Table S1. PEA3 subfamily regulates the expression of genes associated with cell migration and invasion

Cancer type	PEA3 member	Gene	Finding	Reference
Bladder cancer	ETV4	P3H4	ETV4 binds directly to the promoter region of P3H4 and activates its transcription, prompting cancer proliferation and invasion.	[1]
Bladder cancer	ETV5	TAZ	ETV5 is involved in cancer invasion and metastasis by upregulating TAZ expression and activating Hippo pathway.	[2]
Breast cancer	ETV1	hTERT	HER2 interacts with ETV1 to synergistically activate hTERT transcription, conferring the aggressive biologic behavior in breast cancer.	[3]
Breast cancer	ETV5	hTERT	ETV5 and c-Myc synergistically mediate hTERT activation via composite Ets/E-box motifs.	[4]
Breast cancer	ETV1	Rcl	ETV1 and HER2/Neu coordinate to upregulate the Rcl expression. ETV1 binds to the Rcl promoter and increases tumor grade.	[5]
Breast cancer	ETV1	Smad7	HER2/Neu collaborates with ETV1 to activate Smad7 transcription.	[6]
Breast cancer	ETV4	MMP13	ETV4 promotes cancer proliferation, migration, invasion, and anchorage-independent growth by targeting its target gene MMP13.	[7]
Breast cancer (ER-negative)	ETV4	MMP1, CXCR4	ETV4 could promote cancer progression and metastasis by activating its well-characterized target genes CXCR4 and MMP1.	[8]
Chondrosarcoma	ETV5	MMP2	ETV5 upregulates MMP2 expression and promotes chondrosarcoma metastasis.	[9]
ccRCC	ETV4	FOSL1	ETV4 promotes ccRCC metastasis by activating the pro-metastatic gene FOSL1 in a PI3K-AKT dependent manner.	[10]
Colorectal cancer	ETV4	MMP7, MMP14	ETV4 acts as a mediator of cancer metastasis by regulating MMP7 and MMP14 expression.	[11]
Colorectal cancer	ETV4	COX2, MMP7	ETV4 activates transcriptional activity of COX-2 and MMP-7, leading to cancer progression.	[12]
Colorectal cancer	ETV4	MMP1, MMP7, COX2, iNOS	ETV4 expression is positively correlated with the expression of MMP1, MMP7, COX2, and iNOS, ETV4-MMP1-MMP-7-COX-2-iNOS axis contributes to colorectal cancer progression.	[13, 14]
Colorectal cancer	ETV5	PDGF-BB	ETV5 directly binds to the promoter region of PDGF-BB, which mediates colorectal cancer angiogenesis.	[15]
Endometrial cancer	ETV4	ER	ETV4 is a candidate factor regulating ER in endometrial cancer cells. The high level of ER contributes to cancer progression.	[16]
Endometrial cancer	ETV5	MMP2	ETV5 regulates MMP2 expression to confer tumor invasion ability.	[17]
Endometrial cancer	ETV5	NID1, NUPR1	ETV5 promotes cancer migration and invasion by directly upregulating NID1 and NUPR1 transcriptional activity in vitro and in vivo.	[18]
Gastric cancer	ETV4	KDM5D*	ETV4 might promote gastric cancer cell metastasis by negatively modulating KDM5D.	[19]
Gastric cancer	ETV4	KIF2A	ETV4 directly upregulates the expression of KIF2 to promote cell migration and invasion.	[20]

Gastric cancer	ETV4	ME1	ETV4 directly binds to ME1 promoter to promote cancer metastasis.	[21]
Glioma	ETV4	GalT V	ETV4 physically interacts with Sp1 transcription factor and forms an ETV4/Sp1 complex, the ETV4/Sp1 complex binds to the GalT V promoter, inducing glioma invasion.	[22]
Hepatocellular carcinoma	ETV4	uPAR	PBK promotes migration invasion by enhancing the binding of ETV4 to the uPAR promoter.	[23]
Hepatocellular carcinoma	ETV4	MMP1	CIC deficiency increases the expression of its downstream target ETV4, which further upregulates MMP1 expression and promotes hepatocellular carcinoma progression.	[24]
Lung adenocarcinoma	ETV4	MSI2	ETV4 increases MSI2 expression by directly binding to the promoter of MSI2, which promotes the proliferation and invasion of lung adenocarcinoma.	[25]
Lung cancer	ETV1/4/5	MMP2	ETV1/ETV4/ETV5 overexpression upregulates MMP2 target gene, which leads to the migration and invasion of lung cancer cells.	[26]
Lung cancer (NSCLC)	ETV4	PXN, MMP1	ETV4 overexpression promotes cancer progression by upregulating PXN and MMP1 transcriptionally.	[27]
Lung cancer (NSCLC)	ETV4	Rho	ETV4 activates the Rho protein in an HGF-enhanced manner, which further increases the phosphorylation of MLC and induces the malignancy potential of NSCLC cells.	[28]
Melanoma	ETV4	MMP25	ETV4 induces MMP25 overexpression and leads to melanoma metastasis.	[29]
Neuroblastoma	ETV5	RET	ETV5 promotes RET gene transcription by binding to the RET promoter, which drives neuroblastoma oncogenesis.	[30]
Oesophageal adenocarcinoma	ETV4	MMP1	ETV4 promotes cancer proliferation and invasive by targeting MMP1.	[31]
Oesophageal squamous cell carcinoma	ETV4	MMP2, MMP9	ETV4 induces cancer metastasis by enhancing MMP-2 and MMP-9 expression.	[32]
Oral squamous cell carcinoma	ETV4	MMP1/3/9	HGF induces the expression of ETV4, which in turn activates MMP1/3/9 and leads to oral cancer cell invasion.	[33]
Ovarian cancer	ETV5	FOXM1	ETV5 upregulates FOXM1 expression by binding to the proximal promoter region of FOXM1, which promotes cancer progression.	[34]
Pancreatic cancer	ETV1	Sparc, Has2	By regulating two novel downstream factors Sparc and Has2, ETV1 increases the invasive capacity of pancreatic cancer cells.	[35]
Prostate cancer	ETV1	β-catenin	ETV1 could stabilize β-catenin, which leads to the increased accumulation of β-catenin within prostate cancer cells, promoting malignant transformation in cancer.	[36]
Prostate cancer	ETV1	MMP1, MMP7	ETV1 activates transcription of its target genes MMP-1 and MMP-7, which regulates cell migration and invasion.	[37, 38]

Prostate cancer	ETV1	CHK1*	ETV1 contributes to DNA damage accumulation, genetic instability, and prostate tumor progression by directly repressing the expression of CHK1.	[39]
Prostate cancer	ETV4	uPA, MMP2, MMP9	ETV4 regulates uPA expression by directly binding to the uPA promoter region. Besides, uPA binds to its receptor uPAR, activating MMP2 and MMP9 expression and inducing tumor metastasis.	[40]
Prostate cancer	ETV4	MYC	ETV4 directly binds to the 5' and 3' MYC enhancers and regulates MYC expression to increase cellular motility.	[41]
Prostate cancer	ETV4	TAZ	ETV4 directly binds to the TAZ promoter region. TAZ upregulates its target gene SH3BP1, which promots cell migration and anchorage-independent growth.	[42]
Thyroid cancer	ETV1/4/5	TERT	ETV5 directly binds to the TERT promoter in a mutation-dependent manner, which increases the invasiveness of thyroid carcinoma.	[43, 44]
Thyroid cancer	ETV5	PIK3A	ETV5 promotes cell growth and migration by targeting and activating PIK3CA transcriptionally.	[45]

ER, estrogen receptor; MMP, matrix metalloproteinase; ccRCC, Clear cell renal cell carcinoma; PDGF-BB, platelet-derived growth factor BB; NID1, Nidogen 1; NUPR1, Nuclear Protein 1; MLC, myosin light chain; NSCLC, non-small-cell lung cancer; CHK1, Checkpoint kinase 1. *Genes downregulated by PEA3 subfamily.

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Table S2. miRNAs and drugs targeting PEA3 subfamily

Cancer type	PEA3 member	miRNA/drug	Patient samples	In-vitro model	Functions
Prostate cancer	ETV1	miR-129-5p	30 tumor tissues and matched adjacent normal tissues	RWPE-1, PC-3, DU145, and LNCaP	Through the repression of ETV1 expression, miR-129-5p could inactivate YAP signaling and inhibit cell proliferation.
Lung adenocarcinoma	ETV1	miR-1224-3p	52 tumor tissues and matched adjacent normal tissues	HBE, HCC827, NCI-H23, SPC-A1, H1975, H1299, and A549	Circ-ZNF609 enhances lung adenocarcinoma progression by increasing oncogenic EVT1 expression via sponging miR-1224-3p.
Glioma	ETV1	miR-195-5p	/	hCMEC/D3, HEK293T, U87, NHAs	miR-195-5p directly targets ETV1 3'-UTR and reduces its expression.
Lung cancer	ETV1	miR-582-5p	Blood samples of 38 lung cancer and 23 healthy controls	/	ETV1 is regulated by miR-582-5p in lung cancer.
Triple-negative breast cancer	ETV1	miR-17-5p	105 tumor tissues and matched adjacent normal tissues	MCF 10A, MDA-MB-231, BT-549, Hs578 T	miR-17-5p suppresses cell proliferation and invasion by directly targeting ETV1.
Gastrointestinal stromal tumors	ETV1	miR-17/20a	50 primary GIST tissues and10 GI-LMS tissues	GIST-T1, GIST-882	Overexpression of miR-17 and miR-20a affects the cell cycle and induces apoptosis by targeting ETV1 in GIST cells.
Glioblastoma	ETV5	miR-8067	3 tumor tissues and matched adjacent normal tissues	/	Low expression of ETV5, regulated by miR-8067, is significantly associated with a good prognosis.
Melanoma	ETV1	miR 17	/	WM-266-4, 624mel	miR-17 enhances the migration of melanoma cells by downregulating its target gene ETV1.
Prostate cancer	ETV1	YK-4-279	/	LNCaP, PC3	YK-4-279 inhibits ETV1 biological activity in fusion-positive prostate cancer cells, leading to decreased motility and invasion.
Melanoma and prostate cancer	ETV1	BRD32048	/	501mel, SK-MEL-28, LNCaP, PC3	BRD32048 binds to ETV1 directly, modulating the transcriptional activity of ETV1.
Breast cancer	ETV4, ETV5	Tamoxifen	69 women at increased risk for breast cancer (37 received tamoxifen and 32 received placebo)	/	Tamoxifen significantly downregulates the expression of ETV4 and ETV5, which are known to play a central role in stem cell renewal and differentiation.
Gastrointestinal stromal tumors	ETV1	trifluoperazine and thioridazine	/	GIST882	Trifluoperazine and thioridazine are potential ETV1 targeting drugs. Combined of phenothiazine and MEK inhibitors exerts strong anticancer effect in GISTs.
Cervical carcinoma	ETV1	p-anisidine	/	HeLa	p-anisidine is a promising anticancer agent targeting ETV1 with an IC50 of 27.769 mg/mL in HeLa cells.

GIST, gastrointestinal stromal tumors; GI-LMS, gastrointestinal leiomyosarcomas.