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The expression and clinical value of LRP11, FUBP1 and TET1 in cervical cancer

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ABSTRACT

Cervical cancer is the second leading cause of cancer death among women worldwide. Identification of effective genes along with biological markers as targeting agents is very necessary for the diagnosis and treatment of this disease. Bioinformatics techniques along with genetic and molecular investigations have provided the possibility of studying different levels of information such as the genome, transcriptome, proteome, and metabolize with high depth and accuracy. The collection of these data provides comprehensive and valuable information about the investigated phenotypes, including complex diseases such as cancer. In this study, we examined three genes *LRP11*, *FUBP1*, and *TET1* related to cervical cancer. The results of this study showed that the level of expression of these genes is high in lymph nodes and the thyroid and is less in the pancreas and liver. Also, the expression level of the *FUBP1* gene is higher than that of *LRP11*, and the expression level of the *LRP11* gene is higher than that of *TET1*. Regarding the structure and proteomics of the studied genes, it can be seen that due to the presence of more domains in the *LRP11* and *FUBP1* genes, these genes probably independently participate in various functions and have a wider range of activity than the *TET1* gene. Also, the analysis of the stability of the examined genes showed that the stability of the *FUBP1* gene is relatively higher than that of the *TET1* gene, and this gene is also more stable than the *LRP11* gene. Considering that these genes are effective key genes for the early detection of cervical cancer, it is hoped that they will be used as markers in the diagnosis and treatment of cervical cancer.

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Introduction

In 2018, about 18 million new cancers were registered, and according to the statistics and information mentioned in the same year, cervical cancer ranked fourth among women's cancers in terms of disease incidence and mortality rate (1). It is one of the most dangerous and deadly diseases of the 20th century and it is expected to be one of the great challenges to human health in the 21st century. While infection with human papillomaviruses plays an important role in the development of cervical cancer, the presence of the virus alone is not sufficient to cause cancer. Genetics and environmental factors such as smoking and unhealthy eating habits also play a role in this. Today, mankind is constantly exposed to various carcinogenic factors such as mutations, radioactive substances, and chemical and environmental pollution (2). Every year, approximately 470,000 new cases of cervical cancer are diagnosed, and approximately 230,000 women around the world are diagnosed due to this. Most of the deaths (approximately 80%) occur in developing countries (3). The prevalence of cervical cancer is different all over the world the highest rate is in East Africa and the lowest in West Asia (4).

In addition to tumor suppressors and carcinogenic oncogenes, various receptors such as EPHA4, EPHA5, and EPHB2, endothelin receptors EDNRB and EDNRA, as well as nuclear receptors NR2C1 and NCOA3 are involved in cervical cancer disease (5). The use of new approaches, such as microarray gene expression profiles and RNA-seq, has provided an unprecedented look at the function of the genome. The accurate extraction of such data and their analysis makes it possible to accurately identify the genes and biological pathways involved in various diseases, including cancer. Considering the vast amount of information available in these data and their huge dimensions, the analysis of these data requires the use of information and bioinformatics networks that both facilitate the understanding of information for biologists and provide many tools for the analysis of existing networks.

Although infection with the human virus is necessary for the development of cervical cancer, it alone is not sufficient to explain cervical cancer; therefore, other risk factors such as genetic factors, specific host and their importance in the induction of cervical cancer should be known. Considering that gene expression profile studies in the last decade have provided significant molecular findings about oral cancer, sufficient screening and effective treatment strategies have not yet been achieved (5). In the investigations, genes such as *LRP11*, *FUBP1*, and *TET1* have been identified in cervical cancer. The present study was conducted to investigate the effect of these genes on cervical cancer. In general, the bioinformatics analysis and expression analysis of these influential genes can be further evaluated in order to develop new therapeutic and

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diagnostic methods.

LRP11 gene

The *LRP11* gene with accession number NM_032832 is located on chromosome 6 (6q25.1). This gene activates the binding of phosphoproteins and it is predicted that its location is in the plasma membrane. The number of amino acids, molecular weight, and isoelectric point of the number of exons were determined in Table 1 for the *LRP11* gene. *LRP11* has an effective role in proliferation, migration, and invasion and can be used as a useful prognostic marker for cancer diagnosis. Also, the *LRP11* gene is known as one of the therapeutic targets for patients with HSIL and cervical cancer (6-7). Figure 1(A) shows the location of this gene on the chromosome.

FUBP1 gene

The *FUBP1* gene with accession number NM_032832 is located on chromosome 1 (1p31.1). The number of amino acids, molecular weight, and isoelectric point of the number of exons were determined in Table 1 for the *FUBP1* gene. The protein made by this gene is a single-stranded protein that binds to a series of upstream elements such as FUSE and c-myc. Binding to FUSE leads to the up-regulation of the c-myc factor, which occurs mostly in undifferentiated cells. This protein has 3 specialized domains, the N-terminal region and the C-terminal region of the central DNA-binding domain. Evidence suggests that the N-terminal domain may suppress the activity of the C-terminal domain. This gene plays a role in the nervous systems of lung diseases, hepatitis, as well as oral diseases, and cervical cancer, and its expression has been seen in malignant tissues (8-12). Figure 1 (B) shows the location of this gene on the chromosome.

TET1 gene

The *TET1* gene with accession number NM_030625 is located on chromosome 10 (10q21.3). The number of amino acids, molecular weight, and isoelectric point of the number of exons were determined in Table 1 for the *TET1* gene. The *TET1* gene is also known as *LCX* and *KIAA1676*. And they play a role in epigenetic processes such as DNA methylation and gene expression. This gene belongs to the Tet methylcytosine dioxygenase family and plays an effective role in the activation of other genes. Diseases associated with *TET1* include Glioblastoma and Rett Syndrome and cervical cancer. The important paralog of this gene is *TET2* (13-17). Figure 1(C) shows the location of this gene on the chromosome.

Materials and Methods

First, the sequences of *LRP11* (NM_032832), *FUBP1* (NM_003902), and *TET1* (NM_030625) genes were obtained from the NCBI database. The length of these proteins was 500, 644, and 2136 amino acids, respectively. Then the exact location of these genes was determined using the UCSC database. The 3D structure of proteins and Ramachandran plot were determined using the MBC database and the molecular weight and isoelectric point of proteins were determined using the ProtScale database (18-21). Then the cellular comparison of *LRP11*, *FUBP1*, and *TET1* genes and the expression of these genes were analyzed by the Human Protein Atlas OMIM database.

Results

Ontology of *LRP11*, *FUBP1* and *TET1* genes

One of the most important molecular functions of the *LRP11* gene is the binding of phosphoproteins. The effective biological processes of the LRP11 gene include response to heat, cold, hunger, mechanical stimuli and stress. In general, the *LRP11* gene is an integral part of the cell membrane (22-23). The molecular functions of the *FUBP1* gene include binding to nucleic acid, DNA, RNA, and pro-

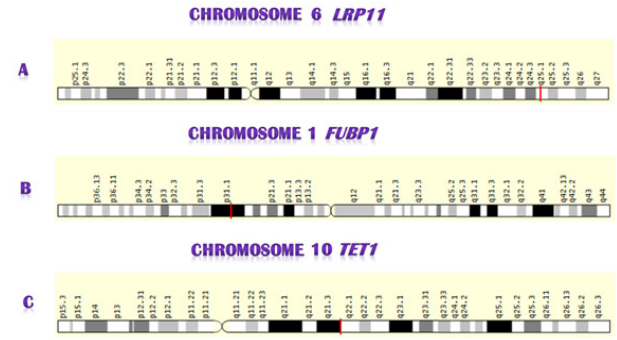

Figure 1. A) Chromosome 6, the red area is where the *LRP11* gene is located (6q25.1). B) Chromosome 1, the red area is where the *FUBP1* gene is located (1p31.1). C) Chromosome 10, the red area is where the *TET1* gene is located (10q21.3).

Table 1. Genes sequence results of *LRP11, FUBP1, and TET1.*

Name	*LRP11*	*FUBP1*	*TET1*
ORGANISM	Homo sapiens (Human)	Homo sapiens (Human)	Homo sapiens (Human)
Accession number nucleotide	NM_032832	NM_003902	NM_030625
Accession number protein	NP_116221.3	NP_003893.2	NP_085128.2
Gene ID	84918	8880	80312
Chromosome	6	1	10
Cytogenetic location	6q25.1	1p31.1	10q21.3
Chromosome location bp	149818757-149864359	77944055-77979072	68560337-68694487
nucleotide length	3634bp	6714bp	9612 bp
protein length	500aa	644aa	2136aa
Molecular weight (Da)	53311.35	67560.39	235308.68
Isoelectric point	6.04	7.18	8.53
Total Exon	7	20	12

tein and acting as a transcription factor. Biological processes related to the *FUBP1* gene also include transcriptional regulation, transcription from RNA polymerase II promoter and positive regulation of gene expression. Also, the *FUBP1* gene is a cellular component of the nucleus and nucleoplasm (24). The *TET1* gene is also a cellular component of the nucleus. Its molecular functions include the activation of RNA polymerase II transcription factor, DNA binding to specific sequences, binding to metal ions such as iron and zinc, oxidoreductase activity, dioxygenase and methylcytosine dioxygenase. The effective biological process in the gene also includes chromatin organization and negative regulation and silencing of chromatin dependent on methylation, DNA demethylation, cell differentiation, transcription regulation, and glycosylation, positive regulation of cell proliferation and methylation of histones and maintenance of stem cell population (25-27).

Three-dimensional structure

Molecular homology modeling using the SWISS-MODEL database in Expasy led to the prediction of the three-dimensional structure of *LRP11*, *FUBP1*, and *TET1* proteins based on sample 1a02 with the highest percentage of similarity (Figure 2). Then the proteins related to *LRP11*, *FUBP1*, and *TET1* were determined (Figure 3). QMEAN-DisCo Global and GMQE numbers showed the overall quality of the model, which usually varies between zero and one, and higher numbers indicate high model quality. The value of QMEANDisCo Global and GMQE for the *LRP11* gene is equal to 0.45 ± 0.05 and 0.27, for the *FUBP1* gene it is equal to 0.71 ± 0.07 and 0.21, and for the *TET1* gene, it is equal to 0.64 ± 0.05 and 0.09. The estimation of protein quality was determined based on the QMEAN z-scores scale. According to the QMEAN Z-scores, it was found that there is a good match between the model structure and the experimental structures of the same size.

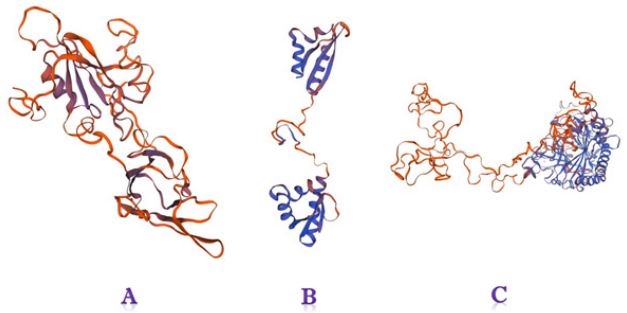

Figure 2. A) Three-dimensional structure of *LRP11* protein. B) Three-dimensional structure of *FUBP1* protein. C) Three-dimensional structure of *TET1* protein.

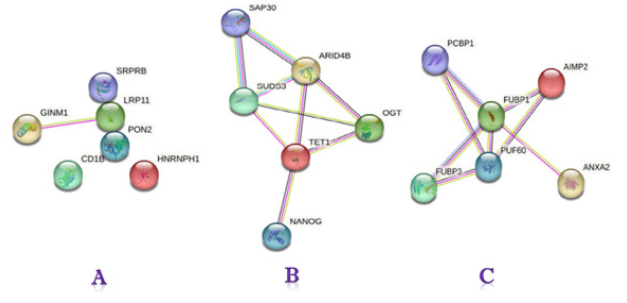

Figure 3. A) Interacting proteins for *LRP11* Gene. B) Interacting proteins for *FUBP1* Gene. C) Interacting proteins for *TET1* Gene.

Figures 4, 5, and 6 show the different QMEAN z-scores, including QMEAN, Cβ interactions, all-atom interactions, solvation, and torsion for the *LRP11*, *FUBP1*, and *TET1* genes. Then the Ramachandran diagram related to *LRP11*, *FUBP1*, and *TET1* proteins was determined to determine the energy level and stability in terms of two angles φ and ψ in the proteins (Figure 7). Considering that in *LRP11* protein, the percentage of Ramachandran's favorite amino acids was 77.10%, in *FUBP1* protein, the percentage of Ramachandran's favorite amino acids was 93.45%, and in TET1 protein, the percentage of Ramachandran's favorite amino acids was 84.06%. Therefore, the proposed model is suitable for the three-dimensional structure of proteins.

Investigation of molecular domains in *LRP11*, *FUBP1* and *TET1* genes

The *LRP11* gene has 3 protein domains. The first domain is MANEC, which is between 84 and 184 amino acids and has an E-value of 6.74e-44. The second domain is PKD, located between 215 and 299 amino acids with an E-value=1.72e-03. The third domain is LDLa, which is between 309 and 346 amino acids with an E-value=1.09e-05. *FUBP1* gene contains 4 KH domains, located in the distances of 99-169, 184-256, 274-344, and 375-448, respectively, E-value1=1.09e-17, E-value2=2.33e-17, E-value3=1.86e-16 and E-value4=1.019e-14. The second

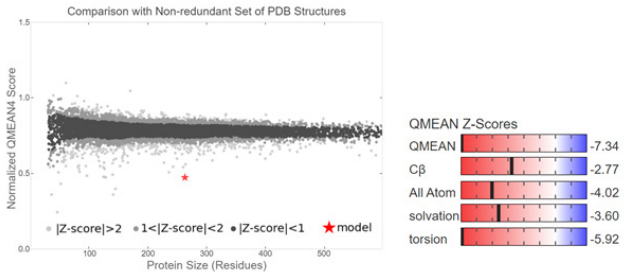

Figure 4. Plot showing the QMEAN value and Z-score for the *LRP11* gene.

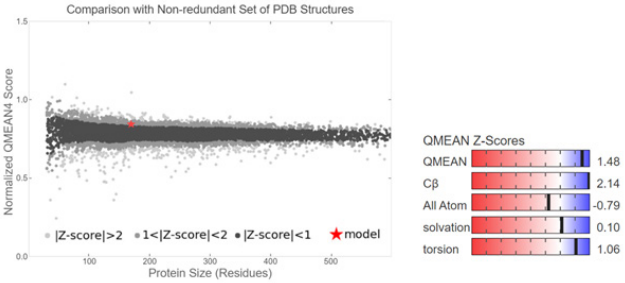

Figure 5. Plot showing the QMEAN value and Z-score for the *FUBP1* gene.

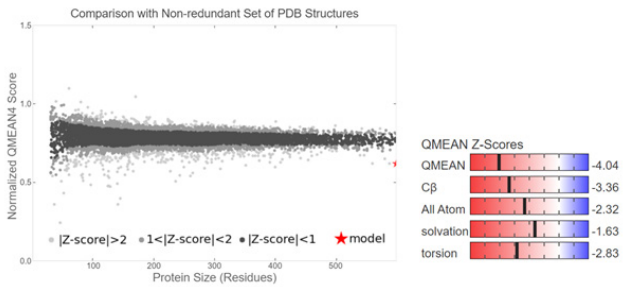

Figure 6. Plot showing the QMEAN value and Z-score for the *TET1* gene.

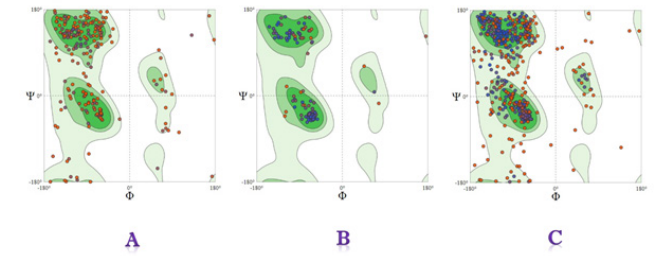

Figure 7. A) The *LRP11* protein Ramachandran diagram. B) The *FUBP1* protein Ramachandran diagram. C) The *TET1* protein Ramachandran diagram.

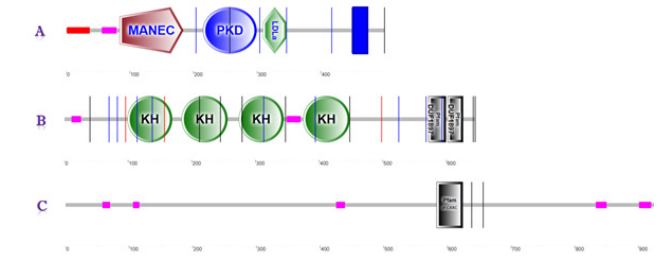

Figure 8. Molecular domains in the investigated genes. A) *LRP11* gene. B) *FUBP1* gene. C) *TET1* gene.

domain is called DUF1897, which is located between 572-599 and 602-626, E-value DUF1897 (1)= 2.80e-08, E-value DUF1897 (2)= 2.70e-10. *TET1* gene has a zf-CXXC domain located between 583 and 624 and E-value=3.70e-11 (Figure 8).

The results of examining the expression of LRP11, FUBP1, and TET1 genes in different organs

Figures 9, 10, and 11 show the expression of LRP11, FUBP1, and TET1 genes in different organs. According to the graphs, it can be seen that the expression of the LRP11 gene is the highest in the organs of the brain, prostate, and thyroid gland, and the lowest in the bone marrow. In the FUBP1 gene, the highest level of expression was observed in the lymph node and the lowest level of expression was observed in the pancreas and liver. In the case of the TET1 gene, the highest level of expression was observed in the placenta and the lowest level of similar expression of the FUBP1 gene was observed in the pancreas and liver.

Discussion

Cervical cancer, as one of the challenges facing women's health and treatment, is of particular importance. The molecular and bioinformatics technique has provided the possibility of studying different levels of information such as the genome, transcriptome, proteome, and metabolome with high depth and accuracy, which provides comprehensive and valuable information about the investigated phenotypes, including complex diseases such as cancer. Comprehensive databases such as GEO and NCBI contain bioinformatics data for different phenotypes and organisms. Extracting valuable and comprehensive information also requires the use of appropriate and accurate methods. Since the genes examined in this research are closely related to cervical cancer, it is very necessary to examine the expression of these genes in different organs and lead to the prediction and improvement of the field of medicine and treatment, especially in cancer (28). In general, gene expression analysis of *LRP11*, *FUBP1*, and *TET1* genes showed that the expression level of these genes is high in lymph nodes and thyroid, and lower in the pancreas and liver. Also, the expression level of the *FUBP1* gene is higher than that of *LRP11*, and the expression level of the *LRP11* gene is higher than that of *TET1*. Regarding the structure and proteomics of the studied genes, it can be seen that due to the presence of more domains in the *LRP11* and *FUBP1* genes, these genes probably independently participate in various functions and have a wider range of activity than the *TET1* gene. Also, the matching of QMEANDisCo Global and GMQE figures showed that the stability of the FUBP1 gene is relatively higher than the *TET1* gene, and the *TET1* gene is more stable than the *LRP11* gene. These results were completely consistent with the data obtained from the Ramachandran chart. Considering that these genes are effective key genes for the early detection of cervical cancer and there is much evidence that they are effective in suppressing tumors related to cervical cancer, they can be used as markers in the diagnosis and treatment of cervical cancer.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018 Nov;68(6):394-424. doi: 10.3322/caac.21492. Epub 2018 Sep 12. Erratum in: CA Cancer J Clin. 2020 Jul;70(4):313. PMID: 30207593.
2. Roy PS, Saikia BJ. Cancer and cure: A critical analysis. Indian J Cancer. 2016 Jul-Sep;53(3):441-442. doi: 10.4103/0019-509X.200658. PMID: 28244479.
3. Beaudenon S, Huibregtse JM. HPV E6, E6AP and cervical cancer. BMC Biochem. 2008 Oct 21;9 Suppl 1(Suppl 1):S4. doi: 10.1186/1471-2091-9-S1-S4. PMID: 19007434; PMCID: PMC2582798.
4. Shrestha AD, Neupane D, Vedsted P, Kallestrup P. Cervical Cancer Prevalence, Incidence and Mortality in Low and Middle Income Countries: A Systematic Review. Asian Pac J Cancer Prev.

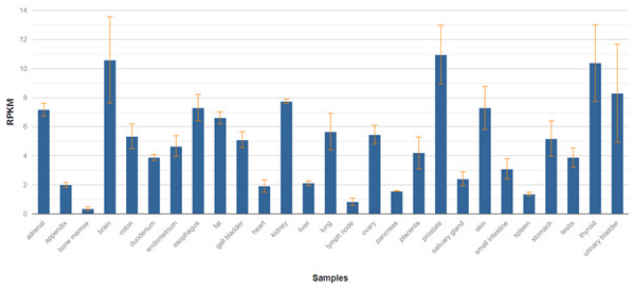

Figure 9. Results of the study of *LRP11* gene expression.

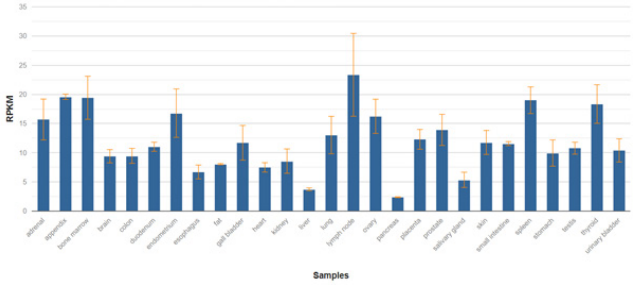

Figure 10. Results of the study of *FUBP1* gene expression.

2018 Feb 26;19(2):319-324. doi: 10.22034/APJCP.2018.19.2.319. PMID: 29479954; PMCID: PMC5980914.

5. Kori M, Yalcin Arga K. Potential biomarkers and therapeutic targets in cervical cancer: Insights from the meta-analysis of transcriptomics data within network biomedicine perspective. PLoS One. 2018 Jul 18;13(7):e0200717. doi: 10.1371/journal.pone.0200717. PMID: 30020984; PMCID: PMC6051662.
6. Wang Y, Han S, You X, Shi X, Liu L, Sun Y, Ma Y, Qian Q, Liu H, Cui B, Zhang Y. The role of low density lipoprotein receptor-related protein 11 as a tumor promoter in cervical cancer. Cancer Manag Res. 2019 Aug 30;11:8081-8093. doi: 10.2147/CMAR.S211912. PMID: 31507330; PMCID: PMC6719843.
7. Kattan RE, Han H, Seo G, Yang B, Lin Y, Dotson M, Pham S, Menely Y, Wang W. Interactome Analysis of Human Phospholipase D and Phosphatidic Acid-Associated Protein Network. Mol Cell Proteomics. 2022 Feb;21(2):100195. doi: 10.1016/j.mcpro.2022.100195. Epub 2022 Jan 8. PMID: 35007762; PMCID: PMC8864472.
8. Li X, Yu H, Xu F, Wu Y, Sheng J. Differentially Expressed Long Noncoding RNAs Involved in FUBP1 Promoting Hepatocellular Carcinoma Cells Proliferation. Biomed Res Int. 2021 Apr 14;2021:6664519. doi: 10.1155/2021/6664519. PMID: 33954195; PMCID: PMC8063849.
9. Ma C, Huang Z, Wu Z, Di C, Lin X, Huang M, Hong H, Yin H. Overexpression of FUBP1 is associated with human cervical carcinoma development and prognosis. Life Sci. 2021 Mar 15;269:119098. doi: 10.1016/j.lfs.2021.119098. Epub 2021 Jan 18. PMID: 33476628.
10. Liu W, Xiong X, Chen W, Li X, Hua X, Liu Z, Zhang Z. High expression of FUSE binding protein 1 in breast cancer stimulates cell proliferation and diminishes drug sensitivity. Int J Oncol. 2020 Aug;57(2):488-499. doi: 10.3892/ijo.2020.5080. Epub 2020 Jun 10. Erratum in: Int J Oncol. 2021 Jun;58(6): PMID: 32626933; PMCID: PMC7307591.
11. Jiang P, Huang M, Qi W, Wang F, Yang T, Gao T, Luo C, Deng J, Yang Z, Zhou T, Zou Y, Gao G, Yang X. FUBP1 promotes neuroblastoma proliferation via enhancing glycolysis-a new possible marker of malignancy for neuroblastoma. J Exp Clin Cancer Res. 2019 Sep 11;38(1):400. doi: 10.1186/s13046-019-1414-6. PMID: 31511046; PMCID: PMC6737630.
12. Khageh Hosseini S, Kolterer S, Steiner M, von Manstein V, Gerlach K, Trojan J, Waidmann O, Zeuzem S, Schulze JO, Hahn S, Steinhilber D, Gatterdam V, Tampé R, Biondi RM, Proschak E, Zörnig M. Camptothecin and its analog SN-38, the active metabolite of irinotecan, inhibit binding of the transcriptional regulator and oncoprotein FUBP1 to its DNA target sequence FUSE. Biochem Pharmacol. 2017 Dec 15;146:53-62. doi: 10.1016/j.bcp.2017.10.003. Epub 2017 Oct 13. PMID: 29031818.
13. Yang S, Yu J, Yang H, Zheng W, Zhou Y, Huang Y, Chen G, Zheng S. Aberrant high expression of the TET1 gene in Hirschsprung's disease. Pediatr Neonatol. 2022 Jul;63(4):348-354. doi: 10.1016/j.pedneo.2022.03.003. Epub 2022 Mar 29. PMID: 35650007.
14. Zhu T, Brown AP, Cai LP, Quon G, Ji H. Single-Cell RNA-Seq Analysis Reveals Lung Epithelial Cell Type-Specific Responses to HDM and Regulation by Tet1. Genes (Basel). 2022 May 14;13(5):880. doi: 10.3390/genes13050880. PMID: 35627266; PMCID: PMC9140484.
15. Adamczyk M, Rawłuszko-Wieczorek AA, Wirstlein P, Nowicki M, Jagodziński PP, Wender-Ozegowska E, Kedzia M. Assessment of TET1 gene expression, DNA methylation and H3K27me3 level of its promoter region in eutopic endometrium of women with endometriosis and infertility. Biomed Pharmacother. 2022 Jun;150:112989. doi: 10.1016/j.biopha.2022.112989. Epub 2022 Apr 27. PMID: 35489280.
16. Qiu T, Wang X, Du F, Hu X, Sun F, Song C, Zhao J. TET1 mutations as a predictive biomarker for immune checkpoint inhibitors in colon adenocarcinoma. World J Surg Oncol. 2022 Apr 8;20(1):115. doi: 10.1186/s12957-022-02581-7. PMID: 35395805; PMCID: PMC8991851.
17. Schagdarsurengin U, Luo C, Slanina H, Sheridan D, Füssel S, Böğürcü-Seidel N, Gattenloehner S, Baretton GB, Hofbauer LC, Wagenlehner F, Dansranjav T. Tracing TET1 expression in prostate cancer: discovery of malignant cells with a distinct oncogenic signature. Clin Epigenetics. 2021 Nov 29;13(1):211. doi: 10.1186/s13148-021-01201-7. PMID: 34844636; PMCID: PMC8630881.
18. Mirzaei A R, Shakoory-Moghadam V. Bioinformatics analysis and pharmacological effect of Stevia rebaudiana in the prevention of type-2 diabetes. Cell Mol Biomed Rep. 2022; 2(2), 64-73. doi: 10.55705/cmbr.2022.336232.1035.
19. Mirzaei A R, Fazeli F. Bioinformatics analysis of microtubule-associated protein-1 light chain 3 (MAP1LC3A) and (BECN1) genes in autophagy. Cell Mol Biomed Rep. 2022; 2(3), 129-137. doi: 10.55705/CMBR.2022.345001.1046.
20. Alhashimi R A, Mirzaei A, Alsaedy H. Molecular and clinical analysis of genes involved in gastric cancer. Cell Mol Biomed Rep. 2021; 1(3), 138-146. doi: 10.55705/CMBR.2021.355860.1056.
21. Al-Zaidi H M H, Mousavinasab F, Radseresht N, Mirzaei A R, Moradi Y, Mahmoudifar M. Investigation of GJB2 and SLC26A4 genes related to pendred syndrome genetic deafness patients. Cell Mol Biomed Rep. 2023; 3(3), 163-171. doi: 10.55705/cmbr.2023.379262.1093.
22. Mravec B, Lukackova R, Bodnar I, Kiss A, Pacak K, Palkovits M, Kvetnansky R. Stress-induced alterations in catecholamine enzymes gene expression in the hypothalamic dorsomedial nucleus are modulated by caudal brain and not hypothalamic paraventricular nucleus neurons. Brain Res Bull. 2007 Sep 14;74(1-3):147-54. doi: 10.1016/j.brainresbull.2007.06.005. Epub 2007 Jun 29. PMID: 17683801.
23. Gavrilovic L, Spasojevic N, Zivkovic M, Dronjak S. Effect of immobilization stress on gene expression of catecholamine biosynthetic enzymes in heart auricles of socially isolated rats. Braz J Med Biol Res. 2009 Dec;42(12):1185-90. doi: 10.1590/s0100-879x2009005000040. Epub 2009 Nov 6. PMID: 19893991.
24. Marceau AH. Functions of single-strand DNA-binding proteins in DNA replication, recombination, and repair. Methods Mol Biol. 2012;922:1-21. doi: 10.1007/978-1-62703-032-8_1. PMID: 22976174.
25. Ito S, Shen L, Dai Q, Wu SC, Collins LB, Swenberg JA, He C, Zhang Y. Tet proteins can convert 5-methylcytosine to 5-formylcytosine and 5-carboxylcytosine. Science. 2011 Sep 2;333(6047):1300-3. doi: 10.1126/science.1210597. Epub 2011 Jul 21. PMID: 21778364; PMCID: PMC3495246.
26. Mondal T, Rasmussen M, Pandey GK, Isaksson A, Kanduri C. Characterization of the RNA content of chromatin. Genome Res. 2010 Jul;20(7):899-907. doi: 10.1101/gr.103473.109. Epub 2010 Apr 19. PMID: 20404130; PMCID: PMC2892091.
27. Zhu J, Kapoor A, Sridhar VV, Agius F, Zhu JK. The DNA glycosylase/lyase ROS1 functions in pruning DNA methylation patterns in Arabidopsis. Curr Biol. 2007 Jan 9;17(1):54-9. doi: 10.1016/j.cub.2006.10.059. PMID: 17208187.
28. Wang Y, Han S, You X, Shi X, Liu L, Sun Y, Ma Y, Qian Q, Liu H, Cui B, Zhang Y. The role of low density lipoprotein receptor-related protein 11 as a tumor promoter in cervical cancer. Cancer Manag Res. 2019 Aug 30;11:8081-8093. doi: 10.2147/CMAR.S211912. PMID: 31507330; PMCID: PMC6719843.