignant breast cancer cell line MCF-7 in an opposing manner, *BMC Cancer* (2016) 16:628.

57. Jinliang Liu , 2016 Reciprocal Regulation Of Long Non coding Rnas Thbs4-003 And Thbs4 Control Migration And Invasion In Prostate Cancer Cell Lines, *Molecular Medicine Report*s 14: 1451-1458, 2016.

58. Sung Han Kim, regulated expression of BCL2, MCM7, and CCNE1 indicate cisplatin-resistance in the set of two human bladder cancer cell lines: T24 cisplatin sensitive and T24R2 cisplatin resistant bladder cancer cell lines, Basic and Translational Research, *Investig ClinUrol* 2016, 57, 63-72.

59. YouqingXu, 2015, Microrna-140 Inhibits Cell Proliferation In Gastric Cancer Cell Line HGC-27 By Suppressing SOX4, Med *Science* Monitor 2016, 22, 2243-2252.

60. Stephen Charnock-Jones, 1993, Identification and Localization of Alternately Spliced Mrnas For Vascular Endothelial Growth Factor In Human Uterus And Estrogen Regulation In Endometrial Carcinoma Cell Lines, *Biology Of Reproductio*n 48, 1120-1128 (1993).

Source of Support: Nil, **Conflict of Interest:** None.