Journal of Health Science Research, *Vol 4(1), 2019, 10-15*
ISSN (Online) : 2456-2688
DOI: 10.18311/jhsr/2019/23361

Telomere Length Alterations Associated with Breast, Thyroid and Cervical Cancers

Zorawar Singh* **and Priya Khangotra**

Department of Zoology, Khalsa College, Amritsar – 143001, Punjab, India; zorawarsinghs@rediffmail.com

Abstract

Telomeres are specialised structures of eukaryotic chromosomes that are present at each end of chromosomes. Telomeric length acts as a biological clock which helps to determine the life span of a cell and an organism. Telomeric shortening is also associated with various disease patterns including Dyskeratosis Congenita, Parkinson's disease, Ulcerative Colitis and chronic hepatitis. Any anomality in the telomeric function initiates genomic instability which increases the risk of cancer. Individuals with short telomeres are at increased risk for cancer. This review paper aims to find out the studies pointing out the relation of telomeric length and different types of cancers including breast, thyroid and cervical cancer. A positive correlation has been found in between telomeric shortening and cancer occurrence. Further studies are suggested to strengthen the association of telomere length alterations with specific cancer type.

Keywords: Biomarker, Breast Cancer, Cervical Cancer, Telomere, Telomeric Shortening, Telomerase, Thyroid Cancer

1. Introduction

Telomeres are specialised structures of eukaryotic chromosomes that are present at each end of chromosomes. Telomeres are TTAGGG tandem repeats capping chromosomal ends[1]. The sequence of nucleotides is repeated approximately 1500 to 2000 times in human cells. Telomeres are essential for providing protection to genome from nucleolytic degradation and inter-chromosomal fusion. Telomeres also maintain the chromosomal and genomic stability[2]. Telomerase is the enzyme that maintains the telomeric length by the addition of guanine rich repetitive sequences. Telomeric length acts as a biological clock which helps to determine the life span of a cell and an organism. The shortening of telomere length can be attributed to various reasons. Stress is one of the main causes of shortening of telomeres[3]. At high stress levels, function of telomerase is impaired and shortening of telomeres gets accelerated[3]. Smoking is the second reason for reduction in telomeric length. Obesity has also been found in correlation with increased oxidative stress, DNA damage and telomere shortening. An unbalanced dietary habit also enhances the telomere shortening.

Telomeric shortening is also associated with various disease patterns including Dyskeratosis Congenita (DC)[4,5], also known as Zinsser-Cole-Engman Syndrome, Parkinson's disease, Ulcerative Colitis[6] and chronic hepatitis[7]. Chronic Obstructive Pulmonary Disease (COPD)[8,9] and Type 2 diabetes[10–12] have also been found related with telomeric shortening. Leukocyte Telomere Length (LTL) is a biological marker of aging and shorter LTL is associated with adverse cardiovascular outcomes[13–17]. Telomere shortening was shown to parallel Alzheimer's Disease (AD) associated dementia[18]. Various other studies also reported the association of telomere shortening and AD[18–22].

*Author for correspondence

2. Telomeres as Biomarkers

Telomere alteration and telomerase activity have been observed in most human cancers and are known to be a feature of malignancy[23]. Individuals with short telomeres are at an increased risk for cancer, since short telomeres lead to genomic instability[24]. Hence, telomeres may act as biomarkers for the prediction and progression of a cancer type. The studies reporting the telomere length being associated in different cancer types are summarized below.

3. Breast Cancer

Breast cancer risk is affected by Telomere Length (TL). Telomere dysfunction plays a significant role in the initiation of genomic instability during carcinogenesis in human breast cancer[25]. Working schedule may impact risk of breast cancer as TL is affected by intensive night work schedule. Working continuously for six consecutive nights for more than 5 years was found to decrease TL (-3.18, 95% CI: -6.46 TO -0.58, P = 0.016). There was a lower risk of breast cancer in nurses having longer TL, who worked more than four (OR: 0.37, 95% CI: 0.16 – 0.79, P = 0.014) or five (OR: 0.31, 95% CI: 0.10 – 0.83, P = 0.029) simultaneous night shifts for 5 years or more[26]. In another study by Kammori et al.[27], a total of 44 breast cancer cases including 17 scirrhous, 15 papillotubular and 12 solid tubular carcinomas were investigated. Mean TL was found to be short in patients with large tumours, lymph node metastasis, vascular invasion and with third stage of tumour node metastasis. This data suggested the association of TL of cancer cells with the degree of cancer progression.

3.1 Genetic Polymorphisms in Breast Cancer

Several studies have reported an increase in breast cancer risk when patients are carriers of the CYP19 TTA polymorphism with > / = 10 repeats. In a study, a total of 180 postmenopausal healthy and 70 BC-diagnosed women were checked to understand the relationship between CYP19 TTA repetition polymorphism and telomere length. Patients with a BC diagnosis showed > 10 repetitions more frequently, compared with that of healthy women (50% vs. 23%, chi = 11.44, p = 0.0007)[28]. IGFBP7 promoter methylation status was evaluated by methylation-specific PCR and its expression levels were determined by western blotting. A comparison was done between breast cancer tissues and adjacent normal tissues among Turkish women. GFBP7 methylation was observed in 90% of tumour tissues and 59% of controls (P = 0.0002)[29]. Telomere dysfunction is known to activate ATM (Ataxia Telangiectasia Mutated)-mediated DNA damage response signalling pathways[30]. ATM participates in the signalling of telomere erosion, and inherited mutations in ATM have been associated with increased risk of cancer, particularly breast cancer. Renault et al.[31] measured mean TL and genotyped seven Single-nucleotide Polymorphisms (SNPs) recurrently associated with TL in large population-based studies. ATM mutation carriers (HetAT) individuals were found to be at increased risk of cancer (OR = 2.9, 95% CI = 1.2 – 4.4, P = 0.01), and particularly of breast cancer for women (OR = 2.9, 95% CI = 1.2 – 7.1, P = 0.02), in comparison to their non- HetAT relatives. Similarly, knockdown of HMBOX1 was found associated with increased apoptosis rate and reduced expression of ATM[32]. The non-histone chromatin binding protein High Mobility Group AT-hook protein 2 (HMGA2) plays important roles in the repair and protection of genomic DNA in embryonic stem cells and cancer cells. In a study, HMGA2 was found to prevent ATM-dependent pTRF2T188 phosphorylation and attenuate signalling via the telomere specific ATM-CHK2-CDC25C DNA damage signalling axis[33]. High Mobility Group Box 1 (HMGB1) in tumour cells include replenishing telomeric DNA and maintaining cell immortality. Downregulation of HMGB1 modulated telomere homeostasis by changing the level of telomere-binding proteins, such as TPP1 (PTOP), TRF1 and TRF2. This downregulation also inhibited the ATM signalling pathways[34]. In another study, the role of ATM-mediated DNA damage response signalling in Androgen Receptor (AR)-inactivated prostate cancer cells was investigated. The induction of telomere dysfunction in cells treated with AR-antagonists (Casodex or MDV3100) or AR-siRNA was associated with a dramatic increase in phosphorylation of ATM. ATM inhibitor induces apoptosis in AR-inactivated cells by blocking the repair of damaged DNA at telomeres[30].

4. Thyroid Cancer

Some studies have also been found reporting the association of TL and thyroid cancer[35–37]. Human epidermal growth factor receptor 2 (HER2) proto-

oncogene plays an important role in the development and progression of breast and gastric cancers. Amplification of HER 2 gene in differentiated thyroid cancer was found to be in correlation with telomere shortening[23]. 69 cases of differentiated thyroid cancers were investigated. The telomeres of thyroid cancers, especially follicular carcinomas, were found to be significantly shorter than those of adjacent normal tissues[23]. Similarly, the frequency of HER2 amplification, genetic variations in sporadic Papillary Thyroid Cancer (sPTC) and familial Papillary Thyroid Cancer (fPTC) and association with relative telomere length and BRAF mutational status were investigated. RTL was found to be shorter in fPTCs than sPTCs ($p < 0.001$) and HER2 amplification in fPTCs was found to be invariably associated with BRAF (V600E) mutation[38].

5. Cervical Cancer

Only a few studies reported the association of cervical cancer with telomere shortening. Various compounds may be involved in shortening of TL as Merghoub et al.[39] reported that tomentosin triggered telomere shortening and apoptosis in cervical cancer HeLa and SiHa cells. Similarly, Merghoub et al.[40] reported that the extracts from Inula viscosa L. target telomeres, induce apoptosis and overcome drug resistance in tumour cells. It was also found that extracts raised telomere shortening by suppressing the telomerase activity. Another study reported the association among HMBOX1, telomere length and radiosensitivity in cervical cancer cells. Knock-down of HMBOX1 was found to be associated with increased apoptosis rate and decreased expression of ATM, ATR, p-ATM, p-ATR and BRCA1[41].

6. Conclusion

Telomeric length determines the life span of a cell and an organism. Any change in telomeric function can result in genomic instability which in-turn increases the risk of cancer. Telomeric shortening is also associated with various disease patterns including Parkinson's disease,

Table 1. Studies describing the association of telomere shortening with different cancer types

S. No.	Author	Year	Type of cancer	Inference	Reference no.
	Samulin et al.	2017	Breast cancer	Telomere shortening is associated with breast cancer risk in workers with long periods of consecutive night shifts.	42
	Kammori et al.	2015	Breast cancer	Mean telomere length was found less in patients with TNM third stage; showed positive correlation with degree of cancer progression.	43
	Cassar et al.	2017	Breast cancer	BMP7 induces breast cancer cell ageing by a mechanism involving BMPRII receptor-and Smad3-mediated repression of the hTERT gene.	44
	Finot et al.	2017	Breast cancer	Genotoxic effect of ethyl paraben in the presence of S9 is associated with telomere shortening.	25
	Sugishita et al.	2013	Thyroid cancer	Amplification of the human epidermal growth factor receptor 2 gene in differentiated thyroid cancer correlates with telomere shortening.	23
	Merghoub et al.	2017	Cervical cancer	Tomentosin induced telomere shortening in cervical cancer cells in foetal fibroblast Wi38 and JW10 cells.	39
	Merghoub et al.	2016	Cervical cancer	IV-HE and IV-DF extracts from Inula Viscosa L. induces telomere shortening and apoptosis in cervical cancer cells.	40
	Zhou et al.	2017	Cervical cancer	Knockdown of HMBOX1 increases the radiosensitivity of cervical cancer cells through telomere shortening.	41

qPCR - Quantitative Polymerase Chain Reaction; **Q-FISH** - Quantitative Fluorescence in-situ Hybridization; **TNM** - Tumour Node Metastasis; **BMP7** - Bone Morphogenetic Protein-7; **hTERT** - Human Telomerase Reverse Transcriptase; **MN** - Micronucleus; **FISH** - Fluorescence in-situ Hybridization

ulcerative colitis and chronic hepatitis. Individuals with short telomeres are at increased risk for cancer. This paper reviewed the studies pointing out the relation of telomeric length and different types of cancers including breast, thyroid and cervical cancer. A positive correlation has been found in between telomeric shortening and cancer occurrence. Mean telomere lengths were found lesser in patients with cancer and showed a positive correlation with degree of cancer progression. Further correlative studies are recommended to strengthen the association of telomere length alterations with specific cancer type.

7. Conflict of Interest

None declared

8. References

1. Augustine TA, Baig M, Sood A, Budagov T, Atzmon G, Mariadason JM, Aparo S, Maitra R, Goel S. Telomere length is a novel predictive biomarker of sensitivity to anti-EGFR therapy in metastatic colorectal cancer. Br J Cancer. 2015; 112:313–8. DOI: bjc2014561 [pii];10.1038/bjc.2014.561
2. Augustine T, Maitra R, Goel S. Telomere length regulation through epidermal growth factor receptor signaling in cancer. Genes Cancer. 2017; 8:550–8. DOI: 10.18632/genesandcancer.140 [doi];140 [pii] https://doi.org/10.18632/genesandcancer.140
3. Biegler KA, Anderson AK, Wenzel LB, Osann K, Nelson EL. Longitudinal change in telomere length and the chronic stress response in a randomized pilot biobehavioral clinical study: Implications for cancer prevention. Cancer Prev Res (Phila). 2012; 5:1173–82. DOI: 1940-6207.CAPR-12-0008 [pii];10.1158/1940-6207.CAPR-12-0008
4. Frescas D, de LT. A TIN2 dyskeratosis congenita mutation causes telomerase-independent telomere shortening in mice. Genes Dev. 2014; 28:153–66. DOI: 28/2/153 [pii];10.1101/gad.233395.113
5. Lee JW. Telomere shortening by mutations in the RTEL1 helicase cause severe form of dyskeratosis congenita, Hoyeraal-Hreidarsson syndrome. Clin Genet. 2013; 84:210. DOI: 10.1111/cge.12175 [doi] https://doi.org/10.1111/cge.12175
6. Friis-Ottessen M, Bendix L, Kolvraa S, Norheim-Andersen S, De Angelis PM, Clausen OP. Telomere shortening correlates to dysplasia but not to DNA aneuploidy in long-standing ulcerative colitis. BMC Gastroenterol. 2014; 14:8. DOI: 1471-230X-14-8 [pii];10.1186/1471-230X-14-8
7. Piciocchi M, Cardin R, Cillo U, Vitale A, Cappon A, Mescoli C, Guido M, Rugge M, Burra P, Floreani A, Farinati F. Differential timing of oxidative DNA damage and telomere shortening in hepatitis C and B virus-related liver carcinogenesis. Transl Res. 2016; 168:122–33. DOI: S1931-5244(15)00298-4 [pii];10.1016/j.trsl.2015.08.012
8. Cordoba-Lanus E, Cazorla-Rivero S, Espinoza-Jimenez A, de-Torres JP, Pajares MJ, Aguirre-Jaime A, Celli B, Casanova C. Erratum to Telomere shortening and accelerated aging in COPD: Findings from the BODE cohort. Respir Res. 2017; 18:113. DOI: 10.1186/s12931-017-0589-7 [doi];10.1186/s12931-017-0589-7 [pii] https://doi.org/10.1186/s12931-017-0589-7
9. Cordoba-Lanus E, Cazorla-Rivero S, Espinoza-Jimenez A, de-Torres JP, Pajares MJ, Aguirre-Jaime A, Celli B, Casanova C. Telomere shortening and accelerated aging in COPD: Findings from the BODE cohort. Respir Res. 2017; 18:59. DOI: 10.1186/s12931-017-0547-4 [doi];10.1186/s12931-017-0547-4 [pii] https://doi.org/10.1186/s12931-017-0547-4
10. Liu Z, Zhang J, Yan J, Wang Y, Li Y. Leucocyte telomere shortening in relation to newly diagnosed type 2 diabetic patients with depression. Oxid Med Cell Longev. 2014; 2014:673959. DOI: 10.1155/2014/673959 [doi] https://doi.org/10.1155/2014/673959
11. Ping F, Li ZY, Lv K, Zhou MC, Dong YX, Sun Q, Li YX. Deoxyribonucleic acid telomere length shortening can predict the incidence of non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus. J Diabetes Investig. 2017; 8:174–80. DOI: 10.1111/jdi.12555 https://doi.org/10.1111/jdi.12555
12. Tajbakhsh S, Aliakbari K, Hussey DJ, Lower KM, Donato AJ, Sokoya EM. Differential telomere shortening in blood versus arteries in an animal model of type 2 diabetes. J Diabetes Res. 2015; 2015:153829. DOI: 10.1155/2015/153829 https://doi.org/10.1155/2015/153829
13. Hammadah M, Al M, I, Wilmot K, Ramadan R, Abdelhadi N, Alkhoder A, Obideen M, Pimple PM, Levantsevych O, Kelli HM, Shah A, Sun YV, Pearce B, Kutner M, Long Q, Ward L, Ko YA, Hosny MK, Lin J, Zhao J, Bremner JD, Kim J, Waller EK, Raggi P, Sheps D, Quyyumi AA, Vaccarino V. Telomere shortening, regenerative capacity, and cardiovascular outcomes. Circ Res. 2017; 120:1130–8. DOI: CIRCRESAHA.116.309421 [pii];10.1161/CIRCRESAHA.116.309421
14. Baragetti A, Palmen J, Garlaschelli K, Grigore L, Pellegatta F, Tragni E, Catapano AL, Humphries SE, Norata GD, Talmud PJ. Telomere shortening over 6 years is associated with increased subclinical carotid vascular damage and worse cardiovascular prognosis in the general population. J Intern Med. 2015; 277:478–87. DOI: 10.1111/joim.12282 https://doi.org/10.1111/joim.12282
15. Chang AC, Ong SG, LaGory EL, Kraft PE, Giaccia AJ, Wu JC, Blau HM. Telomere shortening and metabolic com-

promise underlie dystrophic cardiomyopathy. Proc Natl Acad Sci USA. 2016; 113:13120–5. DOI: 1615340113 [pii];10.1073/pnas.1615340113
16. Fyhrquist F, Saijonmaa O, Strandberg T. The roles of senescence and telomere shortening in cardiovascular disease. Nat Rev Cardiol. 2013; 10:274–83. DOI: nrcardio.2013.30 [pii];10.1038/nrcardio.2013.30
17. Guzzardi MA, Iozzo P, Salonen M, Kajantie E, Eriksson JG. Rate of telomere shortening and metabolic and cardiovascular risk factors: A longitudinal study in the 1934-44 Helsinki Birth Cohort Study. Ann Med. 2015; 47:499–505. DOI: 10.3109/07853890.2015.1074718 https://doi.org/10.3109/07853890.2015.1074718
18. Jenkins EC, Marchi EJ, Velinov MT, Ye L, Krinsky-McHale SJ, Zigman WB, Schupf N, Silverman WP. Longitudinal telomere shortening and early Alzheimer's disease progression in adults with down syndrome. Am J Med Genet B Neuropsychiatr Genet. 2017; 174:772–8. DOI: 10.1002/ajmg.b.32575 https://doi.org/10.1002/ajmg.b.32575
19. Boccardi V, Pelini L, Ercolani S, Ruggiero C, Mecocci P. From cellular senescence to Alzheimer's disease: The role of telomere shortening. Ageing Res Rev. 2015; 22:1–8. DOI: S1568-1637(15)00037-9 [pii];10.1016/j.arr.2015.04.003
20. Cai Z, Yan LJ, Ratka A. Telomere shortening and Alzheimer's disease. Neuromolecular Med. 2013; 15:25–48. DOI: 10.1007/s12017-012-8207-9 https://doi.org/10.1007/s12017-012-8207-9
21. Liu M, Huo YR, Wang J, Wang C, Liu S, Liu S, Wang J, Ji Y. Telomere shortening in Alzheimer's disease patients. Ann Clin Lab Sci. 2016; 46:260-26–5. DOI: 46/3/260 [pii]
22. Zhan Y, Song C, Karlsson R, Tillander A, Reynolds CA, Pedersen NL, Hagg S. Telomere length shortening and Alzheimer disease - A mendelian randomization study. JAMA Neurol. 2015; 72:1202–3. DOI: 2452064 [pii];10.1001/jamaneurol.2015.1513
23. Sugishita Y, Kammori M, Yamada O, Poon SS, Kobayashi M, Onoda N, Yamazaki K, Fukumori T, Yoshikawa K, Onose H, Ishii S, Yamada E, Yamada T. Amplification of the human epidermal growth factor receptor 2 gene in differentiated thyroid cancer correlates with telomere shortening. Int J Oncol. 2013; 42:1589–96. DOI: 10.3892/ijo.2013.1848 https://doi.org/10.3892/ijo.2013.1848
24. Aviv A, Anderson JJ, Shay JW, Mutations, cancer and the telomere length paradox. Trends Cancer. 2017; 3:253–8. DOI: S2405-8033(17)30043-2 [pii];10.1016/j.trecan.2017.02.005
25. Finot F, Kaddour A, Morat L, Mouche I, Zaguia N, Cuceu C, Souverville D, Negrault S, Cariou O, Essahli A, Prigent N, Saul J, Paillard F, Heidingsfelder L, Lafouge P, Al JM, Hempel WM, El MM, Colicchio B, Dieterlen A, Jeandidier E, Sabatier L, Clements J, M'Kacher R. Genotoxic risk of ethyl-paraben could be related to telomere shortening. J Appl Toxicol. 2017; 37:758–71. DOI: 10.1002/jat.3425 https://doi.org/10.1002/jat.3425
26. Samulin EJ, Noto HO, Skare O, Lie JS, Petersen-Overleir M, Reszka E, Peplonska B, Zienolddiny S. Mechanisms of breast cancer risk in shift workers: association of telomere shortening with the duration and intensity of night work. Cancer Med. 2017; 6:1988–97. DOI: 10.1002/cam4.1135 https://doi.org/10.1002/cam4.1135
27. Kammori M, Sugishita Y, Okamoto T, Kobayashi M, Yamazaki K, Yamada E, Yamada T. Telomere shortening in breast cancer correlates with the pathological features of tumor progression. Oncol Rep. 2015; 34:627–32. DOI: 10.3892/or.2015.4063 https://doi.org/10.3892/or.2015.4063
28. Murillo-Ortiz B, Martinez-Garza S, Suarez GD, Castillo Valenzuela RD, Garcia Regalado JF, Cano VG. Association between telomere length and CYP19 TTTA repetition polymorphism in healthy and breast cáncer diagnosed women. Breast Cancer (Dove Med Press). 2017; 9:21–7. DOI: 10.2147/BCTT.S125431 [doi];bctt-9-021 [pii] https://doi.org/10.2147/BCTT.S125431
29. Kaya Z, Akkiprik M, Karabulut S, Peker I, Gullu AG, Ozmen T, Gulluoglu BM, Kaya H, Ozer A. Comparison of telomere length and insulin-like growth factor-binding protein 7 promoter methylation between breast cancer tissues and adjacent normal tissues in Turkish women. J Clin Lab Anal. 2017; 31. DOI: 10.1002/jcla.22083 https://doi.org/10.1002/jcla.22083
30. Reddy V, Wu M, Ciavattone N, McKenty N, Menon M, Barrack ER, Reddy GP, Kim SH. ATM inhibition potentiates death of androgen receptor-inactivated prostate cancer cells with telomere dysfunction. J Biol Chem. 2015; 290:25522–33. DOI: M115.671404 [pii];10.1074/jbc.M115.671404
31. Renault AL, Mebirouk N, Cavaciuti E, Le GD, Lecarpentier J, d'Enghien CD, Lauge A, Dondon MG, Labbe M, Lesca G, Leroux D, Gladieff L, Adenis C, Faivre L, Gilbert-Dussardier B, Lortholary A, Fricker JP, Dahan K, Bay JO, Longy M, Buecher B, Janin N, Zattara H, Berthet P, Combes A, Coupier I, Hall J, Stoppa-Lyonnet D, Andrieu N, Lesueur F. Telomere length, ATM mutation status and cancer risk in Ataxia-Telangiectasia families. Carcinogenesis. 2017; 38:994–1003. DOI: 3994029 [pii];10.1093/carcin/bgx074
32. Zhou S, Xiao Y, Zhuang Y, Liu Y, Zhao H, Yang H, Xie C, Zhou F, Zhou Y. Knockdown of homeobox containing 1 increases the radiosensitivity of cervical cancer cells through telomere shortening. Oncol Rep. 2017; 38:515–21. DOI: 10.3892/or.2017.5707 https://doi.org/10.3892/or.2017.5707
33. Natarajan S, Begum F, Gim J, Wark L, Henderson D, Davie JR, Hombach-Klonisch S, Klonisch T. High mobility group

A2 protects cancer cells against telomere dysfunction. Oncotarget. 2016; 7:12761–82. DOI: 6938 [pii];10.18632/oncotarget.6938

34. Ke S, Zhou F, Yang H, Wei Y, Gong J, Mei Z, Wu L, Yu H, Zhou Y. Downregulation of high mobility group box 1 modulates telomere homeostasis and increases the radiosensitivity of human breast cancer cells. Int J Oncol. 2015; 46:1051–8. DOI: 10.3892/ijo.2014.2793 https://doi.org/10.3892/ijo.2014.2793
35. Cantara S, Pisu M, Frau DV, Caria P, Dettori T, Capezzone M, Capuano S, Vanni R, Pacini F. Telomere abnormalities and chromosome fragility in patients affected by familial papillary thyroid cancer. J Clin Endocrinol Metab. 2012; 97:E1327–31. DOI: jc.2011-2096 [pii];10.1210/jc.2011-2096
36. Gramatges MM, Liu Q, Yasui Y, Okcu MF, Neglia JP, Strong LC, Armstrong GT, Robison LL, Bhatia S. Telomere content and risk of second malignant neoplasm in survivors of childhood cancer: A report from the Childhood Cancer Survivor Study. Clin Cancer Res. 2014; 20:904–11. DOI: 1078-0432.CCR-13-2076 [pii];10.1158/1078-0432.CCR-13-2076
37. He M, Bian B, Gesuwan K, Gulati N, Zhang L, Nilubol N, Kebebew E. Telomere length is shorter in affected members of families with familial nonmedullary thyroid cancer. Thyroid. 2013; 23:301–7. DOI: 10.1089/thy.2012.0270 https://doi.org/10.1089/thy.2012.0270
38. Caria P, Cantara S, Frau DV, Pacini F, Vanni R, Dettori T: Genetic heterogeneity of HER2 amplification and telomere shortening in papillary thyroid carcinoma. Int J Mol Sci. 2016; 17. DOI: ijms17101759 [pii];10.3390/ijms17101759
39. Merghoub N, El BH, Benbacer L, Gmouh S, Trentesaux C, Brassart B, Attaleb M, Madoulet C, Wenner T, Amzazi S, Morjani H, El MM. Tomentosin induces telomere shortening and caspase-dependant apoptosis in cervical cancer cells. J Cell Biochem. 2017; 118:1689–98. DOI: 10.1002/jcb.25826 https://doi.org/10.1002/jcb.25826
40. Merghoub N, El BH, Benbacer L, Gmouh S, Trentesaux C, Brassart B, Terryn C, Attaleb M, Madoulet C, Benjouad A, Amzazi S, El MM, Morjani H. Inula viscosa extracts induces telomere shortening and apoptosis in cancer cells and overcome drug resistance. Nutr Cancer. 2016; 68:131–43. DOI: 10.1080/01635581.2016.1115105 https://doi.org/10.1080/01635581.2016.1115105
41. Zhou S, Xiao Y, Zhuang Y, Liu Y, Zhao H, Yang H, Xie C, Zhou F, Zhou Y. Knockdown of homeobox containing 1 increases the radiosensitivity of cervical cancer cells through telomere shortening. Oncol Rep. 2017; 38:515–21. DOI: 10.3892/or.2017.5707 https://doi.org/10.3892/or.2017.5707
42. Samulin EJ, Noto HO, Skare O, Lie JS, Petersen-Overleir M, Reszka E, Peplonska B, Zienolddiny S. Mechanisms of breast cancer risk in shift workers: A.ssociation of telomere shortening with the duration and intensity of night work. Cancer Med 2017; 6:1988–97. DOI: 10.1002/cam4.1135 https://doi.org/10.1002/cam4.1135
43. Kammori M, Sugishita Y, Okamoto T, Kobayashi M, Yamazaki K, Yamada E, Yamada T. Telomere shortening in breast cancer correlates with the pathological features of tumor progression. Oncol Rep. 2015; 34:627–32. DOI: 10.3892/or.2015.4063 https://doi.org/10.3892/or.2015.4063
44. Cassar L, Nicholls C, Pinto AR, Chen R, Wang L, Li H, Liu JP. TGF-beta receptor mediated telomerase inhibition, telomere shortening and breast cancer cell senescence. Protein Cell. 2017; 8:39–54. DOI: 10.1007/s13238-016-0322-1;10.1007/s13238-016-0322-1 [pii] https://doi.org/10.1007/s13238-016-0322-1