Roles of PEG10 in cancer and neurodegenerative disorder (Review)

DACHAO MOU[1,2*], SHASHA WU[1,2*], YANQIONG CHEN[1,2*], YUN WANG[1,2], YUFANG DAI[1,2], MIN TANG[3,4], XIU TENG[1,2], SHIJUN BAI[5] and XIUFENG BAI[1,2]

[1]Laboratory of Human Disease and Immunotherapies, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, P.R. China; [2]Institute of Inflammation and Immunology (I[3]), Frontiers Science Center for Disease-Related Molecular Network, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, P.R. China; [3]Division of Thoracic Tumor Multimodality Treatment and Department of Radiation Oncology, Cancer Center, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, P.R. China; [4]Laboratory of Clinical Cell Therapy, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, P.R. China; [5]Department of Agriculture Forestry and Food Engineering, Yibin University, Lingang Economic and Technological Development Zone, Yibin, Sichuan 644000, P.R. China

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Abstract. Paternally expressed gene 10 (PEG10) is an imprinting gene. In addition to its known roles in placental development, as well as mouse embryonic stem cell and trophoblast stem cell differentiation, PEG10 has recently been shown to have significance in cancers. High expression of PEG10 is observed in various cancer types and is associated with poor prognosis. Of note, disruption of PEG10 expression leads to increased apoptosis, as well as decreased proliferation, invasion and migration of cancer cells. PEG10 is expected to become a target for cancer and neurodegenerative disorder therapy. This article reviewed the latest progress in the role of PEG10 in cancers.

Contents

Correspondence to: Professor Xiufeng Bai, Laboratory of Human Disease and Immunotherapies, West China Hospital, Sichuan University, Building B2, 88 Keyuan South Road, Wuhou, Chengdu, Sichuan 610041, P.R. China
E-mail: baixiufeng@wchscu.cn

Professor Shijun Bai, Department of Agriculture Forestry and Food Engineering, Yibin University, Lingang Economic and Technological Development Zone, 5, 3rd Section of Daxuecheng Road, Yibin, Sichuan 644000, P.R. China
E-mail: bsj11@126.com

*Contributed equally

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1. Introduction

In tumors, certain genes related to proliferation and invasion are upregulated in expression (1). In neurodegenerative diseases, there are also a bulk of genes with abnormal expression, including genes related to the autophagy-lysosomal pathway (2). These abnormally expressed genes may not only serve as biomarkers for disease diagnosis, but also as targets for treatment. Human endogenous retroviruses (HERVs) are derived from ancient retroviruses, which infect and insert viral genes into germline cells. HERVs constitute an estimated 8% of the human genome (3). In general, a complete HERV includes 5' long terminal repeats (5' LTR), a primer-binding site, group-specific antigen gene (gag), a protease gene, a polymerase gene (pol), an envelope gene and 3' LTR elements (4). Paternally expressed imprinted gene 10 (PEG10) is an evolutionarily conserved HERV gene (5) belonging to the Ty3/Gypsy family of retrotransposons. Evolutionarily, PEG10 is a therian-specific gene (6,7), and differentially methylated regions of PEG10 have emerged in the therian ancestor at least 160 million years ago (8). During the evolution of the placenta in mammals, PEG10 was inserted into the genome, as it exists in marsupials but not in egg-laying monotreme species (9). PEG10 is a paternally expressed imprinting gene, which was reported to be located at human chromosome 7q21 in 2001 for the first time (7). Importantly, PEG10 can be used for RNA delivery (10-13). As an imprinting gene, PEG10 is crucial for placental development and plays a key role in mouse embryonic stem cell and trophoblast stem cell differentiation (14-16).

Ono *et al* (17) have reported that PEG10 maintains placental function, and deletion of PEG10 in mice can lead to embryonic lethality. Traditionally, PEG10 expression is limited to the testes, adrenal gland and skin after adulthood (18). During the past few years, knowledge of PEG10 being highly expressed in tumors and neurodegenerative diseases has emerged. Thus, the present article reviewed the recent findings on the roles of PEG10 in these diseases.

2. The structural domains of the PEG10 protein

PEG10 contains 2 overlapping open reading frames (RF1 and RF1/2), and the mRNA of PEG10 utilizes a typical retroviral frameshift mechanism to encode two proteins: RF1 (encoding gag-like protein) and RF1/2 (encoding gag-pol-like polyprotein) (19,20). The frameshifting efficiency of PEG10 is ~22% (19) and a study has identified that the frameshift of PEG10 can be suppressed by a small-molecule compound (21). The ribosomal frameshift element of PEG10 consists of 'slippery' and 'pseudoknot'. The slippery sequence is GGGAAAC, while pseudoknot is composed of multiple stem-loop structures. When ribosomes encounter the pseudoknot, the A- and P-site tRNAs detach from the zero frame codons GGA-AAC, shifting back one nucleotide to GGG-AAA, causing the original encoding of glycine-asparagine to change to glycine-lysine (22). PEG10 has multiple evolutionary conserved functional domains, including a coiled-coil domain, retrotransposon-gag domain, retrovirus zinc finger-like domain, retroviral asparytyl protease domain and reverse transcriptase domain (5,7,23-26). The structure of PEG10 is shown in Fig. 1.

PEG10 as a long non-coding (lnc)RNA. LncRNA is a type of ncRNA with a length exceeding 200 nucleotides. LncRNAs are involved in the occurrence, development and progression of cancer. PEG10 is an upregulated lncRNA in patients with lymphoma (27). In diffuse large B-cell lymphoma (DLBCL), lncRNA PEG10 inhibits microRNA (miR)-101-3p, while miR-101-3p inhibits kinesin family member 2A (KIF2A). Therefore, overexpression of PEG10 leads to an increase in KIF2A expression, promoting DLBCL growth (28,29). LncRNA PEG10 inhibits miR-449a, increases ribosomal protein S2 expression and increases the proliferation, invasion and migration of neuroblastoma cells (30). LncRNA PEG10 and H19 are mutual upstream and downstream regulatory factors, and PEG10 levels are constitutively associated with a high lymph node ratio in gastric cancer (31). Furthermore, knockout of PEG10 causes an increase in miR-3200 and inhibits the proliferation, migration and invasion of gastric cancer cells (32) and glioma cells (33). LncRNA PEG10 inhibits miR-33a in melanoma, thus inhibiting the PI3K/AKT and mTOR pathways (34). Furthermore, overexpression of lncRNA PEG10 also has an essential role in promoting proliferation and invasion in esophageal cancer cells (35) and hypopharyngeal squamous cell carcinoma (36).

PEG10 subcellular localization. PEG10 contains 2 overlapping open reading frames, RF1 and RF2. During embryonic development, PEG10-RF1 and PEG10-RF1/2 proteins are expressed at different stages, suggesting that PEG10-RF1 and PEG10-RF1/2 may have different functions. PEG10-RF1/2 have an aspartate protease domain and new fragments can be generated through self-cutting (19,22). PEG10 is found in multiple cellular components, including the nucleus (24), extracellular vesicles and stress granules (25). PEG10-RF1 has nuclear and cytoplasmic localization and does not enter stress granules under stress conditions. However, PEG10-RF1/2 is only localized in the cytoplasm and enters stress granules under stress conditions (25). PEG10-RF1 contains a retroviral zinc finger domain and is considered a transcription factor, regulates the transcription of genes participates in the progression of cancers and neurodegenerative diseases; these genes include C9orf72-SMCR8 complex subunit, doublecortin like kinase 1, plexin A4, semaphorin 5B, slit guidance ligand 3 and Wnt family member 3A (24).

In addition, PEG10 is a secreted protein produced by Dental-derived mesenchymal stem cells and bone marrow stem cells, which is associated with adipose differentiation. PEG10 expression is generally observed at the immediate early stage of adipocyte differentiation (37).

3. Mechanisms leading to PEG10 activation and inactivation

The increase in PEG10 protein may be caused by various ways, including DNA demethylation, gene duplication, extended RNA half-life, transcriptional activation and inhibition of protein degradation (Fig. 2).

Epigenetic regulation. In the mammalian genome, DNA methylation is an important approach to govern gene expression (38,39). DNA methylation usually inhibits gene expression by recruiting repression proteins or inhibiting transcription factors to DNA. In human parthenogenetic embryonic stem cells, activating transcription factor 7 interacting protein increases PEG10 methylation and inhibits its transcription (40). In $Kras^{G12D}$-induced T-cell neoplasms, imprinting control regions (ICRs) of PEG10 are significantly hypermethylated. Increased DNA methylation at the ICRs of PEG10 is the earliest detectable change in lymphocytic T-cell thymic lymphoma (41). Tet methylcytosine dioxygenase 1 (TET1) is a maintenance DNA demethylase, which promotes PEG10 expression by inhibiting DNA methylation, and deleting TET1 results in an increase of 5-hydroxymethylcytosine in PEG10, leading to a decrease in PEG10 expression (42). Histone methylation is another way to regulate PEG10 expression, and in hepatocellular carcinoma (HCC), menin/mixed-lineage leukemia 1 (MLL) interaction inhibitor MI-503 prevents the display of the menin-MLL1 complex from binding to the PEG10 promoter, reduces the modification of trimethylated H3 lysine 4 in the promoter region and inhibits PEG10 transcription (43).

Gene amplification. Traditionally, gene amplification was identified as one aspect of the genetic instability strongly associated with malignantly transformed cells. Cancer cells use this mechanism to mediate overexpression of certain oncogenes to promote proliferation, anti-apoptosis and resistance to anticancer drugs (44). For instance, genomic amplification of PEG10 at the 7q21.3 locus was found in HCC samples (45,46). In hepatitis B virus-associated HCC, the increase in DNA copy number leads to an increased expression of PEG10 (47).

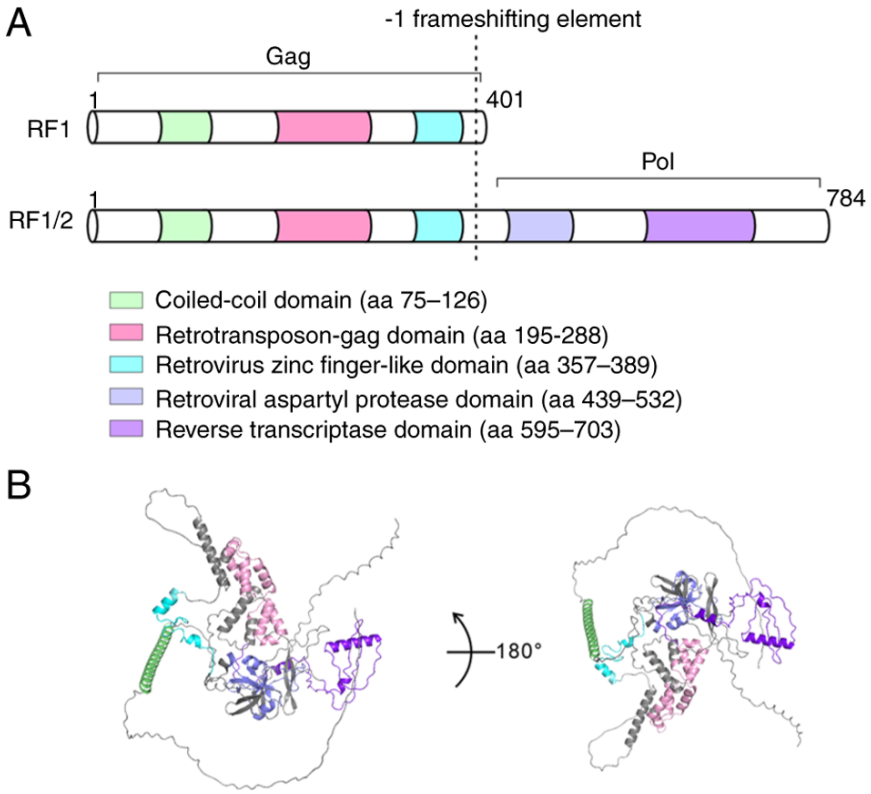

Figure 1. Structure of PEG10. (A) Domain organization of PEG10. PEG10 mRNA produces two proteins, a PEG10-RF1 and a full-length PEG10-RF1/2. (B) Cartoon representation of PEG10-RF1/2 (AlphaFold: AF-I3NHH4-F1). Function of these domains: Coiled-coil domain (homomorphic and heteromorphic protein interaction), retrotransposon-gag domain (RNA binding), retroviruses zinc finger-like domain (DNA binding), retroviral aspartyl protease domain (self-cleavage) and reverse transcriptase domain (RNA binding). Brown ribbons represent the linker domain. RF, reading frame; PEG10, paternally expressed gene 10; pol, polymerase gene; gag, group-specific antigen gene.

RNA stability. The stability of mRNA plays an important role in the control of gene expression (48). PEG10 is a direct target of miRNA-574-5p (30). MiR-138-5p binds to the 3'UTR of PEG10 mRNA, shortening the half-life of PEG10 mRNA (49). In regulating retinoblastoma (RB), the circular RNA Circ:0075804 promotes PEG10 expression by inhibiting miR-138-5p (49). N6-methyladenosine residues on the PEG10 3'UTR are recognized and bind by insulin like growth factor 2 mRNA binding protein 1 to recruit poly (A) Binding Protein Cytoplasmic 1 and enhance the stability of PEG10 mRNA, thereby increasing the protein content of PEG10 (50). In neural progenitor cells, TET3 increases the DNA methylation levels of PEG10 and maintains neural stem cell identity (51). In HCC, miR-122 binds to the PEG10 3'UTR and inhibits PEG10 expression (52). LncRNA SNAI3 antisense RNA 1 increases PEG10 expression through competing endogenous RNA spreading of miR-27a-3p and miR-34a-5p, thereby promoting cancer cell proliferation (53). In human colon cancer cells, miR-491 binds to the 3'UTR of PEG10 mRNA and inhibits PEG10 expression (54). In colorectal cancer, NOTCH1-associated lncRNA in T-cell acute lymphoblastic leukemia 1 increases PEG10 expression to promote tumor progression by sponging miR-574-5p (55).

Transcriptional regulation. Transcription factors can bind to the promoter region of PEG10 and activate its transcription. Myc promotes tumor-cell proliferation by activating PEG10 transcription (56,57). In addition, the E2F family of transcription factors (E2Fs) are transcription factors that promote the transcription of PEG10 and thereby enhance the proliferation of HCC cells (58). Glycogen synthase kinase 3β can phosphorylate and activate E2F transcriptional factor 1 (E2F1). Phosphorylated E2F1 binds to ubiquitin specific peptidase 11, leading to reduced degradation of E2F1 due to deubiquitination. E2F-1 has also been recently shown to be crucial for PEG10 activation in pancreatic cancer, and to further promote cell proliferation, migration and invasion (59). Similarly, in HCC, the expression of PEG10 is positively correlated with lymph node metastasis. Overexpression of PEG10 promotes epithelial-mesenchymal transition, and the expression of PEG10 is influenced by the transforming growth factor β (TGF-β) signaling (60). Furthermore, transcription factor CTR9 homolog, Paf1/RNA polymerase II complex component promotes PEG10 transcription (61).

Although TGF-β promotes PEG10 expression in HCC tissues, in other cancer tissues, the expression of PEG10 is inhibited by TGF-β, e.g. in chondrosarcoma cells (62). Furthermore, the upregulated PEG10 activity in turn inhibits TGF-β and bone morphogenetic protein signaling (63). The transcription factor one cut homeobox 2 binds to the PEG10 promoter and increases the mRNA levels of PEG10 in lethal prostate cancer (64,65), and recent studies demonstrated that androgen receptor (AR) inhibits the transcription of PEG10 (66-68). RB inhibits PEG10 transcription by inhibiting E2F1 activity (26,58). Interestingly, the expression of PEG10 can be regulated by small molecule compounds. For instance,

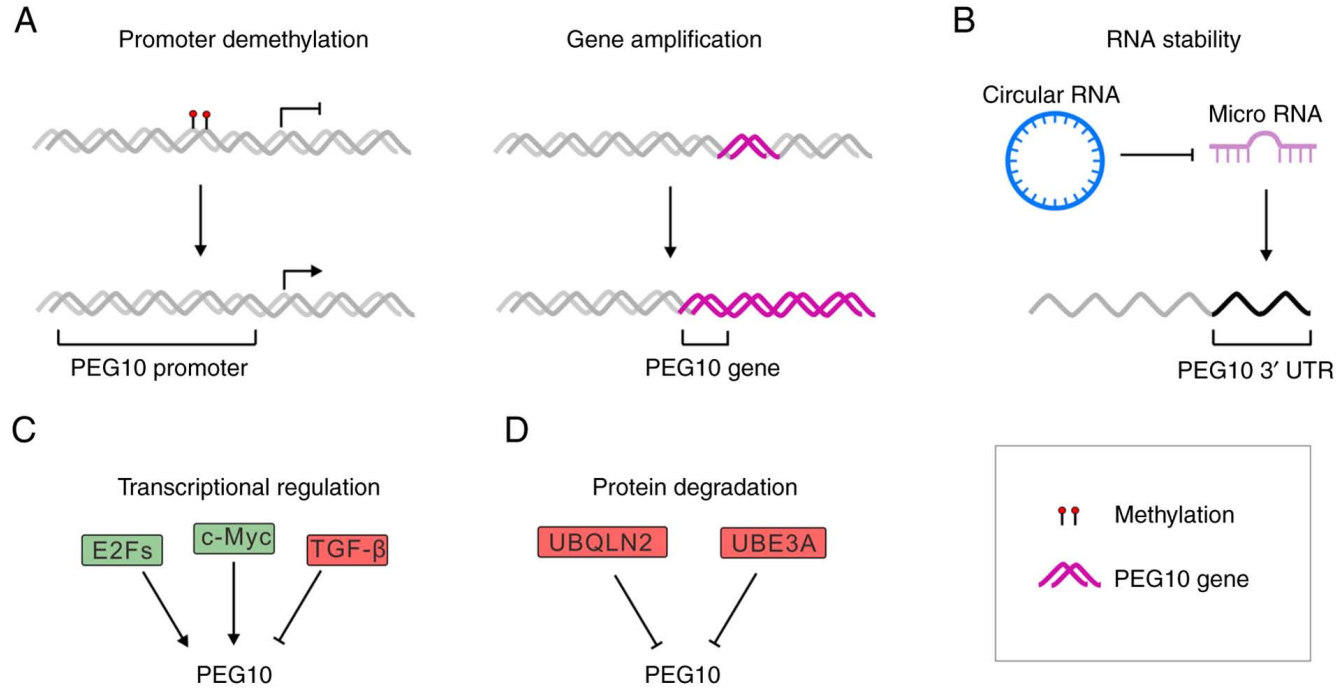

Figure 2. Factors that regulate PEG10 expression. (A) Genetic regulation. (B) miRNAs bind to the 3'UTR of PEG10, which decreases mRNA stability. Circular RNA acts as a sponge for miRNA. (C) Transcriptional regulation of PEG10. (D) Degradation of PEG10 proteins. PEG10, paternally expressed gene 10; miRNA, microRNA; UBE3A, ubiquitin protein ligase E3A; UBQLN2, ubiquilin 2.

curcumin inhibits the expression of PEG10 in an unknown mechanism, thereby inhibiting the growth of breast cancer cells (69). Exposure to cadmium (Cd) can cause a decrease in the expression of Cd-exposed placentas PEG10 (70).

Protein stability. PEG10 has a C-terminal polyproline repeat domain, which may be recognized by human ubiquilin 2 (UBQLN2) and facilitates its proteasomal degradation (24,71). The deficiency of UBQLN2 leads to an increase in PEG10 protein. Furthermore, the ubiquitin protein ligase E3A (UBE3A) is another PEG10 regulating gene. UBE3A inhibits the expression of PEG10 via the proteasome (25)

4. Downstream of PEG10

Nuclear localized PEG10 functions as a transcription factor, mediating the transcription of numerous downstream target genes. Kruppel-like factor 2 (KLF2) is an inhibitory factor of NF-κB and PEG10 activates NF-κB signaling by inhibiting KLF2 expression (23). Upregulated PEG10 expression activates NOTCH signaling and promotes metastatic cancer stem cell self-renewal (72). PEG10 was reported to bind to TGF-β receptor ALK1 and to inhibit ALK1 as well as ALK5 signaling (73). In HCC, TSG101 binds to PEG10 to prevent its degradation, thereby enhancing PEG10 expression and downstream target genes p53, p21 and matrix metalloproteinases (MMPs), leading to cell proliferation, invasion and migration (74). After overexpression of PEG10 in human colon cancer cells, the Wnt1/β-catenin pathway is activated, promoting cell proliferation and inhibiting cell apoptosis (54). In Burkitt's lymphoma cells, PEG10 promotes tumor cell invasion and metastasis by upregulating the expression of MMP-2 and -9 (18,26,59,75). PEG10 promotes the proliferation of endometrial cancer cells by inhibiting the transcription of p16 and p18 genes. PEG10 tends to bind to the TGGGAYTACA and CTCNGCCTCC motifs (50). Of note, it was recently found that PEG10 is an RNA binding protein, promoting trophoblast stem cell differentiation into placental lineages (14).

5. PEG10 in cancer

PEG10 is considered an oncogene and PEG10 protein has been found to be significantly increased in various cancer types to date. Exogenous PEG10 expression leads to increased cellular proliferation and increased cell viability (76).

Liver cancer. The relationship between PEG10 and cancer was first studied in liver cancer. PEG10 is strongly expressed in HCC (77). A machine learning study found that PEG10 is highly expressed in patients unresponsive to transarterial chemotherapy (78). Expression of PEG10 is significantly correlated with poor survival and tumor recurrence in HCC, making PEG10 an independent predictor of early recurrence of HCC (79). However, other studies found that PEG10 has an inhibitory effect on tumor cell growth by activating immune response. For instance, transduction of dendritic cells with PEG10 recombinant adenovirus induced anti-tumor immunity against HCC (80). Another study also identified that androgens activate PEG10 (81). Thereby, PEG10 is the potential biomarker of HCC (82,83).

Lung cancer. An increase in PEG10 content is closely related to the prognosis of lung cancer; therefore, PEG10 is a diagnostic and prognostic gene for lung adenocarcinoma and squamous cell carcinoma (84). E2Fs activate MMPs by upregulating PEG10, leading to lung cancer progression, prognosis and

Table I. Selected PEG10-directed therapies.

Process	Disease	Target	Regulator	(Refs.)
Transcription	HCC	H3K4me3	MI-503	(43)
	HCC	CTR9	shRNA	(61)
RNA stability	Diffuse large B-cell lymphoma	PEG10	shRNA	(23)
	Cutaneous T-cell lymphoma	PEG10	shRNA	(23)
	HCC	PEG10	miR-122	(52)
	Colon cancer	PEG10	miR-491	(54)
	Colon cancer	PEG10	Curcumin	(54)
	HCC	PEG10	miR-27a-3p	(53)
	HCC	PEG10	miR-34a-5p	(53)
	Angelman syndrome	PEG10	shRNA	(25)
	Bladder cancer	PEG10	siRNA	(108)
	Breast cancer	PEG10	siRNA	(112)
	Colorectal cancer	PEG10	miR-574-5p	(55)
	Endometrial cancer	PEG10	siRNA	(50)
	Gastric carcinoma	PEG10	miR-3200	(32)
	Lung cancer	PEG10	siRNA	(85)
	Prostate cancer	PEG10	shRNA	(26)
	Prostate cancer	PEG10	siRNA	(94)
Protein stability	Cutaneous T-cell lymphoma	USP9X	WP1130	(98)
Vaccine	HCC	Dendritic cells	PEG10 recombinant adenovirus	(80)

miR, microRNA; shRNA, short hairpin RNA; PEG10, paternally expressed gene 10; USP9X, ubiquitin specific peptidase 9 X-linked; MI-503, Menin-MLL1 inhibitor 503; HCC, hepatocellular carcinoma.

metastasis (85,86). E2F1 activates PEG10 gene transcription, promoting proliferation of lung epithelial cells (87). Furthermore, transcription termination factor 1 activates receptor tyrosine kinase like orphan receptor 1 (ROR1), which activates PEG10 transcription. Inhibition of ROR1 by small inhibitory (si)RNA in the human lung cancer cell line PC-9 leads to a decrease in the transcription level of PEG10 (88). On the contrary, the expression of PEG10 is also inhibited by certain transcription factors. The expression of PEG10 is inhibited by PI3K/AKT, which leads to a decrease in PEG10 protein levels in lung cancer cells (89).

Prostate cancer. The expression of PEG10 in prostate cancer is usually suppressed, as AR inhibits the transcription of PEG10 (26). However, during the treatment of prostate cancer, AR inhibitors drive cancer cells to evolve into neuroendocrine prostate cancer (NEPC) and the expression of PEG10 gradually increases during the transition from adenocarcinoma to NEPC. Therefore, PEG10 can be used as a predictive indicator for biochemical recurrence of prostate cancer (90). As a characteristic gene of NEPC, silencing PEG10 inhibits the *in vitro* growth of prostate cancer cells (91). In AR activated adenocarcinoma type prostate cancer, full-length RF1/2 is the dominant form, while in NEPC cells, RF1 and RF1/2 are both highly expressed (26). Full-length PEG10 (RF1/2) drive the proliferation of NEPC, while short-length PEG10 (RF1) promotes invasion (26). The expression of PEG10 is associated with short survival of patients with prostate adenocarcinoma (92). Importantly, studies have highlighted the crucial role of PEG10 in promoting the malignant transformation of the highly lethal AR-negative phenotype prostate cancer (93). Silencing PEG10 reduced the expression of neuroendocrine markers and inhibited cell proliferation (94).

Leukemia. Driven by genomic gains and promoter demethylation, PEG10 is highly expressed and is associated with poor patient prognosis in mycosis fungoides-large-cell transformation (23). Furthermore, PEG10 overexpression was observed in B-cell acute lymphoblastic leukemia and B-cell chronic lymphocytic leukemia (95,96). Reducing PEG10 expression leads to a decrease in cell volume and a weakened colony-formation ability in large transformed cutaneous T-cell lymphoma cells; consequently, PEG10 inhibition may be a promising treatment for advanced invasive T-cell lymphoma (23). In thymoma, the DNA methylation level of the promoter region of PEG10 is higher than that of T-cell lymphoblastic leukemia (97,98). Abnormal DNA methylation in PEG10 ICRs is expected to become a prognostic marker for T-cell neoplasm and B-cell chronic lymphocytic leukemia (41,99).

Other cancer types. To date, PEG10 has been shown to be crucial in several types of cancer, such as Ewing sarcoma (ES), esophageal squamous cell carcinoma (ESCC) and metastatic thymic adenocarcinoma. In ES, PEG10 inhibits the TGF-β pathway and reduces cell growth. In the human skin epidermoid carcinoma cell line A431, miR-145, miR-432 and miR-1972 inhibit

PEG10 expression (100). Besides, genetic mutations can also affect PEG10 activity. In metastatic thymic adenocarcinoma, PEG10 was found to have a somatic p.R207H mutation (101). LncRNA PEG10 is elevated in serum exosomes of patients with ESCC (102). Higher PEG10 levels are associated with unfavorable overall and progression-free survival (103). Therefore, PEG10 can serve as a marker of carcinogenesis, progression and poor prognosis, as well as a putative drug target in ovarian cancer (72,104,105), rectal adenocarcinoma (106), early-onset colorectal cancer (107), neuroendocrine muscle-invasive bladder cancer (108), bladder cancer (108), adenosquamous carcinomas (109), gallbladder adenocarcinoma (110), breast cancer (111,112), adenocarcinoma (113), oral squamous cell carcinoma (114) and glioma (115).

6. Neurodegenerative disorder

Amyotrophic lateral sclerosis (ALS). ALS is a chronic neurodegenerative disease that mainly causes damage to upper and lower motor neurons. Mutations in the ubiquitin-adaptor protein UBQLN2 is considered one of the causes of ALS (116,117). PEG10 is a substrate of UBQLN2 (118); UBQLN2 binds to the C-terminus of PEG10 and initiates its degradation (24).

Angelman syndrome. Angelman syndrome is caused by UBE3A defect; patients with Angelman syndrome often experience developmental delay, balance disorders, limb incoordination and gait instability. The UBE3A mutation causes PEG10 aggregation, alters neuronal migration and ultimately leads to Angelman syndrome (25).

7. Therapeutic strategies to target PEG10-driven diseases

Although no targeted small-molecule inhibitors to block PEG10 have been developed, there are still numerous ways to inhibit PEG10, including inhibitors that target its transcription factors, siRNAs, shRNAs or miRNAs that target PEG10 mRNA, as well as using PEG10 as an antigen to develop vaccines (119). PEG10-related treatment methods are listed in Table I. The functional diversity of PEG10 poses multiple challenges to drug development, and ensuring target specificity is key in drug development to avoid unnecessary damage to embryo development or normal tissue function.

8. Conclusions

PEG10 can be used for RNA delivery (10). PEG10 is an imprinting gene expressed in the placenta and tumors. Silencing PEG10 expression in cancer cells slows cell growth, increases apoptosis, and reduces invasion and metastasis. PEG10 is a promising therapeutic target and prognostic marker for cancer. However, due to its nuclear distribution, PEG10 is not suitable for antibody drug development. Synthetic PEG10 siRNA is a potential therapeutic agent. In addition, small molecules targeting the ribosomal frameshift of PEG10 are a promising approach (120,121).

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Availability of data and materials

Not applicable.

Authors' contributions

DM, SB and XB were involved in the conceptualization of the study. SW and YC wrote the original draft. YW and YD prepared the figures. MT and XT reviewed and revised the manuscript. All authors reviewed the manuscript and have read and approved the final version. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Hanahan D: Hallmarks of cancer: New dimensions. Cancer Discov 12: 31-46, 2022.
2. Lee MS, Kim JW, Park DG, Heo H, Kim J, Yoon JH and Chang J: Autophagic signatures in peripheral blood mononuclear cells from Parkinson's disease patients. Mol Cells 48: 100173, 2024.
3. Dopkins N and Nixon DF: Activation of human endogenous retroviruses and its physiological consequences. Nat Rev Mol Cell Biol 25: 212-222, 2024.
4. Jakobsson J and Vincendeau M: SnapShot: Human endogenous retroviruses. Cell 185: 400-400.e1, 2022.
5. Youngson NA, Kocialkowski S, Peel N and Ferguson-Smith AC: A small family of sushi-class retrotransposon-derived genes in mammals and their relation to genomic imprinting. J Mol Evol 61: 481-490, 2005.
6. Iwasaki S, Suzuki S, Pelekanos M, Clark H, Ono R, Shaw G, Renfree MB, Kaneko-Ishino T and Ishino F: Identification of a novel PNMA-MS1 gene in marsupials suggests the LTR retrotransposon-derived PNMA genes evolved differently in marsupials and eutherians. DNA Res 20: 425-436, 2013.
7. Ono R, Kobayashi S, Wagatsuma H, Aisaka K, Kohda T, Kaneko-Ishino T and Ishino F: A retrotransposon-derived gene, PEG10, is a novel imprinted gene located on human chromosome 7q21. Genomics 73: 232-237, 2001.
8. Renfree MB, Suzuki S and Kaneko-Ishino T: The origin and evolution of genomic imprinting and viviparity in mammals. Philos Trans R Soc Lond B Biol Sci 368: 20120151, 2013.
9. Suzuki S, Ono R, Narita T, Pask AJ, Shaw G, Wang C, Kohda T, Alsop AE, Marshall Graves JA, Kohara Y, *et al*: Retrotransposon silencing by DNA methylation can drive mammalian genomic imprinting. PLoS Genet 3: e55, 2007.

10. Segel M, Lash B, Song J, Ladha A, Liu CC, Jin X, Mekhedov SL, Macrae RK, Koonin EV and Zhang F: Mammalian retrovirus-like protein PEG10 packages its own mRNA and can be pseudotyped for mRNA delivery. Science 373: 882-889, 2021.
11. Tang R, Guo L, Wei T, Chen T, Yang H, Ye H, Lin F, Zeng Y, Yu H, Cai Z and Liu X: Engineering PEG10 assembled endogenous virus-like particles with genetically encoded neoantigen peptides for cancer vaccination. Elife 13: RP98579, 2024.
12. Campodonico W, Mohan HM, Huynh PT, Black HH, Lau CI, Paulson HL, Sharkey LM and Whiteley AM: The gag-like gene RTL8 antagonizes PEG10-mediated virus like particles. PLoS One 19: e0310946, 2024.
13. Li M, Liu Z, Wang D, Ye J, Shi Z, Pan C, Zhang Q, Ju R, Zheng Y and Liu Y: Intraocular mRNA delivery with endogenous MmPEG10-based virus-like particles. Exp Eye Res 243: 109899, 2024.
14. Abed M, Verschueren E, Budayeva H, Liu P, Kirkpatrick DS, Reja R, Kummerfeld SK, Webster JD, Gierke S, Reichelt M, *et al*: The Gag protein PEG10 binds to RNA and regulates trophoblast stem cell lineage specification. PLoS One 14: e0214110, 2019.
15. Pollard KS, Serre D, Wang X, Tao H, Grundberg E, Hudson TJ, Clark AG and Frazer K: A genome-wide approach to identifying novel-imprinted genes. Hum Genet 122: 625-634, 2008.
16. Smallwood A, Papageorghiou A, Nicolaides K, Alley MK, Jim A, Nargund G, Ojha K, Campbell S and Banerjee S: Temporal regulation of the expression of syncytin (HERV-W), maternally imprinted PEG10, and SGCE in human placenta. Biol Reprod 69: 286-293, 2003.
17. Ono R, Nakamura K, Inoue K, Naruse M, Usami T, Wakisaka-Saito N, Hino T, Suzuki-Migishima R, Ogonuki N, Miki H, *et al*: Deletion of Peg10, an imprinted gene acquired from a retrotransposon, causes early embryonic lethality. Nat Genet 38: 101-106, 2006.
18. Xie T, Pan S, Zheng H, Luo Z, Tembo KM, Jamal M, Yu Z, Yu Y, Xia J, Yin Q, *et al*: PEG10 as an oncogene: Expression regulatory mechanisms and role in tumor progression. Cancer Cell Inte 18: 112, 2018.
19. Clark MB, Jänicke M, Gottesbühren U, Kleffmann T, Legge M, Poole ES and Tate WP: Mammalian gene PEG10 expresses two reading frames by high efficiency-1 frameshifting in embryonic-associated tissues. J Biol Chem 282: 37359-37369, 2007.
20. Manktelow E, Shigemoto K and Brierley I: Characterization of the frameshift signal of Edr, a mammalian example of programmed-1 ribosomal frameshifting. Nucleic Acids Res 33: 1553-1563, 2005.
21. Cardno TS, Shimaki Y, Sleebs BE, Lackovic K, Parisot JP, Moss RM, Crowe-McAuliffe C, Mathew SF, Edgar CD, Kleffmann T and Tate WP: HIV-1 and human PEG10 frameshift elements are functionally distinct and distinguished by novel small molecule modulators. PLoS One 10: e0139036, 2015.
22. Lux H, Flammann H, Hafner M and Lux A: Genetic and molecular analyses of PEG10 reveal new aspects of genomic organization, transcription and translation. PLoS One 5: e8686, 2010.
23. Liu F, Gao Y, Xu B, Xiong S, Yi S, Sun J, Chen Z, Liu X, Li Y, Lin Y, *et al*: PEG10 amplification at 7q21.3 potentiates large-cell transformation in cutaneous T-cell lymphoma. Blood 139: 554-571, 2022.
24. Black HH, Hanson JL, Roberts JE, Leslie SN, Campodonico W, Ebmeier CC, Holling GA, Tay JW, Matthews AM, Ung E, *et al*: UBQLN2 restrains the domesticated retrotransposon PEG10 to maintain neuronal health in ALS. Elife 12: e79452, 2023.
25. Pandya NJ, Wang C, Costa V, Lopatta P, Meier S, Zampeta FI, Punt AM, Mientjes E, Grossen P, Distler T, *et al*: Secreted retrovirus-like GAG-domain-containing protein PEG10 is regulated by UBE3A and is involved in Angelman syndrome pathophysiology. Cell Rep Med 2: 100360, 2021.
26. Akamatsu S, Wyatt AW, Lin D, Lysakowski S, Zhang F, Kim S, Tse C, Wang K, Mo F, Haegert A, *et al*: The placental gene PEG10 promotes progression of neuroendocrine prostate cancer. Cell Rep 12: 922-936, 2015.
27. Yang J and Wang X: Role of long non-coding RNAs in lymphoma: A systematic review and clinical perspectives. Crit Rev Oncol Hematol 141: 13-22, 2019.
28. Zhao J, Su L and Jiang J: Long Non-coding RNA paternally expressed imprinted gene 10 (PEG10) elevates diffuse large B-Cell lymphoma progression by regulating kinesin family member 2A (KIF2A) via targeting MiR-101-3p. Med Sci Monit 26: e922810, 2020.
29. Peng W, Fan H, Wu G, Wu J and Feng J: Upregulation of long noncoding RNA PEG10 associates with poor prognosis in diffuse large B cell lymphoma with facilitating tumorigenicity. Clin Exp Med 16: 177-182, 2016.
30. Zhang J, Liu W, Ji P and Zhang Y: Silencing of long chain noncoding RNA paternally expressed gene (PEG10) inhibits the progression of neuroblastoma by regulating microRNA-449a (miR-449a)/ribosomal protein S2 (RPS2) axis. Bioengineered 13: 6309-6322, 2022.
31. Ishii S, Yamashita K, Harada H, Ushiku H, Tanaka T, Nishizawa N, Yokoi K, Washio M, Ema A, Mieno H, *et al*: The H19-PEG10/IGF2BP3 axis promotes gastric cancer progression in patients with high lymph node ratios. Oncotarget 8: 74567-74581, 2017.
32. Wang J, Chu XQ, Zhang D and Kong DF: Knockdown of long non-coding RNA PEG10 inhibits growth, migration and invasion of gastric carcinoma cells via up-regulating miR-3200. Neoplasma 65: 769-778, 2018.
33. Xiao H, Ding N, Liao H, Yao Z, Cheng X, Zhang J and Zhao M: Prediction of relapse and prognosis by expression levels of long noncoding RNA PEG10 in glioma patients. Medicine (Baltimore) 98: e17583, 2019.
34. Fu Y, Bi Y, Wang F, Chen X and Liu H: Declination of long noncoding RNA paternally expressed gene 10 inhibits A375 cells proliferation, migration, and invasion via mediating microRNA-33a. J Cell Biochem 120: 19868-19877, 2019.
35. Zang W, Wang T, Huang J, Li M, Wang Y, Du Y, Chen X and Zhao G: Long noncoding RNA PEG10 regulates proliferation and invasion of esophageal cancer cells. Cancer Gene Ther 22: 138-144, 2015.
36. Zhao M, Sun D, Li X, Xu Y, Zhang H, Qin Y and Xia M: Overexpression of long noncoding RNA PEG10 promotes proliferation, invasion and metastasis of hypopharyngeal squamous cell carcinoma. Oncol Lett 14: 2919-2925, 2017.
37. Kumar A, Kumar V, Rattan V, Jha V and Bhattacharyya S: Secretome proteins regulate comparative osteogenic and adipogenic potential in bone marrow and dental stem cells. Biochimie 155: 129-139, 2018.
38. Jung S and Lee JS: Single-cell genomics for investigating pathogenesis of inflammatory diseases. Mol Cells 46: 120-129, 2023.
39. Wu YL, Lin ZJ, Li CC, Lin X, Shan SK, Guo B, Zheng MH, Li F, Yuan LQ and Li ZH: Epigenetic regulation in metabolic diseases: Mechanisms and advances in clinical study. Signal Transduct Target Ther 8: 98, 2023.
40. Bar S, Vershkov D, Keshet G, Lezmi E, Meller N, Yilmaz A, Yanuka O, Nissim-Rafinia M, Meshorer E, Eldar-Geva T and Benvenisty N: Identifying regulators of parental imprinting by CRISPR/Cas9 screening in haploid human embryonic stem cells. Nat Commun 12: 6718, 2021.
41. Bretz CL, Langohr IM, Lee S and Kim J: Epigenetic instability at imprinting control regions in a Kras(G12D)-induced T-cell neoplasm. Epigenetics 10: 1111-1120, 2015.
42. Yamaguchi S, Shen L, Liu Y, Sendler D and Zhang Y: Role of Tet1 in erasure of genomic imprinting. Nature 504: 460-464, 2013.
43. Kempinska K, Malik B, Borkin D, Klossowski S, Shukla S, Miao H, Wang J, Cierpicki T and Grembecka J: Pharmacologic inhibition of the Menin-MLL interaction leads to transcriptional repression of PEG10 and blocks hepatocellular carcinoma. Mol Cancer Ther 17: 26-38, 2018.
44. Shoshani O, Brunner SF, Yaeger R, Ly P, Nechemia-Arbely Y, Kim DH, Fang R, Castillon GA, Yu M, Li JSZ, *et al*: Chromothripsis drives the evolution of gene amplification in cancer. Nature 591: 137-141, 2021.
45. Dong H, Zhang H, Liang J, Yan H, Chen Y, Shen Y, Kong Y, Wang S, Zhao G and Jin W: Digital karyotyping reveals probable target genes at 7q21.3 locus in hepatocellular carcinoma. BMC Med Genomics 4: 60, 2011.
46. Tsuji K, Yasui K, Gen Y, Endo M, Dohi O, Zen K, Mitsuyoshi H, Minami M, Itoh Y, Taniwaki M and Tanaka S: PEG10 is a probable target for the amplification at 7q21 detected in hepatocellular carcinoma. Cancer Genet Cytogenet 198: 118-125, 2010.
47. Huang J, Sheng HH, Shen T, Hu YJ, Xiao HS, Zhang Q, Zhang QH and Han ZG: Correlation between genomic DNA copy number alterations and transcriptional expression in hepatitis B virus-associated hepatocellular carcinoma. FEBS Lett 580: 3571-3581, 2006.
48. Kwon HC, Bae Y and Lee SV: The role of mRNA quality control in the aging of caenorhabditis elegans. Mole Cells 46: 664-671, 2023.

49. Zhang Y, Dou X, Kong Q, Li Y and Zhou X: Circ_0075804 promotes the malignant behaviors of retinoblastoma cells by binding to miR-138-5p to induce PEG10 expression. Int Ophthalmol 42: 509-523, 2022.
50. Zhang L, Wan Y, Zhang Z, Jiang Y, Gu Z, Ma X, Nie S, Yang J, Lang J, Cheng W and Zhu L: IGF2BP1 overexpression stabilizes PEG10 mRNA in an m6A-dependent manner and promotes endometrial cancer progression. Theranostics 11: 1100-1114, 2021.
51. Santiago M, Antunes C, Guedes M, Iacovino M, Kyba M, Reik W, Sousa N, Pinto L, Branco MR and Marques CJ: Tet3 regulates cellular identity and DNA methylation in neural progenitor cells. Cell Mol Life Sci 77: 2871-2883, 2020.
52. Shyu YC, Lee TL, Lu MJ, Chen JR, Chien RN, Chen HY, Lin JF, Tsou AP, Chen YH, Hsieh CW and Huang TS: miR-122-mediated translational repression of PEG10 and its suppression in human hepatocellular carcinoma. J Transl Med 14: 200, 2016.
53. Li Y, Guo D, Lu G, Mohiuddin Chowdhury ATM, Zhang D, Ren M, Chen Y, Wang R and He S: LncRNA SNAI3-AS1 promotes PEG10-mediated proliferation and metastasis via decoying of miR-27a-3p and miR-34a-5p in hepatocellular carcinoma. Cell Death Dis 11: 685, 2020.
54. Li B, Shi C, Li B, Zhao JM and Wang L: The effects of Curcumin on HCT-116 cells proliferation and apoptosis via the miR-491/PEG10 pathway. J Cell Biochem 119: 3091-3098, 2018.
55. Ye M, Zhao L, Zhang L, Wu S, Li Z, Qin Y, Lin F and Pan L: LncRNA NALT1 promotes colorectal cancer progression via targeting PEG10 by sponging microRNA-574-5p. Cell Death Dis 13: 960, 2022.
56. Jiménez Martín O, Schlosser A, Furtwängler R, Wegert J and Gessler M: MYCN and MAX alterations in Wilms tumor and identification of novel N-MYC interaction partners as biomarker candidates. Cancer Cell Int 21: 555, 2021.
57. Li CM, Margolin AA, Salas M, Memeo L, Mansukhani M, Hibshoosh H, Szabolcs M, Klinakis A and Tycko B: PEG10 is a c-MYC target gene in cancer cells. Cancer Res 66: 665-672, 2006.
58. Wang C, Xiao Y, Hu Z, Chen Y, Liu N and Hu G: PEG10 directly regulated by E2Fs might have a role in the development of hepatocellular carcinoma. FEBS Lett 582: 2793-2798, 2008.
59. Peng YP, Zhu Y, Yin LD, Zhang JJ, Wei JS, Liu X, Liu XC, Gao WT, Jiang KR and Miao Y: PEG10 overexpression induced by E2F-1 promotes cell proliferation, migration, and invasion in pancreatic cancer. J Exp Clin Cancer Res 36: 30, 2017.
60. Zhang M, Sui C, Dai B, Shen W, Lu J and Yang J: PEG10 is imperative for TGF-β1-induced epithelial-mesenchymal transition in hepatocellular carcinoma. Oncol Rep 37: 510-518, 2017.
61. Zhang B, Liu ZY, Wu R, Zhang CM, Cao K, Shan WG, Liu Z, Ji M, Tian ZL, Sethi G, *et al*: Transcriptional regulator CTR9 promotes hepatocellular carcinoma progression and metastasis via increasing PEG10 transcriptional activity. Acta Pharmacol Sin 43: 2109-2118, 2022.
62. Yahiro Y, Maeda S, Shinohara N, Jokoji G, Sakuma D, Setoguchi T, Ishidou Y, Nagano S, Komiya S and Taniguchi N: PEG10 counteracts signaling pathways of TGF-β and BMP to regulate growth, motility and invasion of SW1353 chondrosarcoma cells. J Bone Miner Metab 37: 441-454, 2019.
63. Shinohara N, Maeda S, Yahiro Y, Sakuma D, Matsuyama K, Imamura K, Kawamura I, Setoguchi T, Ishidou Y, Nagano S and Komiya S: TGF-β signalling and PEG10 are mutually exclusive and inhibitory in chondrosarcoma cells. Sci Rep 7: 13494, 2017.
64. Rotinen M, You S, Yang J, Coetzee SG, Reis-Sobreiro M, Huang WC, Huang F, Pan X, Yáñez A, Hazelett DJ, *et al*: ONECUT2 is a targetable master regulator of lethal prostate cancer that suppresses the androgen axis. Nat Med 24: 1887-1898, 2018.
65. Chatterjee A, Gallent B, Katiki M, Qian C, Harter MR, Silletti S, Komives EA, Freeman MR and Murali R: The homeodomain regulates stable DNA binding of prostate cancer target ONECUT2. Nat Commun 15: 9037, 2024.
66. Akamatsu S, Inoue T, Ogawa O and Gleave ME: Clinical and molecular features of treatment-related neuroendocrine prostate cancer. Int J Urol 25: 345-351, 2018.
67. Feng H, Cheng AS, Tsang DP, Li MS, Go MY, Cheung YS, Zhao GJ, Ng SS, Lin MC, Yu J, *et al*: Cell cycle-related kinase is a direct androgen receptor-regulated gene that drives β-catenin/T cell factor-dependent hepatocarcinogenesis. J Clin Invest 121: 3159-3175, 2011.
68. Qin J, Liu M, Ding Q, Ji X, Hao Y, Wu X and Xiong J: The direct effect of estrogen on cell viability and apoptosis in human gastric cancer cells. Mol Cell Biochem 395: 99-107, 2014.
69. Kreutz D, Sinthuvanich C, Bileck A, Janker L, Muqaku B, Slany A and Gerner C: Curcumin exerts its antitumor effects in a context dependent fashion. J Proteomics 182: 65-72, 2018.
70. Xu P, Wu Z, Yang W and Wang L: Dysregulation of DNA methylation and expression of imprinted genes in mouse placentas of fetal growth restriction induced by maternal cadmium exposure. Toxicology 390: 109-116, 2017.
71. Wu JJ, Cai A, Greenslade JE, Higgins NR, Fan C, Le NTT, Tatman M, Whiteley AM, Prado MA, Dieriks BV, *et al*: ALS/FTD mutations in UBQLN2 impede autophagy by reducing autophagosome acidification through loss of function. Proc Natl Acad Sci USA 117: 15230-15241, 2020.
72. Zhao H, Gao Y, Miao J, Chen S, Li J, Li Z, Yin C and Yue W: Single-cell RNA-seq highlights a specific carcinoembryonic cluster in ovarian cancer. Cell Death Dis 12: 1082, 2021.
73. Lux A, Beil C, Majety M, Barron S, Gallione CJ, Kuhn HM, Berg JN, Kioschis P, Marchuk DA and Hafner M: Human retroviral gag- and gag-pol-like proteins interact with the transforming growth factor-beta receptor activin receptor-like kinase 1. J Biol Chem 280: 8482-8493, 2005.
74. Liu Z, Tian Z, Cao K, Zhang B, Wen Q, Zhou X, Yang W, Wang T, Shi H and Wang R: TSG101 promotes the proliferation, migration and invasion of hepatocellular carcinoma cells by regulating the PEG10. J Cell Mol Med 23: 70-82, 2019.
75. Xiong J, Qin J, Zheng Y, Peng X, Luo Y and Meng X: PEG10 promotes the migration of human Burkitt's lymphoma cells by up-regulating the expression of matrix metalloproteinase-2 and -9. Clin Invest Med 35: E117-125, 2012.
76. Golda M, Mótyán JA, Mahdi M and Tőzsér J: Functional study of the Retrotransposon-Derived human PEG10 Protease. Int J Mol Sci 21: 2424, 2020.
77. Okabe H, Satoh S, Furukawa Y, Kato T, Hasegawa S, Nakajima Y, Yamaoka Y and Nakamura Y: Involvement of PEG10 in human hepatocellular carcinogenesis through interaction with SIAH1. Cancer Res 63: 3043-3048, 2003.
78. Tang Y, Wu Y, Xue M, Zhu B, Fan W and Li J: A 10-Gene signature identified by machine learning for predicting the response to transarterial chemoembolization in patients with hepatocellular carcinoma. J Oncol 2022: 3822773, 2022.
79. Bang H, Ha SY, Hwang SH and Park CK: Expression of PEG10 is associated with poor survival and tumor recurrence in hepatocellular carcinoma. Cancer Res Treat 47: 844-852, 2015.
80. Peng W, Zhao G, Ma Y, Yu H and Wang X: Dendritic cells transfected with PEG10 recombinant adenovirus elicit anti-tumor immune response in vitro and in vivo. Vaccine 29: 3501-3506, 2011.
81. Jie X, Lang C, Jian Q, Chaoqun L, Dehua Y, Yi S, Yanping J, Luokun X, Qiuping Z, Hui W, *et al*: Androgen activates PEG10 to promote carcinogenesis in hepatic cancer cells. Oncogene 26: 5741-5751, 2007.
82. Jia HL, Ye QH, Qin LX, Budhu A, Forgues M, Chen Y, Liu YK, Sun HC, Wang L, Lu HZ, *et al*: Gene expression profiling reveals potential biomarkers of human hepatocellular carcinoma. Clin Cancer Res 13: 1133-1139, 2007.
83. Ip WK, Lai PB, Wong NL, Sy SM, Beheshti B, Squire JA and Wong N: Identification of PEG10 as a progression related biomarker for hepatocellular carcinoma. Cancer Lett 250: 284-291, 2007.
84. Wu X, Wang L, Feng F and Tian S: Weighted gene expression profiles identify diagnostic and prognostic genes for lung adenocarcinoma and squamous cell carcinoma. J Int Med Res 48: 300060519893837, 2020.
85. Deng X, Hu Y, Ding Q, Han R, Guo Q, Qin J, Li J, Xiao R, Tian S, Hu W, *et al*: PEG10 plays a crucial role in human lung cancer proliferation, progression, prognosis and metastasis. Oncol Rep 32: 2159-2167, 2014.
86. Sinha A, Zou Y, Patel AS, Yoo S, Jiang F, Sato T, Kong R, Watanabe H, Zhu J, Massion PP, *et al*: Early-stage lung adenocarcinoma MDM2 genomic amplification predicts clinical outcome and response to targeted therapy. Cancers (Basel) 14: 708, 2022.
87. Wang D, Zhao J, Li S, Wei J, Nan L, Mallampalli RK, Weathington NM, Ma H and Zhao Y: Phosphorylated E2F1 is stabilized by nuclear USP11 to drive Peg10 gene expression and activate lung epithelial cells. J Mol Cell Biol 10: 60-73, 2018.
88. Nakagawa N, Miyake N, Ochi N, Yamane H, Takeyama M, Nagasaki Y, Ikeda T, Yokota E, Fukazawa T, Nakanishi H, *et al*: Targeting ROR1 in combination with osimertinib in EGFR mutant lung cancer cells. Exp Cell Res 409: 112940, 2021.

89. De Marco C, Laudanna C, Rinaldo N, Oliveira DM, Ravo M, Weisz A, Ceccarelli M, Caira E, Rizzuto A, Zoppoli P, *et al*: Specific gene expression signatures induced by the multiple oncogenic alterations that occur within the PTEN/PI3K/AKT pathway in lung cancer. PLoS One 12: e0178865, 2017.
90. Xing Q, Liu S, Luan J, Wang Y and Ma L: A novel 13 RNA binding proteins (RBPs) signature could predict prostate cancer biochemical recurrence. Pathol Res Pract 225: 153587, 2021.
91. Lundin-Ström KB, Biloglav A, Lazarevic V, Behrendtz M, Castor A and Johansson B: Parental origin of monosomy 7 in acute leukaemia. Br J Haematol 192: e132-e135, 2021.
92. Yoshie H, Sedukhina AS, Minagawa K, Oda K, Ohnuma S, Yanagisawa N, Maeda I, Takagi M, Kudo H, Nakazawa R, *et al*: A bioinformatics-to-clinic sequential approach to analysis of prostate cancer biomarkers using TCGA datasets and clinical samples: A new method for precision oncology? Oncotarget 8: 99601-99611, 2017.
93. Shapovalova M, Lee JK, Li Y, Vander Griend DJ, Coleman IM, Nelson PS, Dehm SM and LeBeau AM: PEG10 Promoter-driven expression of reporter genes enables molecular imaging of lethal prostate cancer. Cancer Res 79: 5668-5680, 2019.
94. Kim S, Thaper D, Bidnur S, Toren P, Akamatsu S, Bishop JL, Colins C, Vahid S and Zoubeidi A: PEG10 is associated with treatment-induced neuroendocrine prostate cancer. J Mol Endocrinol 63: 39-49, 2019.
95. Hu C, Xiong J, Zhang L, Huang B, Zhang Q, Li Q, Yang M, Wu Y, Wu Q, Shen Q, *et al*: PEG10 activation by co-stimulation of CXCR5 and CCR7 essentially contributes to resistance to apoptosis in CD19+CD34+ B cells from patients with B cell lineage acute and chronic lymphocytic leukemia. Cell Mol Immunol 1: 280-294, 2004.
96. Wu H, Luo H, Wang M, Du Y and Li J: NAP1L5 promotes epithelial-mesenchymal transition by regulating PEG10 expression in acute myeloid leukaemia. Leuk Res 148: 107623, 2025.
97. Haider Z, Landfors M, Golovleva I, Erlanson M, Schmiegelow K, Flægstad T, Kanerva J, Norén-Nyström U, Hultdin M and Degerman S: DNA methylation and copy number variation profiling of T-cell lymphoblastic leukemia and lymphoma. Blood Cancer J 10: 45, 2020.
98. Xiong S, Liu F, Sun J, Gao S, Wong CCL, Tu P and Wang Y: Abrogation of USP9X is a potential strategy to decrease PEG10 levels and impede tumor progression in cutaneous T-cell lymphoma. J Invest Dermatol 144: 2778-2788.e9, 2024.
99. Kainz B, Shehata M, Bilban M, Kienle D, Heintel D, Krömer-Holzinger E, Le T, Kröber A, Heller G, Schwarzinger I, *et al*: Overexpression of the paternally expressed gene 10 (PEG10) from the imprinted locus on chromosome 7q21 in high-risk B-cell chronic lymphocytic leukemia. Int J Cancer 121: 1984-1993, 2007.
100. Alanazi I, Hoffmann P and Adelson DL: MicroRNAs are part of the regulatory network that controls EGF induced apoptosis, including elements of the JAK/STAT pathway, in A431 cells. PLoS One 10: e0120337, 2015.
101. Lee Y, Park S, Lee SH and Lee H: Characterization of genetic aberrations in a single case of metastatic thymic adenocarcinoma. BMC Cancer 17: 330, 2017.
102. Yan S, Du L, Jiang X, Duan W, Li J, Xie Y, Zhan Y, Zhang S, Wang L, Li S and Wang C: Evaluation of serum exosomal lncRNAs as diagnostic and prognostic biomarkers for esophageal squamous cell carcinoma. Cancer Manag Res 12: 9753-9763, 2020.
103. Ge H, Yan Y, Wu D, Huang Y and Tian F: Prognostic value of PEG10 in Asian solid tumors: A meta-analysis. Clin Chim Acta 483: 197-203, 2018.
104. Sumitani N, Ishida K, Sawada K, Kimura T, Kaneda Y and Nimura K: Identification of malignant cell populations associated with poor prognosis in High-grade serous ovarian cancer using Single-Cell RNA sequencing. Cancers (Basel) 14: 3580, 2022.
105. Gov E: Co-expressed functional module-related genes in ovarian cancer stem cells represent novel prognostic biomarkers in ovarian cancer. Syst Biol Reprod Med 66: 255-266, 2020.
106. Hua Y, Ma X, Liu X, Yuan X, Qin H and Zhang X: Identification of the potential biomarkers for the metastasis of rectal adenocarcinoma. APMIS 125: 93-100, 2017.
107. Watson KM, Gardner IH, Byrne RM, Ruhl RR, Lanciault CP, Dewey EN, Anand S and Tsikitis VL: Differential expression of PEG10 contributes to aggressive disease in early versus Late-onset colorectal cancer. Dis Colon Rectum 63: 1610-1620, 2020.
108. Kawai Y, Imada K, Akamatsu S, Zhang F, Seiler R, Hayashi T, Leong J, Beraldi E, Saxena N, Kretschmer A, *et al*: Paternally expressed gene 10 (PEG10) promotes growth, invasion, and survival of bladder cancer. Mol Cancer Ther 19: 2210-2220, 2020.
109. Liu Z, Yang Z, Liu D, Li D, Zou Q, Yuan Y, Li J, Liang L, Chen M and Chen S: TSG101 and PEG10 are prognostic markers in squamous cell/adenosquamous carcinomas and adenocarcinoma of the gallbladder. Oncol Lett 7: 1128-1138, 2014.
110. Liu DC, Yang ZL and Jiang S: Identification of PEG10 and TSG101 as carcinogenesis, progression, and poor-prognosis related biomarkers for gallbladder adenocarcinoma. Pathol Oncol Res 17: 859-866, 2011.
111. Li X, Xiao R, Tembo K, Hao L, Xiong M, Pan S, Yang X, Yuan W, Xiong J and Zhang Q: PEG10 promotes human breast cancer cell proliferation, migration and invasion. Int J Oncol 48: 1933-1942, 2016.
112. Katuwal NB, Kang MS, Ghosh M, Hong SD, Jeong YG, Park SM, Kim SG, Sohn J, Kim TH, Moon YW, *et al*: Targeting PEG10 as a novel therapeutic approach to overcome CDK4/6 inhibitor resistance in breast cancer. J Exp Clin Cancer Res 42: 325, 2023.
113. Tang FH, Chang WA, Tsai EM, Tsai MJ and Kuo PL: Investigating novel genes potentially involved in endometrial adenocarcinoma using Next-generation sequencing and bioinformatic approaches. Inte J Med Sci 16: 1338-1348, 2019.
114. Sharan Singh S, Kumar R, Singh Kushwaha V, Bhatt MLBB, Singh A, Mishra A, Ram H, Parmar D and Gupta R: Expression of radioresistant gene PEG10 in OSCC patients and its prognostic significance. Asian Pac J Cancer Prev 18: 1513-1518, 2017.
115. Liang J, Liu N and Xin H: Knockdown long non-coding RNA PEG10 inhibits proliferation, migration and invasion of glioma cell line U251 by regulating miR-506. Gen Physiol Biophys 38: 295-304, 2019.
116. Deng HX, Chen W, Hong ST, Boycott KM, Gorrie GH, Siddique N, Yang Y, Fecto F, Shi Y, Zhai H, *et al*: Mutations in UBQLN2 cause dominant X-linked juvenile and adult-onset ALS and ALS/dementia. Nature 477: 211-215, 2011.
117. Kim SH, Nichols KD, Anderson EN, Liu Y, Ramesh N, Jia W, Kuerbis CJ, Scalf M, Smith LM, Pandey UB and Tibbetts RS: Axon guidance genes modulate neurotoxicity of ALS-associated UBQLN2. Elife 12: e84382, 2023.
118. Whiteley AM, Prado MA, de Poot SAH, Paulo JA, Ashton M, Dominguez S, Weber M, Ngu H, Szpyt J, Jedrychowski MP, *et al*. Global proteomics of Ubqln2-based murine models of ALS. J Biol Chem 296: 100153, 2021.
119. Huber F, Arnaud M, Stevenson BJ, Michaux J, Benedetti F, Thevenet J, Bobisse S, Chiffelle J, Gehert T, Müller M, *et al*: A comprehensive proteogenomic pipeline for neoantigen discovery to advance personalized cancer immunotherapy. Nat Biotechnol: October 11, 2024 (Epub ahead of print).
120. Tang Q and Khvorova A: RNAi-based drug design: Considerations and future directions. Nat Rev Drug Discov 23: 341-364, 2024.
121. Hill CH and Brierley I: Structural and functional insights into viral programmed ribosomal frameshifting. Annu Rev Virol 10: 217-242, 2023.