

Table S1. Significant preclinical and clinical studies on the features of saRNA-based therapeutics - extended characteristics.										
saRNA	Disease Condition	Delivery system	Gene	<i>In vitro</i>	<i>In vivo</i>	Cell lines	Route of administration	Animal models	Comments	Ref.
MTL-CEBPA	Advanced liver cancer	SMARTICLES (liposome)	CEBPA	-	-	-	Intravenous	-	The first clinical trial for saRNA-based therapeutics (NCT ID: NCT02716012; company: Mina Alpha Limited; phase 1). MTL-CEBPA shows favorable safety and promising synergistic effects in combination with TKIs.	[1]
MTL-CEBPA in combination with pembrolizumab	Adult solid tumors	SMARTICLES	CEBPA	-	-	-	Intravenous	-	A new clinical trial of MTL-CEBPA in combination with pembrolizumab (NCT ID: NCT04105335; Phase 1; recruitment status: Recruiting)	[2]
dsP21-322	Prostate cancer	Lipidoid-encapsulated nanoparticle (LNP)	P21	+	+	PC3	Intratumoral	PC3-bearing tumor-xenograft nude mice model	Proliferation inhibition and tumor shrinkage.	[3]
dsP21-322	Hepatocellular carcinoma (HCC)	Lipofectamine RNAiMax reagent (Life Technologies)	P21	+	-	HepG2 and Hep3B	-	-	Cell cycle arrest and inhibition of invasion and migration.	[4]
dsP21-322	Non-small-cell lung carcinomas	LipofectamineTM2000	P21	+	+	A549	Intratumoral	A549 subcutaneously transplanted BALB/c nude mice	<i>In vitro</i> : Proliferation inhibition, cell cycle arrest, and apoptosis induction. <i>In vivo</i> : Inhibition of tumor growth.	[5]
dsP21-322	Pancreatic cancer	Lipofectamine 2000	P21	+	+	PANC-1	Intratumoral	PANC-1 subcutaneously transplanted nude mice	<i>In vitro</i> : Proliferation inhibition, cell cycle arrest, and apoptosis induction. <i>In vivo</i> : Inhibition of tumor growth; high safety.	[6]
dsP21-322	Bladder cancer	Lipofectamine 2000	P21	+	-	T24	-	-	Proliferation inhibition, cell cycle arrest, and apoptosis induction.	[7]

dsWT1-319	HCC	Lipofectamine 2000	WT1	+	-	HepG2	-	-	Proliferation inhibition and apoptosis induction.	[8]
dsEcad-215	Prostate cancer	Lipofectamine 2000	E-cadherin	+	-	PC3	-	-	Inhibition of invasion and migration.	[9]
dsEcad-215	Bladder cancer	Lipofectamine 2000	E-cadherin	+	-	5637	-	-	Inhibition of invasion and migration.	[10]
dsEcad-215, 302	Breast cancer	Lipofectamine 2000	E-cadherin	+	+	MDA-MB-453 and MCF-7	Intratumoral	MDA-MB-453 subcutaneously injected into the BALB/c nude mice	<i>In vitro</i> : Proliferation inhibition, cell cycle arrest, apoptosis induction, and inhibition of invasion and migration. <i>In vivo</i> : Tumor growth inhibition	[11]
dsKLF4-496	Prostate cancer	Lipofectamine 2000	KLF4	+	-	PC-3 and DU145	-	-	Proliferation inhibition, cell cycle arrest, apoptosis induction, and inhibition of invasion and migration.	[12]
dsP53-285	Malignant pheochromocytoma	Lipofectamine RNAiMax	TP53	+	+	PC12	PC12 cells were infected with Lenti-dsP53-285 and subcutaneously injected	PC12 subcutaneously injected xenograft mice model	<i>In vitro</i> : Cell cycle arrest, proliferation inhibition, and apoptosis induction. <i>In vivo</i> : Tumor shrinkage.	[13]
dsHIC1-2998	Breast cancer	Lipofectamine 2000	HIC-1	+	-	MCF-7 and MDA-MB-231	-	-	Proliferation inhibition and apoptosis induction	[14]
dsPAWR-435	Bladder cancer and prostate cancer	Lipofectamine 2000	PAWR	+	-	T24 and PC3	-	-	Proliferation inhibition and apoptosis induction	[15]
dsNKX3-1-381	Prostate cancer	Lipofectamine 2000	NKX3-1	+	+	PC-3, CWR22R, LAPC4, and CWR22RV1	Intratumoral	PC3-bearing tumor-xenograft mice model	<i>In vitro</i> : Proliferation inhibition, cell cycle arrest, apoptosis induction. <i>In vivo</i> : Tumor growth inhibition.	[16]
saRNA ds-320	Nephrolithiasis	Lipofectamine 2000	TRPV5	+	+	NRK-52E	Retrograde ureteral injection	Calcium oxalate stone-forming rat model	<i>In vitro</i> : TRPV5 expression induction. <i>In vivo</i> : TRPV5 expression induction and reduction in the formation of CaOx kidney stone.	[17]

dsVHL-821	Renal cell carcinoma	Lipofectamine RNAiMax	VHL	+	-	769-P	-	-	Cell growth inhibition and apoptosis induction.	[18]
saRNA-482	HCC	Lipofectamine RNAiMax	NIS	+	-	HepG2 and Hep3B	-	-	Apoptosis induction and viability reduction of cancer cells.	[19]
dsP21-322-2'F	Bladder cancer	lipid nanoparticles	P21	-	+	-	Intravesical	Orthoptic bladder cancer mouse	Tumor Shrinkage	[20]
MTL-CEBPA	HCC	SMARTICLES	CEBPA	+	+	AML12, Clone 9, and HEPG2	Intravenous	Diethylnitrosamine-induced cirrhotic HCC rat, carbon-tetrachloride induced liver injury, and fibrosis mouse, and Methionine and choline deficient diet induced nonalcoholic steatohepatitis mouse	<i>In vitro</i> : CEBPA overexpression. <i>In vivo</i> : Tumor growth inhibition and tumor shrinkage.	[21]
C/EBPa-saRNA	HCC	Poly(amidamine) (PAMAM) dendrimers	CEBPA	+	+	HepG2	Intravenous	Rat liver tumor model	<i>In vitro</i> : Proliferation inhibition. <i>In vivo</i> : Tumor burden reduction.	[22]
C/EBPa-saRNA	HCC	PAMAM dendrimers	CEBPA	+	+	HepG2 and SMMC-7721	Intravenous	liver orthotopic xenograft nude mice tumor model	<i>In vitro</i> : Cell migration and invasion inhibition. <i>In vivo</i> : Metastasis inhibition	[23]
dsP21-322	Colorectal cancer	Lipopolyplex (HA anchored PE tumor-selective liposome)	P21	+	+	HT-29	Rectal	Orthotopic-HT29-bearing tumor-xenograft g NOD-SCID mice model colorectal tumor model	<i>In vitro</i> : Apoptosis induction, proliferation inhibition, and cell migration and invasion inhibition. <i>In vivo</i> : Tumor growth inhibition.	[24]

C/EBPa-saRNA	Pancreatic ductal adenocarcinoma	Aptamer	CEBPA	+	+	PANC-1	Intravenous	AsPC-1-bearing mouse xenograft model and PANC-1-bearing mouse xenograft model	<i>In vitro</i> : Proliferation inhibition. <i>In vivo</i> : Tumor shrinkage.	[25]
saV2-9 RNA	Prostate cancer	Aptamer	DPYSL3	+	+	PC-3	Intraperitoneal	Orthotopic mouse model with xenograft prostate tumor cells	<i>In vitro</i> : Proliferation inhibition and cell migration and invasion inhibition. <i>In vivo</i> : Metastasis inhibition	[26]
iNOS saRNA	Diabetes-induced Erectile dysfunction	Adenoviruses	Nos2	+	+	CSMCs	Intracavernous	Streptozotocin induced diabetes rat model	<i>In vitro</i> : iNos overexpression. <i>In vivo</i> : iNos overexpression and enhancement of peak intracavernous pressure.	[27]
Notch1-saRNA-1480	Human metastatic castration-resistant prostate cancer	Lipofectamine 3000	Notch1	+	+	PC-3	Intratumoral	PC3-bearing tumor-xenograft mice model	<i>In vitro</i> : Cell migration and invasion suppression, cell cycle arrest, and apoptosis inhibition. <i>In vivo</i> : Tumor growth inhibition and suppression of VEGF and AR pathways mechanisms.	[28]
HNF4A-saRNA	Non-alcoholic fatty liver disease	PAMAM dendrimers	HNF4A	+	+	HepG2, Hep3B, and PLCPRF5	Intravenous	NAFLD rat Model (High fat diet rat)	<i>In vitro</i> : Increase in the expression level of HNF4A, CYP450, CYP3A4, CYP3A5, and CYP3A7. <i>In vivo</i> : Liver triglyceride reduction, high-density lipoprotein/low-density lipoprotein (HDL/LDL) ratio enhancement, and white adipose tissue/body weight ratio reduction	[29]
FHIT-saRNA expression vector	Endometrial carcinoma	Lipofectamine 3000	FHIT	+	-	ISK, RL-952, HEC-1-B, and AN3CA	-	-	Proliferation, invasion, and metastasis inhibition	[30]

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