

Supplementary Table S1: Clinicopathological characteristics in public datasets

	TCGA cohort, n (%) (n = 167)	GSE24279 cohort, n (%) (n = 77)	GSE32688 cohort, n (%) (n = 25)
Gender			
Male	92 (55.1)	51 (66.2)	N/A
Female	75 (44.9)	25 (32.5)	N/A
N/A	0 (0.0)	1 (1.3)	25 (100.0)
Age (years)			
median (range)	65 (35-88)	65 (40-85)	N/A
N/A	0 (0.0)	3 (3.9)	25 (100.0)
Tumor location			
Ph	141 (84.4)	N/A	N/A
Pbt	26 (15.6)	N/A	N/A
T status			
T1-2	28 (10.8)	4 (5.2)	N/A
T3-4	139 (89.2)	73 (94.8)	N/A
Lymph node metastases			
Negative	46 (27.5)	8 (10.4)	8 (32.0)
Positive	121 (72.5)	69 (89.6)	17 (68.0)
UICC stage (ver.7)			
IA, IB	18 (10.8)	1 (1.3)	2 (8.0)
IIA	26 (15.6)	7 (9.1)	6 (24.0)
IIB	119 (71.2)	64 (83.1)	17 (68.0)
III	4 (2.4)	5 (6.5)	0 (0.0)
IV	0 (0.0)	0 (0.0)	0 (0.0)

N/A, Not available; UICC, International Union Against Cancer

Supplementary Table S2: Clinicopathological characteristics of Pre-Neoadjuvant therapy EUS-FNA biopsy cohort

Characteristics	Pre-Neoadjuvant therapy EUS-FNA biopsy specimens, n (%) (n = 62)
Gender	
Male	37 (59.7)
Female	25 (40.3)
Age (years)	
median (range)	70 (47-79)
Pre-Neoadjuvant therapy CA19-9 (U/mL)	
median (range)	80.5 (1-4956)
Tumor location	
Ph	32 (51.6)
Pbt	30 (48.4)
Pre-Neoadjuvant therapy tumor size (CT, mm)	
median (range)	25 (9-80)
Pre-Neoadjuvant therapy Resectability status	
Resectable	52 (83.9)
Borderline resectable	10 (16.1)
ypT status (Post-Neoadjuvant therapy)	
T0	1 (1.6)
T1	12 (19.4)
T2	2 (3.2)
T3	47 (75.8)
T4	0 (0.0)
ypN status (Post-Neoadjuvant therapy)	
N0	53 (85.5)
N1	9 (14.5)
IICC ypStage (ver.7, Post-Neoadjuvant therapy)	
0	1 (1.6)
IA	12 (19.4)
IB	2 (3.2)
IIA	38 (61.3)
IIB	9 (14.5)
III	0 (0.0)
IV	0 (0.0)
Neoadjuvant therapy	
Gemcitabine + Radiation	58 (93.5)
Gemcitabine + S-1 + Radiation	4 (6.5)
Adjuvant therapy	
Yes	62 (100.0)
No	0 (0.0)

EUS-FNA, Endoscopic ultrasound - guided fine needle aspiration

IICC, International Union Against Cancer

Supplementary Table S3: Recent studies reporting the clinical significance of 6 candidate miRNAs as cancer biomarkers

miRNA	Cancers	Clinical significance	Reference
miR-155-5p	Pancreatic ductal adenocarcinoma	Cancer detection, Prognosis (unfavorable)	69-72
	Gastric cancer	Tumor penetration through serosa and lymph node metastasis	67
	Colorectal cancer	Poor Prognosis (unfavorable) and treatment resistance	73
	Hepatocellular carcinoma	Cancer detection, Prognosis (unfavorable)	74
	Lung cancer	Cancer detection, recurrence and metastasis	75, 76
	Bladder cancer	Detection for invasive cancer	77
	Sinonasal Squamous Cell Carcinoma	Regional recurrence	78
	Neuroglioma	Prognosis (unfavorable)	79
miR-196b-5p	Pancreatic ductal adenocarcinoma	Cancer detection, Prognosis (unfavorable)	72, 80-82
	Gastric cancer	Cancer detection, Prognosis (unfavorable)	83, 84
	Colorectal cancer	Cancer detection, Prognosis (unfavorable), Chemoresistance	85-88
	Hepatocellular carcinoma	Prognosis (unfavorable), Tumor size, multiple tumor, vascular invasion	89, 90
	Oral cancer	Cancer detection	91
miR-365a-5p	Lung cancer	Prognosis (unfavorable)	92
miR-629-5p	Pancreatic ductal adenocarcinoma	Cancer detection, Advanced stage, Distant metastasis, Prognosis (unfavorable)	93
	Gastric cancer	Cancer detection	94
miR-675-3p			No reports
miR-92b-3p	Pancreatic ductal adenocarcinoma	Prognosis (favorable), Small tumor size, Lymph node metastasis negative	68
	Esophageal cancer	Prognosis (favorable), Prognosis (unfavorable)	95
	Gastric cancer	Cancer detection	96
	Colorectal cancer	Cancer detection, Chemotherapy response	97-99
	Hepatocellular carcinoma	Recurrence prediction, Microvascular invasion	100, 101
	Nasopharyngeal cancer	Prognosis (favorable)	102
	Breast cancer	Prognosis (favorable)	103
	Oral squamous cell carcinoma	Recurrence prediction (favorable), Prognosis (unfavorable)	104, 105
	Glioblastoma	Prognosis (unfavorable)	106

Supplementary Table S4: miRNA-mRNA network analysis of 6 candidate miRNAs

miRNA-mRNA regulatory analysis					
miRNA	Target Genes	miRNA	Target Genes	miRNA	Target Genes
hsa-miR-155-5p	KANSL1		KCNC4		NECTIN1
	PATJ		NOL4L		KCNA1
	FAM135A		DBT		ZNF512B
	BCAT1		DNAJB12		LRCH1
	ARL5B		GIT2		GPR180
	UQCR11		MAN2A1		GDF11
	KLF3		MEF2D		PIP4K2C
	VAV3		MYO5A		PPP1R12A
	CYB561D1		GLYR1		CALN1
	ATXN1L		SPOCK2		FAM133B
	FBXO33		GNAQ		PPP1R9A
	MIER3		MAP2K4		TBL1XR1
	RELA		PTAR1		PCDH11Y
	TENM3		SLC7A11		DESI1
	GABRA1		RSBN1		EFR3A
	TM9SF3		SERTAD3		NFIB
	CPEB4		RBFOX2		SFMBT2
	CDC73		DKK3		CELF2
hsa-miR-92b-3p	MYLK	TULP4		hsa-miR-92b-3p	PLXDC2
	DENND1B	YIPF4			MARCHF8
	DPY19L1	ATP7A			PIK3R3
	SP1	DAB2IP			NFIA
	CCR9	E2F3			TOR1AIP2
	GLIPR1	FXR1			QKI
	ZNF561	SPRYD4			ATXN3
	NR6A1	PTPRJ			FAM110B
	IGF2BP1	INSIG1			FRYL
	NXPE3	PAPD7			CXCL5
	MIEF1	BCL2L11			LIN54
	BACH1	PPP1R37			LIN28A
	LCOR	RAB8B			GAS2L3
hsa-miR-196b-5p	SLC31A1	TECPR2			TPCN1
	MRS2	GATAD2B			KCNK3
	NEDD4L	PLEKHA1			SOCS5
	RASGRP1	PCMTD1			CEP41
	EEF2K	FOXN3			TSSK6
	TMEM143	DNAJC30			ATL3
	SOX11	LDLRAD4			ELOVL6

	SOCS4	TMEM87A	PPARGC1B
	HIP1	PDS5B	CAMK2A
	CASK	DCX	GRM7
	ZDHHC21	CCNLJL	EIF4G2
	SOX12	C20orf194	SLC17A6
	MAPK8	LPP	ZBTB20
	YY1	ANGPTL2	TMCC1
	SFMBT1	COL5A1	SEC31B
	AAK1	PLEKHB2	C2CD4C
	HAND1	NCKAP5	HOXC8
	NME4	NPC1	PAWR
	PSMD11	SOCS6	CNOT2
	CDV3	TRAF3	SMARCA5
	YIPF6	SEMA6D	EIF1
	SLC30A6	ARPP19	XPR1
	DFFA	LUZP1	GAN
hsa-miR-365a-5p	HNRNPC	RORA	KDM2A
hsa-miR-629-5p	MTRF1L	NEO1	NACC2
	EIF1AD	RNF157	APOBEC3F
hsa-miR-675-3p	OPCML	ATRX	ZNF24
	ZNF268	PCDH11X	

Supplementary Table S5: Pathway enrichment analysis

SourceDB	Term.id	Term.name	Pathway enrichment analysis	
			Intersection	P value
Gene Ontology	GO:0019216	regulation of lipid metabolic process	DKK3;DAB2IP;INSIG1;VAV3;SOCS6;RORA;TBL1XR1;PIK3R3;SOC55;ELOVL6;ZBTB20;SP1;GLIPR1	0.00
KEGG	hsa04917	Prolactin signaling pathway	RELA;SOCS4;MAPK8;SOCS6;PIK3R3;SOC55	0.00
KEGG	hsa04668	TNF signaling pathway	MAP2K4;DAB2IP;RELA;MAPK8;TRAF3;PIK3R3;CXCL5	0.00
KEGG	hsa05169	Epstein-Barr virus infection	MAP2K4;E2F3;BCL2L11;RELA;MAPK8;PSMD11;TRAF3;PIK3R3	0.00
Gene Ontology	GO:0062012	regulation of small molecule metabolic process	SLC7A11;DKK3;ATP7A;INSIG1;DNAJC30;ARPP19;RORA;ELOVL6;ZBTB20;SP1	0.00
Gene Ontology	GO:0048880	sensory system development	MAN2A1;SLC7A11;TENM3;SOX11;YY1;PDS5B;DCX;COL5A1;NECTIN1;GDF11	0.00
Gene Ontology	GO:0035148	tube formation	DAB2IP;BCL2L11;SOX11;HAND1;LUZP1;NFIB	0.00
Gene Ontology	GO:0090596	sensory organ morphogenesis	MAN2A1;INSIG1;TENM3;SOX11;YY1;COL5A1;NECTIN1;GDF11	0.00
KEGG	hsa04210	Apoptosis	DAB2IP;BCL2L11;RELA;MAPK8;PIK3R3;DFFA	0.00
KEGG	hsa05142	Chagas disease (American trypanosomiasis)	GNAQ;MAP2K4;RELA;MAPK8;PIK3R3	0.00
KEGG	hsa04620	Toll-like receptor signaling pathway	MAP2K4;RELA;MAPK8;TRAF3;PIK3R3	0.00
Gene Ontology	GO:0098732	macromolecule deacylation	MIER3;MAPK8;TBL1XR1;ATXN3;NACC2	0.00
KEGG	hsa04664	Fc epsilon RI signaling pathway	MAP2K4;VAV3;MAPK8;PIK3R3	0.00
Gene Ontology	GO:0030323	respiratory tube development	MAN2A1;SLC7A11;ATP7A;ATXN1L;SOX11;NFIB	0.01
Gene Ontology	GO:0048705	skeletal system morphogenesis	MEF2D;INSIG1;PLEKHA1;FOXN3;SOX11;PPARGC1B;HOXC8	0.01
Gene Ontology	GO:0002931	response to ischemia	EEF2K;CAMK2A;CPEB4	0.01
Gene Ontology	GO:0061614	pri-miRNA transcription by RNA polymerase II	RELA;YY1;NFIB	0.01
Gene Ontology	GO:0060541	respiratory system development	MAN2A1;SLC7A11;ATP7A;ATXN1L;SOX11;NFIB	0.01
Gene Ontology	GO:0060021	roof of mouth development	INSIG1;PLEKHA1;SOX11;GDF11	0.01
Gene Ontology	GO:0034248	regulation of cellular amide metabolic process	IGF2BP1;SLC7A11;FXR1;QKI;LIN28A;EIF4G2;CNOT2;CPEB4;EIF1	0.01
Gene Ontology	GO:0038127	ERBB signaling pathway	DAB2IP;PTPRJ;SOCS4;HIP1;SOC55	0.01
Gene Ontology	GO:0061448	connective tissue development	MEF2D;ATP7A;RELA;HAND1;COL5A1;TBL1XR1;NFIB	0.01
Gene Ontology	GO:0048008	platelet-derived growth factor receptor signaling pathway	PTPRJ;PLEKHA1;HIP1	0.01
Gene Ontology	GO:0071241	cellular response to inorganic substance	ATP7A;EEF2K;MAPK8;ATRX;KCNA1;KCNK3	0.01
Gene Ontology	GO:0009896	positive regulation of catabolic process	DAB2IP;BCL2L11;NEDD4L;SOCS4;PIP4K2C;ATXN3;TPCN1;SOC55;ZBTB20	0.01
KEGG	hsa05212	Pancreatic cancer	E2F3;RELA;MAPK8;PIK3R3	0.01
KEGG	hsa04611	Platelet activation	GNAQ;RASGRP1;PPP1R12A;PIK3R3;MYLK	0.01
KEGG	hsa05167	Kaposi sarcoma-associated herpesvirus infection	MAP2K4;E2F3;RELA;MAPK8;TRAF3;PIK3R3	0.01
KEGG	hsa04012	ErbB signaling pathway	MAP2K4;MAPK8;PIK3R3;CAMK2A	0.01
KEGG	hsa04930	Type II diabetes mellitus	SOCS4;MAPK8;PIK3R3	0.01
KEGG	hsa04024	cAMP signaling pathway	VAV3;RELA;MAPK8;PPP1R12A;PIK3R3;CAMK2A	0.01
KEGG	hsa04657	IL-17 signaling pathway	RELA;MAPK8;TRAF3;CXCL5	0.01
KEGG	hsa04912	GnRH signaling pathway	GNAQ;MAP2K4;MAPK8;CAMK2A	0.01
KEGG	hsa05222	Small cell lung cancer	E2F3;RELA;TRAF3;PIK3R3	0.01
KEGG	hsa05161	Hepatitis B	MAP2K4;E2F3;RELA;MAPK8;PIK3R3	0.01

KEGG	hsa04932	Non-alcoholic fatty liver disease (NAFLD)	BCL2L11;UQCR11;RELA;MAPK8;PIK3R3	0.01
KEGG	hsa01522	Endocrine resistance	E2F3;MAPK8;PIK3R3;SP1	0.01
KEGG	hsa04750	Inflammatory mediator regulation of TRP channels	GNAQ;MAPK8;PIK3R3;CAMK2A	0.01
KEGG	hsa04921	Oxytocin signaling pathway	GNAQ;EEF2K;PPP1R12A;CAMK2A;MYLK	0.01
KEGG	hsa04934	Cushing syndrome	GNAQ;E2F3;KCNK3;CAMK2A;SP1	0.01
KEGG	hsa04660	T cell receptor signaling pathway	VAV3;RELA;RASGRP1;PIK3R3	0.01
Gene Ontology	GO:0010948	negative regulation of cell cycle process	DAB2IP;FOXN3;ATRX;CNOT2;NACC2;CDC73;ZNF268	0.02
Gene Ontology	GO:0009895	negative regulation of catabolic process	IGF2BP1;DAB2IP;RELA;NPC1;EIF4G2;DFFA;HNRNPC	0.02
Gene Ontology	GO:0016358	dendrite development	RBFOX2;DAB2IP;NEDD4L;EEF2K;PPP1R9A;CAMK2A	0.02
Gene Ontology	GO:0071216	cellular response to biotic stimulus	DAB2IP;BCL2L11;RELA;MAPK8;CXCL5;CDC73	0.02
KEGG	hsa04931	Insulin resistance	RELA;MAPK8;PIK3R3;PPARGC1B	0.02
Gene Ontology	GO:0019748	secondary metabolic process	MYO5A;SLC7A11;SP1	0.02
Gene Ontology	GO:0000041	transition metal ion transport	ATP7A;SLC31A1;NECTIN1;SLC30A6	0.02
Gene Ontology	GO:0032606	type I interferon production	RELA;YY1;TRAF3;ZBTB20	0.02
Gene Ontology	GO:0042303	molting cycle	MYO5A;ATP7A;RELA;ZDHHC21	0.02
KEGG	hsa04927	Cortisol synthesis and secretion	GNAQ;SP1;KCNK3	0.02
Gene Ontology	GO:0035459	cargo loading into vesicle	INSIG1;SEC31B	0.02
KEGG	hsa04137	Mitophagy	SP1;RELA;MAPK8	0.02
Gene Ontology	GO:0055094	response to lipoprotein particle	NPC1;SOCS5	0.02
Gene Ontology	GO:0050769	positive regulation of neurogenesis	MAN2A1;DAB2IP;RELA;TEMN3;NEDD4L;EEF2K;SOX11;PPP1R9A;LIN28A	0.02
KEGG	hsa04071	Sphingolipid signaling pathway	GNAQ;RELA;MAPK8;PIK3R3	0.02
Gene Ontology	GO:0010498	proteasomal protein catabolic process	DNAJ12;DAB2IP;FBXO33;NEDD4L;SOCS4;SOCS6;TBL1XR1;ATXN3;SOCS5	0.03
Gene Ontology	GO:0008202	steroid metabolic process	DKK3;INSIG1;PLEKHA1;SP1;NPC1;RORA;ELOVL6	0.03
KEGG	hsa04722	Neurotrophin signaling pathway	RELA;MAPK8;PIK3R3;CAMK2A	0.03
KEGG	hsa05120	Epithelial cell signaling in Helicobacter pylori infection	MAP2K4;RELA;MAPK8	0.03
KEGG	hsa05200	Pathways in cancer	GNAQ;E2F3;BCL2L11;SP1;RELA;RASGRP1;MAPK8;TRAF3;PIK3R3;CAMK2A	0.03
Gene Ontology	GO:0010657	muscle cell apoptotic process	MAP2K4;E2F3;CAMK2A	0.03
KEGG	hsa04622	RIG-I-like receptor signaling pathway	RELA;MAPK8;TRAF3	0.03
Gene Ontology	GO:0021591	ventricular system development	SLC7A11;SEMA6D	0.03
Gene Ontology	GO:0071402	cellular response to lipoprotein particle stimulus	NPC1;SOCS5	0.03
Gene Ontology	GO:0050808	synapse organization	MYO5A;SPOCK2;SLC7A11;DAB2IP;EEF2K;NECTIN1;PPP1R9A;NFIA	0.03
Gene Ontology	GO:0044843	cell cycle G1/S phase transition	BACH1;BCAT1;CNOT2;NACC2;CDC73;CAMK2A	0.03
KEGG	hsa04662	B cell receptor signaling pathway	VAV3;RELA;PIK3R3	0.03
KEGG	hsa05214	Glioma	E2F3;PIK3R3;CAMK2A	0.03
Gene Ontology	GO:0048545	response to steroid hormone	NR6A1;RBFOX2;BCL2L11;CNOT2;RELA;NPC1;RORA;PPARGC1B	0.03
Gene Ontology	GO:0055088	lipid homeostasis	INSIG1;NPC1;RORA;ZBTB20	0.03
Gene Ontology	GO:0010586	miRNA metabolic process	RELA;LIN28A	0.03

Gene Ontology	GO:0036314	response to sterol	INSIG1;RORA	0.03
Gene Ontology	GO:0042476	odontogenesis	MYO5A;BCL2L11;HAND1;NECTIN1	0.03
KEGG	hsa01524	Platinum drug resistance	ATP7A;SLC31A1;PIK3R3	0.03
Gene Ontology	GO:0016569	covalent chromatin modification	KANSL1;KDM2A;NACC2;CDC73;MIER3;MAPK8;ATRX;TBL1XR1 ;ATXN3	0.03
KEGG	hsa04062	Chemokine signaling pathway	CCR9;VAV3;RELA;PIK3R3;CXCL5	0.03
KEGG	hsa04971	Gastric acid secretion regulation of cellular	GNAQ;MYLK;CAMK2A	0.03
Gene Ontology	GO:0090287	response to growth factor stimulus	DKK3;DAB2IP;SOX11;CASK;LDLRAD4;NEO1	0.03
KEGG	hsa04926	Relaxin signaling pathway	MAP2K4;RELA;MAPK8;PIK3R3	0.03
KEGG	hsa05133	Pertussis	RELA;MAPK8;CXCL5	0.03
KEGG	hsa05220	Chronic myeloid leukemia	E2F3;RELA;PIK3R3	0.03
KEGG	hsa05160	Hepatitis C	RELA;MAPK8;TRAF3;PIK3R3	0.03
Gene Ontology	GO:0090559	regulation of membrane permeability	BCL2L11;MAPK8;CAMK2A	0.04
Gene Ontology	GO:2000272	negative regulation of signaling receptor activity	SOCS4;SOC5S	0.04
KEGG	hsa04215	Apoptosis	BCL2L11;MAPK8	0.04
Gene Ontology	GO:0001505	regulation of neurotransmitter levels	KCNC4;SLC7A11;ATP7A;CASK;RORA;PPP1R9A;CAMK2A	0.04
Gene Ontology	GO:0002764	immune response-regulating signaling pathway	DAB2IP;PTPRJ;PLEKHA1;PAWR;DENND1B;VAV3;RELA;MAPK8; TRAF3	0.04
Gene Ontology	GO:1903311	regulation of mRNA metabolic process	IGF2BP1;RBFOX2;FXR1;HNRNPC;CDC73;CELF2	0.04
Gene Ontology	GO:0010608	posttranscriptional regulation of gene expression	IGF2BP1;FXR1;HNRNPC;CNOT2;CPEB4;EIF1;QKI;LIN28A;EIF4G 2	0.04
KEGG	hsa04510	Focal adhesion	MYLK;VAV3;MAPK8;PPP1R12A;PIK3R3	0.04
Gene Ontology	GO:0044772	mitotic cell cycle phase transition	BACH1;FOXN3;BCAT1;CNOT2;NACC2;CDC73;ARPP19;CEP41;C AMK2A	0.04
Gene Ontology	GO:0006836	neurotransmitter transport	KCNC4;SLC7A11;CASK;PPP1R9A;CAMK2A;SLC17A6	0.04
KEGG	hsa05418	Fluid shear stress and atherosclerosis	MAP2K4;RELA;MAPK8;PIK3R3	0.04
Gene Ontology	GO:0002683	negative regulation of immune system process	DAB2IP;PTPRJ;PAWR;CDC73;SOX11;SOC5S;LRCH1;SOC5	0.04
Gene Ontology	GO:0048144	fibroblast proliferation	DAB2IP;PAWR;CDC73	0.04
Gene Ontology	GO:0042092	type 2 immune response	DENND1B;SOC5S	0.04
Gene Ontology	GO:0060627	regulation of vesicle-mediated transport	PTPRJ;INSIG1;RAB8B;NEDD4L;EEF2K;HIP1;CASK;AAK1;CAMK2 A	0.04
Gene Ontology	GO:0035690	cellular response to drug	GNAQ;PLEKHA1;PAWR;RELA;SLC31A1;ATRX;PPP1R12A	0.05
KEGG	hsa05210	Colorectal cancer	BCL2L11;MAPK8;PIK3R3	0.05
KEGG	hsa04960	Aldosterone-regulated sodium reabsorption	NEDD4L;PIK3R3	0.05
Gene Ontology	GO:0051668	localization within membrane	SLC7A11;INSIG1;HIP1;SEC31B	0.05
Gene Ontology	GO:0098727	maintenance of cell number	IGF2BP1;CNOT2;CDC73;LIN28A	0.05
KEGG	hsa05170	Human immunodeficiency virus 1 infection	GNAQ;APOBEC3F;RELA;MAPK8;PIK3R3	0.05
Gene Ontology	GO:0006979	response to oxidative stress	SLC7A11;ATP7A;PLEKHA1;PAWR;SP1;RELA;MAPK8;PPARGC1 B	0.05
KEGG	hsa04810	Regulation of actin cytoskeleton	MYLK;VAV3;PIP4K2C;PPP1R12A;PIK3R3	0.05
Gene Ontology	GO:0010038	response to metal ion	ATP7A;NEDD4L;EEF2K;MAPK8;NPC1;KCNA1;KCNK3	0.05

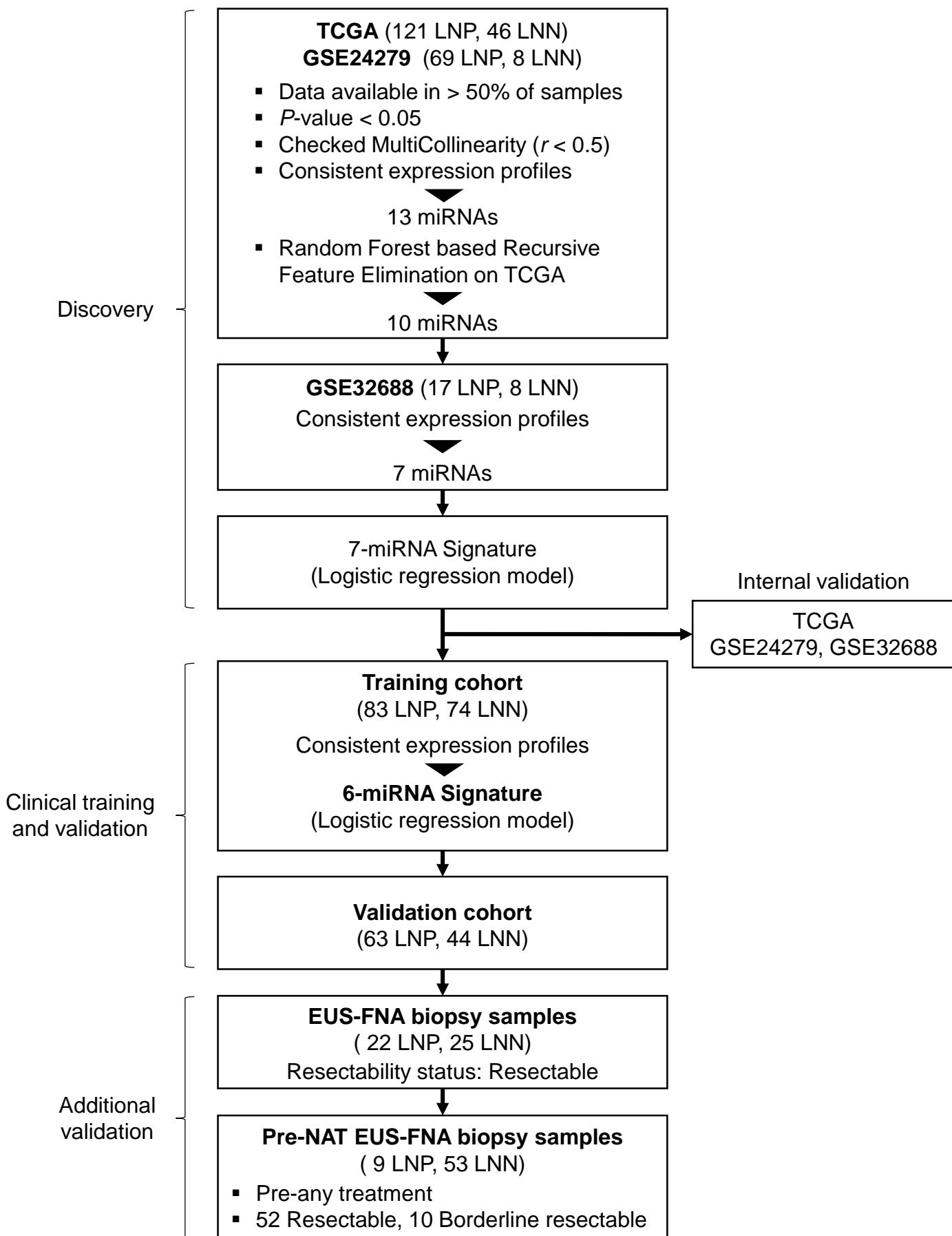
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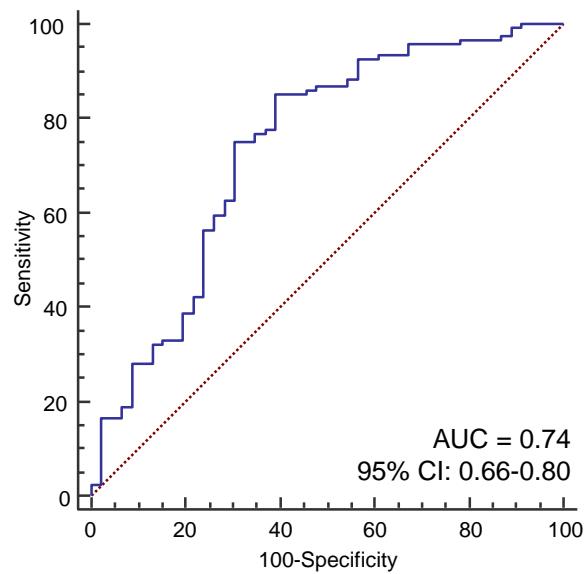
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Supplementary Figure 1

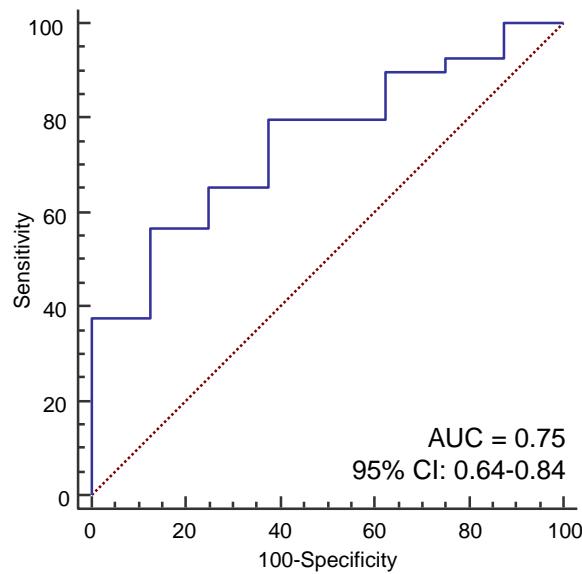


Supplementary Figure 2

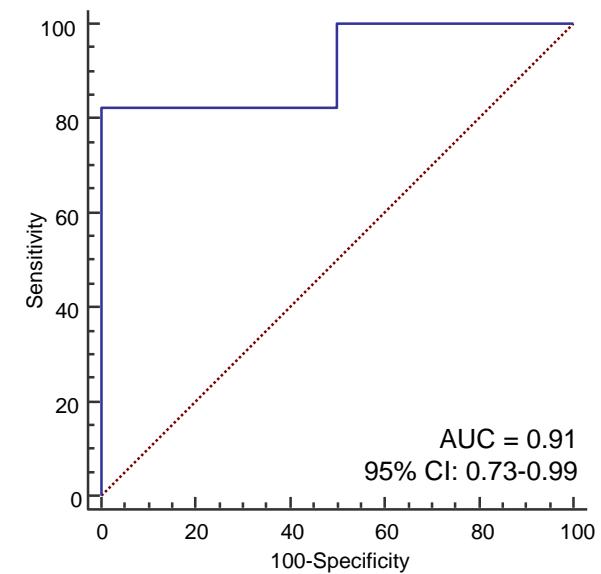
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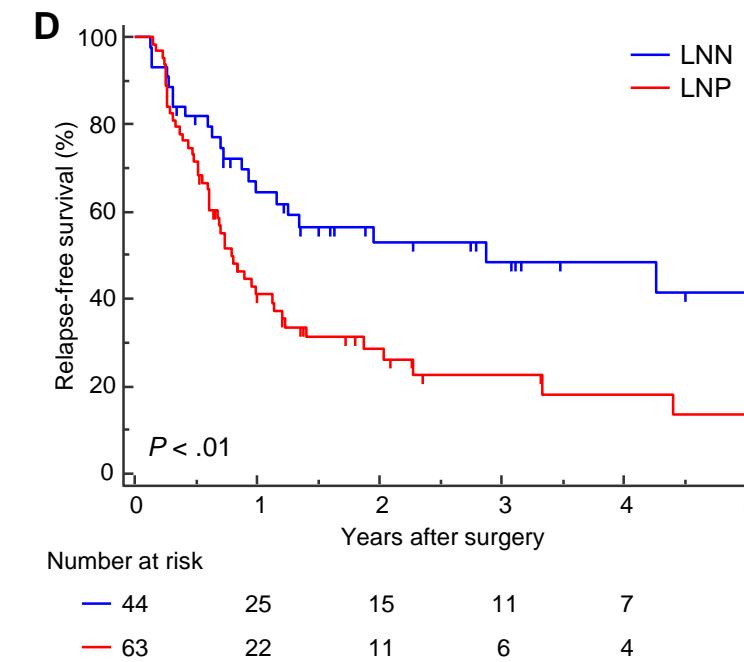
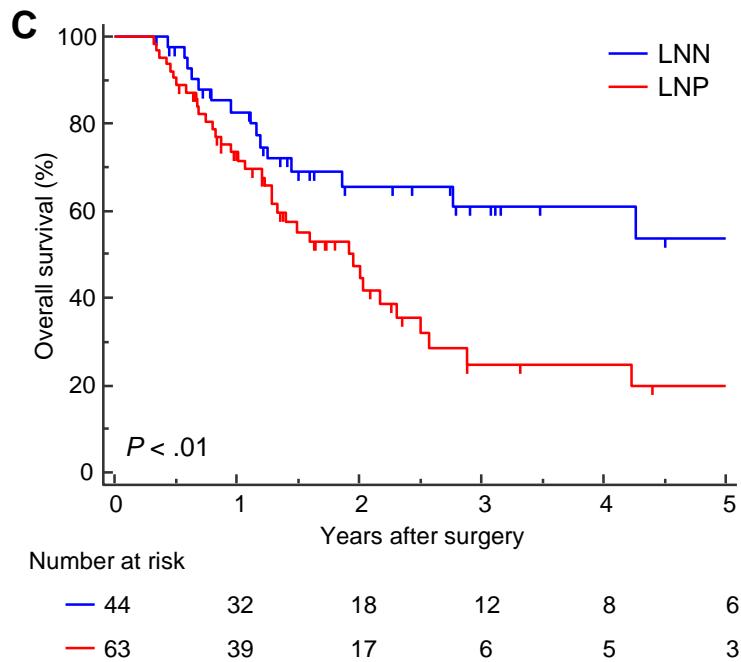
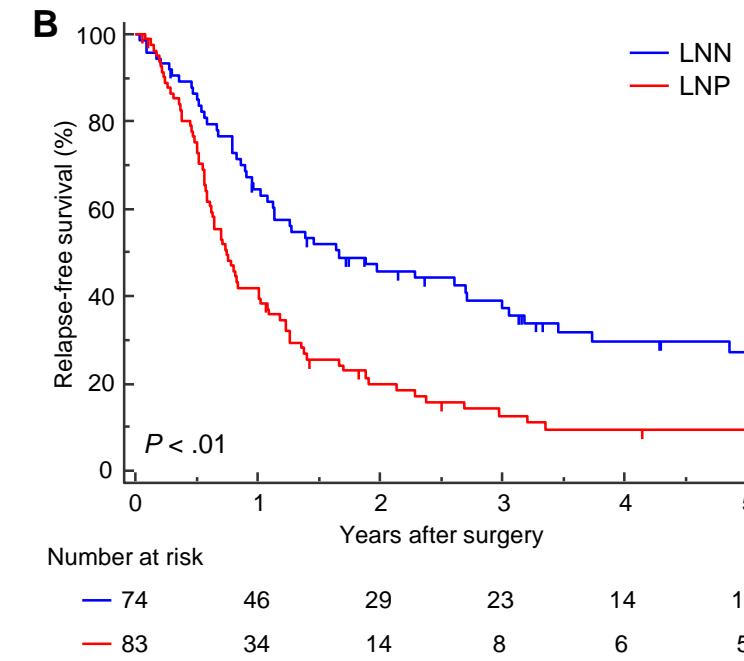
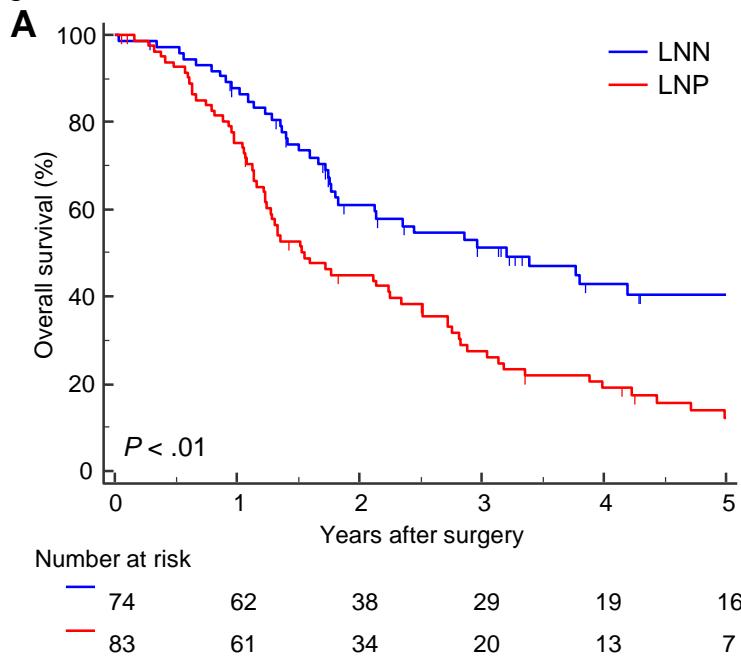
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C



Supplementary Figure 3



Supplementary Figure 4

