

Table SI. Representative EV-associated circRNA programs in immune and myeloid cell communication.

Authors, year	circRNA	EV donor or transferred component	Recipient	Intra-recipient mechanism	Measured endpoint	Transfer status	Cancer	(Refs.)
Chen <i>et al</i> , 2021	circFARSA	NSCLC-cell EV circFARSA	Macrophage	PTEN-PI3K-AKT signaling	CD163- and CD206-associated macrophage polarization and NSCLC metastasis	EV circRNA delivered to macrophages	NSCLC	(48)
Yao <i>et al</i> , 2023	circATP9A	NSCLC-cell EV circATP9A loaded by hnRNPA2B1	Macrophage	EV exposure induced M2-associated features. The HuR-NUCKS1-PI3K-AKT-mTOR route was measured in tumor cells	Macrophage polarization and NSCLC growth and metastasis	EV circRNA delivered to macrophages. The molecular route in macrophages was not resolved	NSCLC	(49)
Lu <i>et al</i> , 2020	circ0048117	Hypoxic ESCC-cell EV circ0048117	Macrophage	miR-140-TLR4	CD206, Arg1, IL-10 and TGF- β expression and increased ESCC-cell invasion and migration	EV uptake and circRNA-dependent activity measured in macrophages	ESCC	(50)
Zhang <i>et al</i> , 2023	circASPH	CRC-cell circASPH increased EV-associated STING	Macrophage	Tumor-cell circASPH stabilized IGF2BP2 and increased m6A-modified STING RNA, followed by EV transfer of STING	M2-associated macrophage features and CRC progression	STING was transferred. Transfer of circASPH was not shown	CRC	(53)
Wang <i>et al</i> , 2023	circATP2B4	EOC-cell EV circATP2B4	Macrophage	miR-532-3p-SREBF1 and PI3K-AKT signaling	M2-associated macrophage polarization and EOC metastasis	EV circRNA uptake and recipient-cell mechanism measured	EOC	(51)
Wang <i>et al</i> , 2021	circ_0074854	HCC-cell EV circ_0074854	Macrophage	EV circ_0074854 induced M2-associated features. HuR binding was measured in HCC cells	Macrophage polarization and HCC-cell migration and invasion	EV circRNA delivered to macrophages. The HuR route was tumor intrinsic	HCC	(52)

Gao <i>et al</i> , 2022	circZNF451	LUAD-cell EV circZNF451	Macrophage	TRIM56–FXR1 complex, FXR1 degradation and ELF4–IRF4 activation	Macrophage reprogramming, impaired CD8+ T-cell proliferation and effector function, and reduced anti-PD-1 activity in mice	EV-dependent circRNA increase in macrophages with donor perturbation and rescue	LUAD	(17)
Sun <i>et al</i> , 2024	circPOLQ	CRC-cell EV circPOLQ	Macrophage	miR-379-3p–IL-10–STAT3	M2-associated macrophage polarization and metastatic nodule formation	EV circRNA entered macrophages and was perturbed in donor cells	CRC	(54)
Wang <i>et al</i> , 2025	circUBQLN1	CRC-cell EV circUBQLN1	Macrophage	miR-34c-5p–CSF1R	M2-associated macrophage polarization and CRC progression	EV circRNA-dependent recipient-cell activity	CRC	(55)
Zhuang <i>et al</i> , 2024	circ-0100519	Breast-cancer-cell EV circ-0100519	Macrophage	circ-0100519 scaffolded USP7 and NRF2 and increased NRF2 deubiquitination	M2-associated macrophage polarization and breast cancer invasion and metastasis	EV circRNA delivered to macrophages with donor-cargo perturbation	Breast cancer	(56)
Cao <i>et al</i> , 2024	circ-001422	Glioma-cell EV circ-001422	Macrophage	p300-dependent STAT3 acetylation and STAT3-NF-κB transcription	TAM polarization and glioma progression	EV circRNA-dependent macrophage activity	Glioma	(57)
Song <i>et al</i> , 2022	circ_0017252	GC-cell EV circ_0017252	Macrophage	Reduced CD163- and CD206-associated macrophage features	Reduced M2-associated polarization and GC growth	EV-associated circRNA exposure. Absolute delivery was not quantified	GC	(58)
Liu <i>et al</i> , 2024	circFTO	M2-macrophage sEV circFTO	NSCLC cell	miR-148a-3p–PDK4	Tumor-cell proliferation, migration and glycolysis	Macrophage sEV circRNA delivered to tumor cells	NSCLC	(59)
Fan <i>et al</i> , 2023	circRNA_CC DC66	M2-macrophage EV circRNA_CCDC66	CRC cell	miR-342-3p–metadherin	Tumor-cell immune evasion and CRC progression	Macrophage EV circRNA delivered to tumor cells	CRC	(60)
Chen <i>et al</i> , 2022	circ_0020256	TAM EV circ_0020256	CCA cell	miR-432-5p–E2F3	Tumor-cell proliferation, migration and invasion and xenograft growth	TAM EV circRNA delivered to tumor cells	CCA	(61)

Gao <i>et al</i> , 2022	circMID1	MDSC EV S100A9 protein	Prostate-cancer cell	S100A9 reduced DHX9 and increased recipient-cell circMID1, followed by circMID1–miR-506-3p–MID1 signaling	CRPC-cell proliferation, migration, invasion and tumor growth	S100A9 was transferred. circMID1 was induced in recipient cells and was not the EV cargo	CRPC	(74)
Shi <i>et al</i> , 2024	circRNA_0013936	Bladder-cancer-cell EV circRNA_0013936	PMN-MDSC	miR-320a–JAK2–FATP2 and miR-301b–CREB1–RIPK3	PMN-MDSC suppressive activity and reduced CD8+ T-cell function	EV circRNA entered PMN-MDSCs and recipient pathways were perturbed	Bladder cancer	(75)
Zhang <i>et al</i> , 2020	circUHRF1	HCC-cell EV circUHRF1	NK cell	miR-449c-5p–TIM-3	Reduced IFN- γ and TNF- α secretion, NK-cell dysfunction and lower anti-PD-1 activity	EV-dependent recipient function was measured. Labeled uptake and absolute circRNA dose were not reported	HCC	(13)
Chen <i>et al</i> , 2021	circUSP7	NSCLC-cell EV circUSP7	CD8 ⁺ T cell	miR-934–SHP2	Reduced IFN- γ , TNF- α , granzyme B and perforin and lower anti-PD-1 activity	Recipient function followed EV exposure and donor perturbation. Labeled vesicle uptake was not reported	NSCLC	(15)
Hu <i>et al</i> , 2023	circCCAR1	HCC-cell EV circCCAR1 loaded by hnRNPA2B1	CD8 ⁺ T cell	Direct binding to PD-1 protein, reduced PD-1 ubiquitination and prolonged PD-1 stability	Reduced proliferation and cytotoxicity, increased inhibitory receptors and anti-PD-1 resistance	PKH-labeled EV uptake, donor-cargo perturbation and recipient mechanism measured	HCC	(14)
Yang <i>et al</i> , 2022	circTRPS1	Bladder-cancer-cell EV circTRPS1	CD8 ⁺ T cell and tumor cell	miR-141-3p–GLS1 with redox and glutamine-metabolism changes	CD8 ⁺ T-cell exhaustion and bladder-cancer progression	EV-associated circRNA was linked to T-cell dysfunction. Several metabolic steps were measured in tumor cells	Bladder cancer	(16)
Wang <i>et al</i> , 2024	circ_0001947	GC-cell sEV circ_0001947	CD8 ⁺ T cell	miR-661 and miR-671-5p–CD39	CD8 ⁺ T-cell exhaustion and reduced anti-PD-1 response	PKH-labeled sEV uptake and circRNA-dependent recipient activity measured	GC	(39)

Huang <i>et al</i> , 2022	circGSE1	HCC-cell EV circGSE1	T cell	miR-324-5p-TGFBR1-S mad3	FOXP3 ⁺ Treg expansion, immune escape and metastasis	EV-associated circRNA-dependent Treg expansion	HCC	(151)
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CCA, cholangiocarcinoma. CRC, colorectal cancer. CRPC, castration-resistant prostate cancer. EOC, epithelial ovarian cancer. ESCC, esophageal squamous cell carcinoma. EV, extracellular vesicle. GC, gastric cancer. HCC, hepatocellular carcinoma. LUAD, lung adenocarcinoma. MDSC, myeloid-derived suppressor cell. NK, natural killer. NSCLC, non-small cell lung cancer. PMN-MDSC, polymorphonuclear myeloid-derived suppressor cell. sEV, small extracellular vesicle. TAM, tumor-associated macrophage. Treg, regulatory T cell.

Table SII. EV-associated circRNAs in CAF, stromal and vascular communication.

Authors, year	circRNA or EV product	Direction	Recipient	Mechanism	Measured stromal, vascular or treatment endpoint	Immune or ICI endpoint	Cancer	(Refs.)
He <i>et al</i> , 2023	circEHD2	RCC cell EV to fibroblast	Fibroblast	hnRNPA2B1-dependent loading. circEHD2 bound YWHAH, recruited YAP and activated SOX9	Fibroblast activation, IL-6 secretion, collagen contraction and RCC metastasis	Not measured	RCC	(23)
Mu <i>et al</i> , 2024	circ_0011496	Benzo[a]pyrene-exposed HCC cell EV to lung fibroblast	Lung fibroblast	miR-486-5p-TWF1 with MMP9-associated stromal signaling	Lung fibroblast activation, premetastatic niche formation and organotropic metastasis	Not measured	HCC	(98)
Qiao <i>et al</i> , 2025	circNRIP1	Hypoxic ESCC cell EV to fibroblast	Fibroblast	Binding to TRMT6	CAF activation, inflammatory cytokine release and increased ESCC-cell migration and invasion	Not measured	ESCC	(99)
Yang <i>et al</i> , 2021	circEIF3K	Hypoxic CAF EV to CRC cell	CRC cell	miR-214-PD-L1	CRC-cell proliferation and invasion, endothelial tube formation and xenograft growth	Tumor-cell PD-L1 was measured. T-cell function, infiltration and ICI response were not measured	CRC	(24)
Yang <i>et al</i> , 2022	circN4BP2L2	CAF sEV to CRC cell	CRC cell	miR-664b-3p-HMGB3	Proliferation, migration, tube formation, xenograft growth and liver metastasis	Not measured	CRC	(102)
Yang <i>et al</i> , 2024	circ_0067557	CAF EV to CRC cell	CRC cell	Lin28A and Lin28B	Proliferation, invasion, stemness, chemoresistance and xenograft growth	Not measured	CRC	(103)
Payervand <i>et al</i> , 2024	circ_0084043	CAF EV to endothelial cell	Endothelial cell	miR-140-3p-HIF-1 α -VEGF	Endothelial proliferation, migration and tube formation <i>In vitro</i>	No immune, <i>in vivo</i> angiogenesis or treatment endpoint was measured	CRC	(104)

Zhan <i>et al</i> , 2021	circHIF1A	Hypoxic CAF EV to breast-cancer cell	Breast-cancer cell	miR-580-5p-CD44	Tumor-cell stemness	Not measured	Breast cancer	(105)
Yang <i>et al</i> , 2025	circSTAT3	Hypoxic CAF EV to TNBC cell	TNBC cell	miR-671-5p-NOTCH1	Proliferation, migration, epithelial-mesenchymal transition, stemness and cisplatin resistance	Not measured	TNBC	(106)
Xun <i>et al</i> , 2025	circFOXO1	CAF EV to TNBC cell	TNBC cell	miR-27a-3p-BNIP3	Autophagy and radioresistance	Not measured	TNBC	(107)
Kang <i>et al</i> , 2025	circ_0076535	CAF EV to ESCC cell	ESCC cell	CAF EV-mediated transfer to ESCC cells	ESCC progression	Not measured	ESCC	(108)
Ye <i>et al</i> , 2023	circTBPL1	CAF EV to breast-cancer cell	Breast-cancer cell	miR-653-5p-TPBG	Proliferation, migration and invasion	Not measured	Breast cancer	(109)
Zheng <i>et al</i> , 2023	circBIRC6	CAF EV to PDAC cell	PDAC cell	XRCC4 binding and SUMOylation at K115, followed by non-homologous end joining	Oxaliplatin resistance. circBIRC6 inhibition plus olaparib reduced resistant tumor growth	Not measured	PDAC	(111)
Tan <i>et al</i> , 2025	circTAX1BP1	ITGA11+ CAF EV to CRC cell	CRC cell	AARS2 recruitment, VIRMA K1713 lactylation, SP1 mRNA m6A stabilization and TGF- β secretion	CRC growth, liver metastasis and TGF- β -dependent maintenance of ITGA11+ CAFs	CD8+ T-cell localization and ICI response were not measured	CRC	(113)
Jiang <i>et al</i> , 2023	circDennd1b	Tumor-associated fibroblast EV to pituitary-adenoma cell	Pituitary-adenoma cell	miR-145-5p-ONECUT2 and MAPK signaling	Tumor progression and temozolomide response	Not measured	Pituitary adenoma	(110)
Gu <i>et al</i> , 2020	circSLC7A6	CAF EV to CRC cell	CRC cell	Matrine reduced CAF EV circSLC7A6 through CXCR5	Tumor-cell migration and invasion	Not measured	CRC	(114)

Du <i>et al</i> , 2025	NGR-modified CAF EVs	Engineered CAF EV to tumor vasculature and osteosarcoma cell	Vascular and tumor compartments	NGR-mediated vascular targeting and ferroptosis	Reduced osteosarcoma chemoresistance	No endogenous circRNA cargo or ICI endpoint was tested	Osteosarcoma	(115)
Huang <i>et al</i> , 2020	circRNA-100338	HCC cell EV to endothelial cell	Endothelial cell	Recipient-cell molecular route was not defined	Endothelial proliferation, permeability, angiogenesis, vasculogenic mimicry and HCC metastasis	Not measured	HCC	(46)
Jiang <i>et al</i> , 2022	circKIF18A	Glioblastoma-associated microglia EV to endothelial cell	Endothelial cell	FOXC2	Angiogenesis and glioblastoma progression	Not measured	Glioblastoma	(47)

CAF, cancer-associated fibroblast. CRC, colorectal cancer. ESCC, esophageal squamous cell carcinoma. EV, extracellular vesicle. HCC, hepatocellular carcinoma. ICI, immune checkpoint inhibitor. PDAC, pancreatic ductal adenocarcinoma. RCC, renal cell carcinoma. sEV, small extracellular vesicle. TNBC, triple-negative breast cancer.

Table SIII. Translational and engineered circRNA strategies adjacent to endogenous EV-circRNA biology.

Authors, year	Application or method	Example	Experimental basis	Intended use	Current boundary	Platform class	(Refs.)
Wang <i>et al</i> , 2023	Exploratory plasma EV biomarker	circ-PTPN22 and circ-ADAMTS6	Plasma EV circRNA profiling in six of 14 Asian iCCA patients linked these circRNAs to exhausted T-cell and neutrophil extracellular-trap programs	Hypothesis generation for immune-state biomarkers	Small discovery set without prospective diagnostic or treatment-response validation	Endogenous EV biomarker	(78)
He <i>et al</i> , 2023	ASO targeting	ASO against circEHD2	Systemic circEHD2 ASO reduced RCC growth and fibroblast activation in preclinical models	Block tumor-to-fibroblast signaling	Delivery to tumor and stromal cells, off-target activity and pharmacodynamic EV measurements remain unresolved	Endogenous EV-circRNA intervention	(23)
Zhou <i>et al</i> , 2023	Nanoparticle siRNA delivery	PLGA nanoparticles carrying si-cSERPINE2	Silencing cSERPINE2 reduced the macrophage MALT1–NF-κB–IL-6 program and breast-tumor growth <i>in vivo</i>	Disrupt tumor–macrophage feedback	Preclinical delivery and safety. The therapeutic carrier was a nanoparticle and not an EV	Synthetic carrier targeting endogenous EV cargo	(70)
Zhou <i>et al</i> , 2024	Donor-cell circRNA suppression	Ginsenoside Rb1 and circ-0034880-enriched EVs	Reduced circ-0034880 biogenesis decreased SPP1 ^{high} CD206 ⁺ macrophages, liver premetastatic niche formation and CRLM	Interfere with metastatic-niche formation	Preclinical intervention. Direct selectivity for circ-0034880 biogenesis requires further definition	Drug modulation of endogenous EV cargo	(71)
Guo <i>et al</i> , 2022	Engineered EV delivery	RGD-modified EVs carrying circDIDO1	Systemic delivery increased SOCS2 through miR-1307-3p and reduced GC xenograft growth	Restore a tumor-suppressive circRNA	Manufacturing, loading consistency, biodistribution and repeated-dose safety	Engineered EV	(171)
Fu <i>et al</i> , 2025	Local hydrogel-assisted delivery	GelMA hydrogel carrying circNEFM-engineered EVs	Local EV release reduced glioma growth in preclinical models	Sustain local delivery in the brain	Release kinetics, tissue distribution, immune compatibility and scale-up	Engineered EV plus biomaterial	(172)

Zhang <i>et al</i> , 2025	Engineered EV microenvironment intervention	circPRKD3-loaded EVs	EV delivery inhibited STAT3 signaling, reduced glioblastoma growth and altered the tumor microenvironment	Combine tumor suppression with local microenvironment change	Preclinical efficacy and incomplete long-term toxicity and biodistribution data	Engineered EV	(173)
Li <i>et al</i> , 2022	circRNA cancer vaccine	Antigen-encoding circRNA in LNPs	Sustained antigen expression induced innate and adaptive immunity in several mouse tumor models	Therapeutic vaccination	Antigen selection, innate sensing, formulation consistency and clinical safety	LNP circRNA vaccine	(176)
Amaya <i>et al</i> , 2023	circRNA vaccine platform	Antigen-encoding circRNA vaccine	CircRNA vaccination induced antigen-specific T-cell responses in preclinical models	Active antitumor immunization	Human dose, duration, manufacturing and immune safety	Non-EV circRNA vaccine	(177)
Wang <i>et al</i> , 2024	Neoantigen vaccine	HCC neoantigen-encoding circRNA	CircRNA activated dendritic cells and T cells and inhibited tumors in mouse models	Personalized neoantigen immunotherapy	Neoantigen selection, production time and patient-specific release testing	LNP circRNA vaccine	(178)
Alshehry <i>et al</i> , 2025	LNP formulation	SM-102, cholesterol, DOPE and DMG-PEG2000 formulation	LNP composition altered lymph-node delivery, dendritic-cell transfection and antigen-specific CD8 ⁺ T-cell responses in mice	Optimize circRNA vaccine delivery	Formulation-dependent activity needs batch-level and species-to-human confirmation	LNP delivery study	(179)
Cai <i>et al</i> , 2025	Dendritic-cell vaccine	circRNA-loaded DC vaccine plus low-dose gemcitabine	The combination reduced Tregs, induced immunogenic cell death and inhibited Panc02 tumors in mice	Extend antigen expression in DC vaccines and reduce suppression	Cell manufacturing, product comparability and clinical safety	Cell vaccine	(180)
Niu <i>et al</i> , 2025	Local cytokine and checkpoint expression	circILNb encoding IL-15 and an anti-PD-L1 nanobody	Local circRNA expression increased antitumor immunity in immune-cold mouse tumors	Local combination immunotherapy	Control of expression duration, cytokine exposure and tissue distribution	Non-EV engineered circRNA	(181)

Lai <i>et al</i> , 2025	Synthetic circRNA decoy and protein expression	Artificial circRNA miRNA sponge and anti-PD-1 scFv platform	The engineered circRNA combined miRNA sequestration with anti-PD-1 scFv expression in HCC models	Combine post-transcriptional regulation with checkpoint blockade	Stoichiometry, off-target miRNA binding, expression control and delivery	Non-EV engineered circRNA	(183)
Hu <i>et al</i> , 2025	Transient CAR-T engineering	Scarless circular mRNA CAR-T cells	Circular mRNA supported transient CAR expression and antitumor activity in preclinical models	Avoid integrating viral vectors and limit CAR duration	Electroporation scale, expression control, persistence and clinical safety	Engineered cell therapy	(187)
Cai <i>et al</i> , 2025	DLL3-targeted CAR-T engineering	CircRNA-electroporated DLL3 CAR-T cells	CircRNA CAR-T cells eliminated SCLC tumors in subcutaneous and orthotopic mouse models	Transient CAR-T therapy for SCLC	Antigen heterogeneity, on-target off-tumor toxicity and manufacturing	Engineered cell therapy	(188)
Welsh <i>et al</i> , 2024	EV study standard	MISEV2023	The guideline defines reporting for EV source, separation, characterization and functional attribution	Improve reproducibility and limit unsupported exosome-specific claims	Application still depends on complete study-level reporting and appropriate controls	Methodological standard	(26)
Luo <i>et al</i> , 2022	Single-EV transcriptomics	Single-vesicle RNA profiling	The study detected 6–148 genes per EV with a mean of 52 genes and showed marked transcriptomic heterogeneity	Resolve heterogeneity hidden by bulk EV preparations	The data do not measure circRNA copies per EV or establish a functional delivered dose	Analytical method	(34)

ASO, antisense oligonucleotide. CAR, chimeric antigen receptor. CRLM, colorectal cancer liver metastasis. DC, dendritic cell. EV, extracellular vesicle. GC, gastric cancer. HCC, hepatocellular carcinoma. iCCA, intrahepatic cholangiocarcinoma. ICI, immune checkpoint inhibitor. GelMA, gelatin methacryloyl. LNP, lipid nanoparticle. PLGA, poly(lactic-co-poly(lactic-co-glycolic acid)). RCC, renal cell carcinoma. scFv, single-chain variable fragment. siRNA, small interfering RNA. SCLC, small cell lung cancer.

Table SIV. Methodological features of representative EV-associated circRNA studies.

Authors, year	Study or axis	Sample or source	EV separation	EV characterization	Cargo or transfer controls	Functional endpoint	Method still unresolved	(Refs.)
Welsh <i>et al</i> , 2024	MISEV2023 benchmark	Not applicable	Report collection, separation and concentration procedures and their recovery and specificity	Report source, abundance, morphology, positive and negative markers and non-EV components	Demonstrate EV association, uptake or delivery and exclude soluble or co-isolated material	Use perturbations that connect the EV preparation to a recipient-cell effect	Use EV or sEV when endosomal origin has not been established	(26)
Zhang <i>et al</i> , 2020	circUHRF1	HCC-cell conditioned medium and patient plasma	Ultracentrifugation for conditioned medium and ExoQuick precipitation for plasma	TEM, NanoSight and EV marker immunoblotting	Donor circUHRF1 perturbation, EV exposure and GW4869-supported EV dependence	NK-cell IFN- γ , TNF- α and TIM-3 and anti-PD-1 activity	Precipitation can retain non-EV material. Labeled uptake and absolute circRNA dose per NK cell were not measured	(13)
Chen <i>et al</i> , 2021	circUSP7	NSCLC-cell conditioned medium and patient plasma	Ultracentrifugation and ExoQuick precipitation	TEM, NanoSight and EV marker immunoblotting	Donor circUSP7 perturbation and exposure of CD8+ T cells to isolated EV preparations	CD8+ T-cell cytokines, granzyme B, perforin and anti-PD-1 activity	A protein-mass EV dose was used. Vesicle number, labeled uptake and delivered circRNA molecules were not reported	(15)
Hu <i>et al</i> , 2023	circCCAR1	HCC-cell conditioned medium and patient serum	EVs were purified from serum and culture supernatant. The main-text procedure was not specified	TEM, NanoSight and CD63 and TSG101	GW4869, hnRNP A2B1-dependent loading, donor-cargo perturbation and PKH-labeled EV uptake by CD8+ T cells	CD8+ T-cell proliferation, apoptosis, cytotoxicity, inhibitory receptors and anti-PD-1 activity	The separation procedure and absolute delivered circRNA dose require fuller reporting	(14)

Gao <i>et al</i> , 2022	circZNF451	LUAD-cell conditioned medium and patient serum	ExoQuick precipitation	Electron microscopy and CD63 and TSG101	GW4869, donor circZNF451 perturbation, recipient circRNA measurement and macrophage-specific rescue	Macrophage state, CD8 ⁺ T-cell function and anti-PD-1 response in mice	Precipitation specificity is limited. The initial response cohort contained three progressive-disease and three partial-response patients	(17)
He <i>et al</i> , 2023	circEHD2	RCC-cell conditioned medium and patient serum	Differential ultracentrifugation	TEM, NanoSight, CD9, CD63, CD81 and TSG101	GW4869, RNase A with and without Triton X-100, EV-depleted medium, hnRNPA2B1 loading and PKH26 uptake	Fibroblast activation, IL-6, collagen contraction and metastasis	Absolute circEHD2 molecules delivered per fibroblast were not measured	(23)
Tan <i>et al</i> , 2025	circTAX1BP1	Primary CAF and normal-fibroblast conditioned medium	EVs were purified from conditioned medium. The main-text procedure was not specified	TEM, nanoparticle tracking, CD63, TSG101 and ALIX with GM130 as a negative marker	CM-DiI uptake, GW4869 and donor circTAX1BP1 knockdown or overexpression	CRC-cell growth, liver metastasis, VIRMA lactylation and CAF feedback	The separation procedure and absolute dose were not reported. CD8 ⁺ T-cell location and ICI response were not measured	(113)
Gao <i>et al</i> , 2022	S100A9-circMID1	MDSC conditioned medium	ExoQuick precipitation after filtration of EV-depleted culture medium	TEM, nanoparticle tracking, CD9, CD63 and Hsp70 with calnexin	CFSE-labeled EV uptake and perturbation of S100A9 and recipient-cell circMID1	CRPC-cell proliferation, migration, invasion and tumor growth	The EV cargo was S100A9 protein. circMID1 was induced in recipient tumor cells and should not be described as transferred	(74)
Wang <i>et al</i> , 2024	circ_0001947	GC-cell conditioned medium and patient plasma	Filtration followed by two 100,000 × g ultracentrifugation steps	TEM, nanoparticle tracking, CD63, CD81 and TSG101 with calnexin	PKH26-labeled sEV uptake by CD8 ⁺ T cells and donor circRNA knockdown	CD39, CD8 ⁺ T-cell exhaustion and anti-PD-1 response	PKH dye does not trace the circRNA itself. Absolute circRNA copies delivered per cell were not measured	(39)

Wang <i>et al</i> , 2023	circ-PTPN22 and circ-ADAMT S6	Plasma from six of 14 iCCA patients	Sequential centrifugation and two 100,000 x g ultracentrifugation steps	TEM, high-sensitivity flow cytometry, CD63 and TSG101 with calnexin	Duplicate sampling in one patient and comparison with tissue and public plasma-EV profiles	Associations with T-cell exhaustion and neutrophil extracellular-trap programs	Discovery sample was small and no functional transfer, diagnostic threshold or treatment-response validation was performed	(78)
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CAF, cancer-associated fibroblast. CRPC, castration-resistant prostate cancer. EV, extracellular vesicle. GC, gastric cancer. HCC, hepatocellular carcinoma. iCCA, intrahepatic cholangiocarcinoma. LUAD, lung adenocarcinoma. MDSC, myeloid-derived suppressor cell. NSCLC, non-small cell lung cancer. RCC, renal cell carcinoma. sEV, small extracellular vesicle. TEM, transmission electron microscopy. MISEV2023, Minimal Information for Studies of Extracellular Vesicles 2023. Terminology follows MISEV2023. The terms EV or sEV are used when endosomal origin has not been established.