

Review

Exosome-Mediated Chemoresistance in Cancers: Mechanisms, Therapeutic Implications, and Future Directions

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Abstract: Chemotherapy resistance represents a formidable obstacle in oncological therapeutics, substantially compromising the efficacy of adjuvant chemotherapy regimens and contributing to unfavorable clinical prognoses. Emerging evidence has elucidated the pivotal involvement of exosomes in the dissemination of chemoresistance phenotypes among tumor cells and within the tumor microenvironment. This review delineates two distinct intra-tumoral resistance mechanisms orchestrated by exosomes: (1) the exosome-mediated sequestration of chemotherapeutic agents coupled with enhanced drug efflux in neoplastic cells, and (2) the horizontal transfer of chemoresistance to drug-sensitive cells through the delivery of bioactive molecular cargo, thereby facilitating the propagation of resistance phenotypes across the tumor population. Furthermore, the review covers current *in vivo* experimental data focusing on targeted interventions against specific genetic elements and exosomal secretion pathways, demonstrating their potential in mitigating chemotherapy resistance. Additionally, the therapeutic potential of inhibiting exosome-mediated transporter transfer strategy is particularly examined as a promising strategy to overcome tumor resistance mechanisms.

Keywords: chemotherapy resistance; exosomes; tumor microenvironment; drug efflux



Academic Editor: Hang Fai (Henry) Kwok

Received: 15 March 2025

Revised: 3 May 2025

Accepted: 5 May 2025

Published: 8 May 2025

Citation: Liu, G.; Liu, J.; Li, S.; Zhang, Y.; He, R. Exosome-Mediated Chemoresistance in Cancers: Mechanisms, Therapeutic Implications, and Future Directions. *Biomolecules* **2025**, *15*, 685. <https://doi.org/10.3390/biom15050685>

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1. Introduction

Exosomes are nanoscale extracellular vesicles (30–150 nm in diameter) characterized by a phospholipid bilayer membrane and a buoyant density of 1.13–1.19 g/mL in sucrose gradients. These vesicles originate through the endosomal pathway, where inward budding of the limiting membrane of late endosomes creates intraluminal vesicles within multivesicular bodies (MVBs). Subsequent fusion of MVBs with the plasma membrane results in exosome release into the extracellular space (Figure 1) [1,2]. Exosomes were first discovered in the maturing mammalian sheep reticulocytes (immature red blood cell) in the mid-1980s [3,4], and were later termed “exosomes” by Johnstone [5] in 1987. Subsequent research has revealed that exosome secretion represents an evolutionarily conserved, ATP-dependent cellular process observed across virtually all mammalian cell types, such as B lymphocytes [6], T lymphocytes [7], natural killer cells [8], dendritic cells [9], mast cells [10], epithelial cells [11], platelets [12], as well as neoplastic cells [13]. Exosomes are stable and widely present in various body fluids, such as circulating blood [14], urine [2], pleural effusion [15], saliva [16], cerebrospinal fluid [17], and nasal secretion [18]. It has even been suggested that amniotic fluid collected by routine amniocentesis could also

contain a large number of exosomes of fetal origin [19]. Initially considered to be cellular “garbage dumpsters” with a mechanism for disposing of cellular components [5], exosomes are now being reconsidered as a rich and stable source of circulating biomarkers. Contemporary research positions these vesicles as critical mediators of intercellular communication through paracrine and endocrine pathways, including but not limited to proteins [20,21], lipids [22,23], mRNAs/microRNA (miRNAs) [24,25], DNA [26,27], as well as other soluble factors capable of interacting with target cells. These molecular payloads enable exosomes to execute targeted modulation of recipient cell functions through multiple mechanisms of cellular interaction. Their inherent stability and disease-specific molecular signatures have established exosomes as promising candidates for applications in clinical diagnostics.

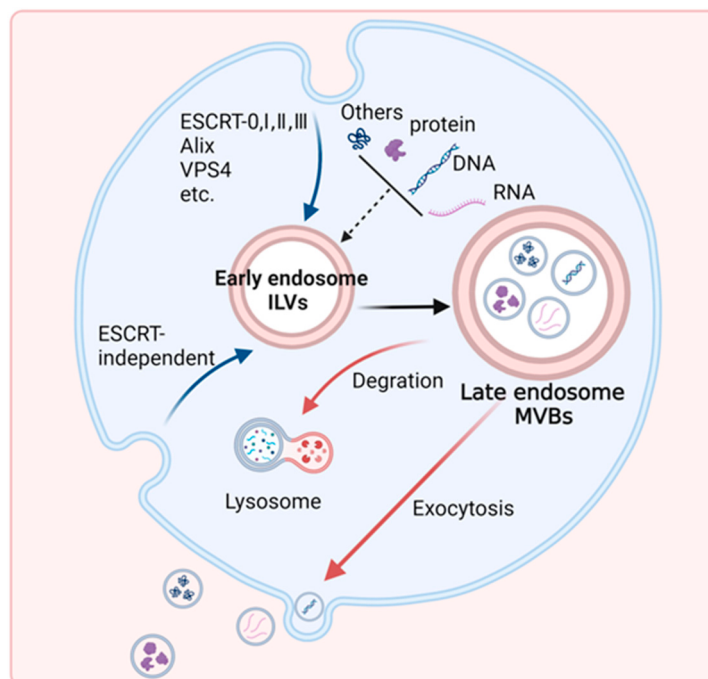


Figure 1. A schematic representation of the exosome production process. The biogenesis of exosomes is associated with the endosomal pathway, which begins with the creation of intraluminal vesicles (ILVs) within MVBs through two mechanisms, and as-formed MVBs can fuse with lysosomes or the plasma membrane for different fates [28].

Exosomes, recognized as pivotal paracrine and endocrine mediators, facilitate intercellular communication by transporting a diverse array of bioactive molecules between donor and recipient cells, thereby enabling long-distance regulatory signaling [29]. As shown in Figure 2, the mechanisms by which recipient cells uptake exosomes involve multiple pathways, including endocytosis, membrane fusion, and receptor-mediated specificity [30,31]. Endocytosis can be further categorized into clathrin-dependent endocytosis, caveolin-mediated endocytosis, and macropinocytosis, all of which rely on membrane dynamics and cytoskeletal reorganization [32]. Additionally, exosomes may directly fuse with the recipient cell membrane to deliver their cargo into the cytoplasm. Specificity in uptake is mediated by interactions between cell surface receptors (e.g., integrins, proteoglycans) and exosome surface ligands (e.g., tetraspanins), which determine tissue or cell tropism [33]. However, this physiological function is frequently co-opted by neoplastic cells to promote chemotherapy resistance. Adjuvant chemotherapy following curative surgery has been established as a standard therapeutic strategy, demonstrating significant clinical benefits by substantially prolonging overall survival in cancer patients [34,35]. However, the emergence of acquired resistance during prolonged and repetitive drug administra-

tion poses a critical limitation to its long-term efficacy, representing the primary cause of treatment failure and mortality in cancer patients despite initial therapeutic success. Chemotherapy resistance has consequently emerged as a paramount challenge in enhancing clinical outcomes for cancer patients. Extensive research indicates that the development of chemoresistance in cancer cells is mediated through multiple genetic and epigenetic mechanisms, including (i) the upregulation of drug resistance-associated proteins; (ii) the modification or mutation of drug targets; (iii) intracellular drug sequestration or enhanced drug efflux; and (iv) the evasion of cell cycle checkpoints (Figure 3) [36,37]. Furthermore, the gradual dissemination of drug-resistant phenotypes within tumor cells and tissues suggests the existence of active mechanisms that facilitate the spread of chemotherapy resistance. Therefore, investigating the specific mechanisms by which exosomes contribute to the development of drug resistance in tumor cells represents one of the critical approaches in cancer therapy.

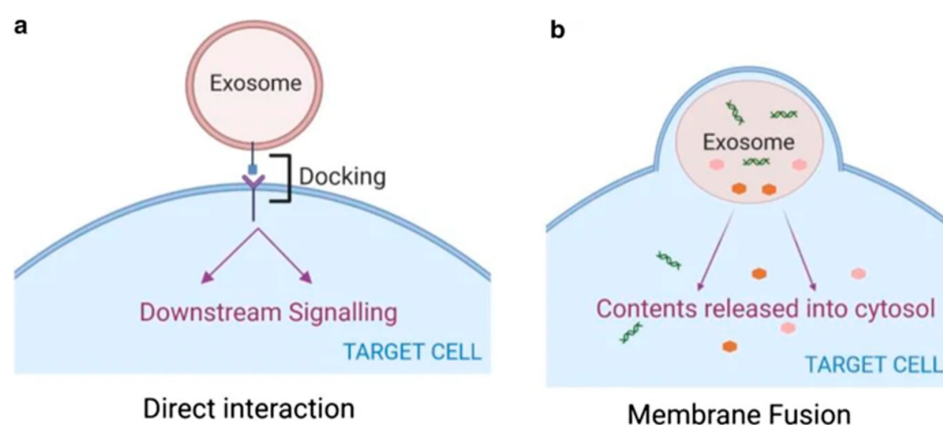


Figure 2. Exosomes mediate intercellular communication through two primary modes: (a) ligand–receptor binding at the cell surface, enabling targeted signal transduction, and (b) structural integration with the plasma membrane, facilitating cargo delivery into the cytosol [31].

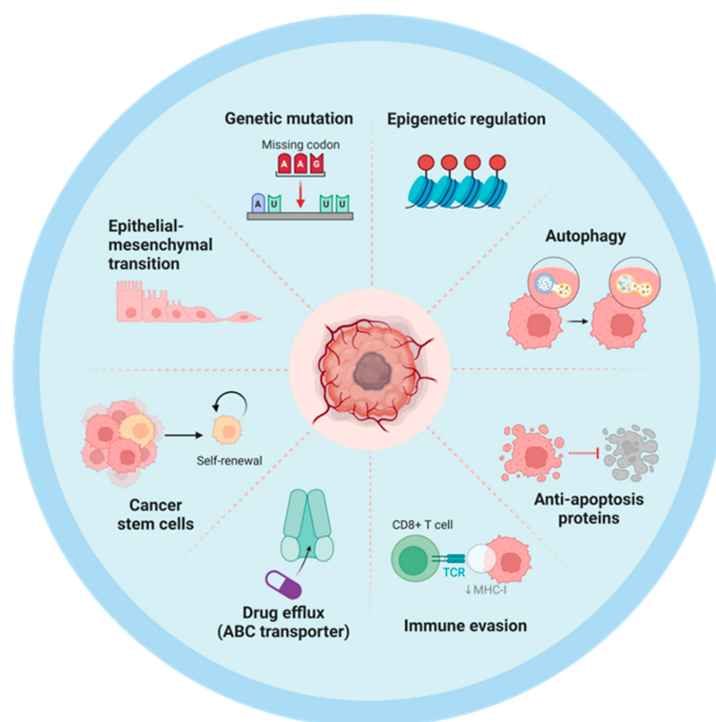


Figure 3. The main pathways and mechanisms underlying the development of drug resistance in tumor cells.

Currently, there are two frequently described mechanisms of exosome-mediated drug resistance: one aspect involves drug sequestration and increased drug efflux to export them out of cells, while the other pertains to exosome-mediated resistance transfer [38,39]. Within the tumor microenvironment, drug-resistant malignant cells and surrounded non-malignant cells (stromal cell [40], mesenchymal stem cell [41], TAMs [42], etc.) derived exosomes have been found to transmit chemoresistance to sensitive cells through the transfer of biologically active molecules including but not limited to DNA [43] and protein [44,45], as well as ncRNAs like miRNAs [46,47], lncRNAs [48], and circRNAs [49,50], which have important roles in the regulation of gene expression, conferring resistance of sensitive cells to the drug of interest. Collectively, accumulating studies suggested that exosome-mediated intercellular communication plays a dominant role in the development of cancer chemoresistance [51,52]. In this review, we systematically summarize the molecular mechanisms underlying exosome-mediated drug resistance in tumor cells, with particular emphasis on recent *in vivo* experimental studies and their associated findings.

2. Dynamic Interplay of Active Molecules Exchanged in Tumor Microenvironment and Chemoresistance

2.1. Intrinsic Mechanisms of Chemoresistance in Tumor Cells

Chemoresistance represents a critical barrier to the advancement of chemotherapeutic interventions, necessitating urgent investigation into the underlying mechanisms of tumor cell resistance to enhance the efficacy of current anticancer therapies. Extensive research has revealed that therapy resistance mechanisms are not solely attributed to intrinsic tumor cell alterations but are also significantly influenced by the dynamic properties of stromal cells within the tumor microenvironment [53,54]. Notably, exosomes, serving as intercellular communication mediators, have been identified as key players in disseminating chemoresistance phenotypes from resistant to sensitive tumor cells through the transfer of biologically active molecules [55,56]. In view of this theory, a feed-forward loop in which tumor cells acquire chemoresistance via exosomes was formed. First of all, with the prolonged chemotherapeutic process, tumor cells struggle to adapt to the changing environment and survive by inducing their own repair mechanisms through the activation of the DNA damage response (DDR) system and a variety of other signaling pathways. However, the majority of tumor cells are unable to repair the lesion damage, leading to cell death through apoptosis or cellular senescence. Residual cancer cells could repair the damage through adjusting the transcription and expression levels of genes and passing/evading cell cycle checkpoints within the tumor cells [57], gradually acquiring drug resistance, called acquired resistance. Incidentally, the counterpart manifests as intrinsic resistance, wherein both the tumor cells and the surrounding cells inherently exhibit chemoresistance [58,59]. For instance, Qin et al. demonstrated that cancer-associated fibroblasts (CAFs) derived from head and neck squamous cell carcinoma (HNSCC) exhibit innate resistance to cisplatin, exemplifying this phenomenon [59]. In addition, exosomes and cancer stem cells (CSCs) collaboratively drive chemoresistance in cancers through dynamic intercellular crosstalk. CSCs, a subpopulation with self-renewal and drug-resistant properties, secrete exosomes enriched with stemness-promoting factors and drug efflux transporters, which propagate resistance to neighboring cells and maintain CSC plasticity [60,61]. Conversely, exosomes from the tumor microenvironment, such as cancer-associated fibroblasts (CAFs), deliver metabolic enzymes (e.g., PKM2) and anti-apoptotic miRNAs (e.g., miR-155) to CSCs, enhancing glycolysis and suppressing chemotherapy-induced cell death. Additionally, exosomal transfer of lncRNAs (e.g., H19) or circular RNAs (e.g., ciRS-122) stabilizes oncogenic transcripts (e.g., c-Myc, PKM2) in CSCs, fostering chemoresistance through metabolic reprogramming and DNA repair activation [62–65].

2.2. Exosomal Crosstalk and Metabolic Reprogramming in Cancer Chemoresistance

The adaptive regulation (up- or down-regulation) of specific biomolecules may orchestrate dual mechanisms of chemoresistance; (i) enhancing intrinsic anti-apoptotic activity and chemoresistance [66]; and (ii) promoting the secretion of exosomes [67,68], the increase in which could facilitate the more rapid expulsion of drugs into the extracellular space, accelerate the interaction between donor-resistant cells and recipient-sensitive cells, and promote the exchange of chemoresistance-related bioactive factors. Meanwhile, the complementary mechanism entails a reciprocal interaction wherein recipient cells upregulate resistance-associated molecules, which are subsequently packaged into exosomes and transferred back to donor cells, thereby facilitating their enrichment within the donor cell-derived extracellular vesicles [69,70]. As an example, Osimertinib promotes the formation and release of exosomes in nonmutEGFR-resistant NSCLC cells by upregulating a member of the Rab GTPase family—RAB17 [71]. Finally, intracellular chemoresistance-related molecules can be specifically packaged into exosomes and transmitted to other cells, thereby facilitating chemoresistance in recipient sensitive cells by altering cellular pathways, including glycolytic and lipid metabolic reprogramming [72,73], enhanced DNA damage repair [74], alleviated endoplasmic reticulum stress [75], apoptosis dysregulation [76,77], autophagy activation [78,79], and enhanced tumor EMT, as well as stem-like property [80,81], thereby disseminating drug resistance. For instance, cisplatin stimulation of NSCLC cells resulted in a significant upregulation of c-Myc expression. c-Myc was identified to directly bind to the miR-425-3p promoter, positively regulating its transcription and facilitating its horizontal transfer in NSCLC cells via exosomes. Exosomal miR-425-3p negatively regulates the AKT/mTOR signaling pathway by targeting AKT1, thereby enhancing autophagic activity in recipient cells and conferring resistance to cisplatin-induced apoptosis [82]. The activation of autophagy eliminates the accumulation of abnormal proteins or organelles induced by chemotherapeutic drug stimulation, thereby promoting tumor cell survival and enhancing resistance to chemotherapy [83]. Another study contributing to the expanding body of evidence on exosome-mediated chemoresistance transfer was conducted by Zhang and collaborators. They investigated the role of lipid metabolic reprogramming and apoptosis dysregulation in this process. Specifically, hnRNPA1, stabilized by USP7 through de-ubiquitination, plays a direct role in mediating miR-522 sorting into CAF exosomes in response to cisplatin and paclitaxel treatment. Consequently, exosomal miR-522 effectively inhibits lipid-ROS production and subsequently suppresses ferroptosis by directly targeting ALOX15 in GC cells [84].

Exosomes critically regulate cancer glycolytic metabolism, a hallmark of the Warburg effect that fuels tumor aggressiveness (Figure 4). By delivering oncogenic miRNAs (e.g., miR-21, miR-155), metabolic enzymes (e.g., HK2, LDHA), and hypoxia-inducible factors (e.g., HIF-1 α), exosomes reprogram recipient cells to enhance glucose uptake and lactate production, fostering an immunosuppressive tumor microenvironment [85,86]. For instance, the exosomal circular RNA ciRS-122 derived from oxaliplatin-resistant cells, which was identified as a sponge for the PKM2-targeting miR-122 in sensitive cells, exhibited a positive correlation with glycolysis and chemoresistance [56]. Of particular note, as a rate-limiting regulator of the Warburg effect, PKM2 promotes aerobic glycolysis in tumor cells, thereby enabling them to thrive [87,88]. Numerous studies have confirmed its close association with metabolic chemoresistance [89,90]. Hypoxia-induced exosomal PKM2 promotes glycolysis in NSCLC cells, generating reductive metabolites that potentially counteract the cisplatin-induced reactive oxygen species (ROS) [91]. Meanwhile, these exosomes could reprogram CAFs to create an acidic microenvironment, promoting sensitive NSCLC cell proliferation and cisplatin resistance [91]. Similarly, other crucial glycolytic enzymes like hexokinase-II and pyruvate dehydrogenase E1 subunit alpha 1 play

analogous roles [92,93]. In targeting these mechanisms, certain treatment strategies for chemotherapy-resistant tumors inhibit exosome biogenesis (e.g., Rab27a knockdown) or block the cargo delivery of glycolytic enzymes, thereby disrupting metabolic symbiosis and reversing chemoresistance [70,89,94]. For instance, Chen et al. demonstrated that ALKBH5 down-regulation, driven by HDAC2-mediated histone deacetylation, promoted colorectal cancer progression via the m6A-dependent stabilization of JMJD8 mRNA, enhancing PKM2-driven glycolysis. To therapeutically exploit this axis, they developed folate receptor-targeted exosome–liposome nanoparticles delivering ALKBH5 mRNA, which suppressed tumor growth in preclinical models by restoring ALKBH5 expression and inhibiting the JMJD8/PKM2 metabolic pathway [95]. Additionally, the mechanisms of exosome-mediated chemoresistance are summarized in Table 1. It is evident that the exosome-mediated transport of molecules associated with resistance predominantly comprises non-coding RNAs (ncRNAs), while proteins and other macromolecules have been less extensively studied. This predominance can be attributed to the multifunctionality of ncRNAs both within and between cells, enabling them to intricately regulate gene expression on a broad scale. Moreover, resistance transfer among identical types of tumor cells to different drugs affects diverse intracellular pathways. Even when exposed to the same drug, the transported molecules and mechanisms of action may vary. In conclusion, understanding the molecular mechanisms involved in chemoresistance could provide promising targets for preventing resistance. Targeted therapy aimed at specific genes or exosome secretion has been validated in both clinical samples and in vivo experiments, proving effective in reducing chemotherapy resistance [96,97].

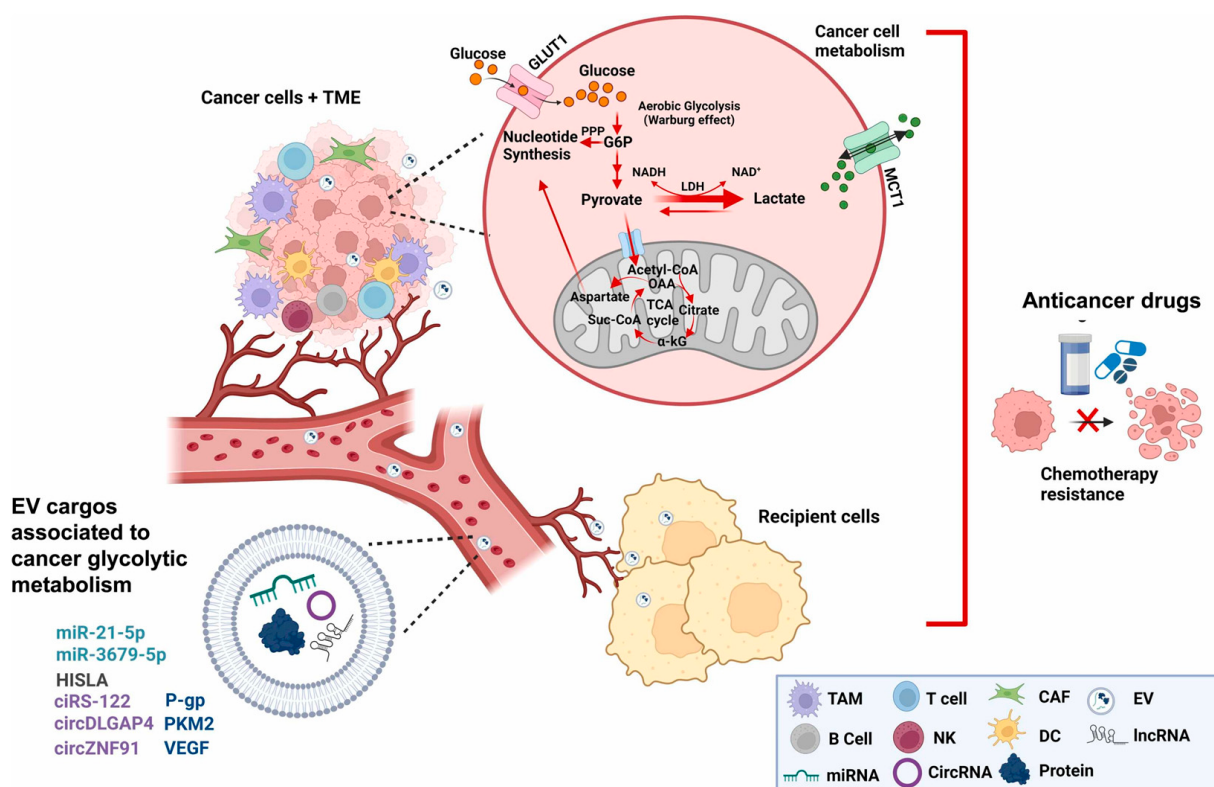


Figure 4. Role of exosomes in transferring chemoresistance by modulation of cancer glycolytic cell metabolism [73].

Table 1. Summary of studies on exosomal components for chemoresistance.

Donor Cell	Recipient Cell	Resistance	Exosomal Components	Molecular Mechanisms	Ref.
Colorectal cancer (R)	Colorectal cancer (S)	Doxorubicin (DOX)	circ_0006174	circ_0006174/miR-1205/CCND2 axis	[98]
		5-fluorouracil	hsa-circ-0004771	hsa-circ-0004771/miR-653/ZEB2 pathway	[99]
		5-FU	circ_0000338	circ_0000338/miR-217, miR-485-3p	[100]
Colorectal cancer (S)	Colorectal cancer (R)	FOLFOX (CRC)	miR-208b	miR-208b/PDCD4 axis	[101]
		Oxaliplatin	circular RNA FBXW7	FBXW7/miR-18b-5p axis	[102]
		Cisplatin	miR-497	PI3K/AKT/mTOR pathway	[103]
Ovarian cancer (OE)	-	Cisplatin (OVA)	circ_C20orf11	circ_C20orf11/miR-527/YWHAZ axis	[104]
Ovarian cancer (R) (KD)	Macrophages	Cisplatin	LncRNA PLADE	LncRNA PLADE/HNRNP/R-loop	[105]
High-grade serous ovarian cancer (OE)	High-grade serous ovarian cancer (R)	Cisplatin	Circ-PAK1	Circ-PAK1/14-3-3 ξ /YAP/Hippo	[106]
		Lenvatinib	Circ-SORE	Circ-SORE/YBX1/PRP19	[107]
		Sorafenib	miR-494-3p	GOLPH3/miR-494-3p/PTEN axis	[108]
Bone marrow mesenchymal stem cell	Acute myeloid leukemia	Cytarabine	miR-10a	miR-10a/RPRD1A/wnt(β)-catenin pathway	[109]
		Cytosine arabinoside	FTO	FTO/LncRNAGLCC1/IGF2BP1/c-Myc axis	[110]
		Temozolomide	circCABIN1	circCABIN1/miR-637/OLFML3/ErbB	[111]
Glioblastoma (R)	Glioblastoma (S)	Temozolomide	Cx43	Bcl-2, Bax and cleaved caspase-3	[112]
		Osimertinib	MSTRG.292666.16	miR-6836-5p/MAPK8IP3 axis	[113]
M2 tumor-associated macrophages	Non-small cell lung cancer	EGFR-TKIs	circRNA_102481	circRNA_102481/miR-30a-5p/ROR1 axis	[114]
Non-small cell lung cancer (KD) (OE)	Non-small cell lung cancer (S)	Gemcitabine	miRNA-222-3p	SOCS3/Stat3 signaling pathway	[115]
		Cisplatin	miR-4443	METTL3/FSP1 pathway	[116]
		Anlotinib	miR-136-5p	PPP2R2A/Akt pathway	[117]
Non-small cell lung cancer (KD)	-	Cisplatin	circ_0008928	miR-488/HK2 Axis	[118]
Non-small cell lung cancer (OE)	-	Everolimus	miR-7-5p	MNK/eIF4E axis	[119]
Non-small cell lung cancer (S)	Non-small cell lung cancer (R)	Gefitinib	miR-7	YAP	[120]
EGFR ⁺ non-small cell lung cancer (R)	EGFR ⁺ non-small cell lung cancer (S)	Osimertinib	miR-210-3p	-	[121]
Small cell lung cancer (KD) (OE)	-	Multidrug	miR-92b-3p	PTEN/AKT pathway	[122]
Tumor associated macrophage (hypoxic)	Epithelial ovarian cancer	Cisplatin	miR-223	miR-223/PTEN/PI3K/AKT pathway	[123]
Omental stromal cells	Ovarian cancer	Paclitaxel	miR-21	miR-21/APAF1 axis	[124]
Esophageal cancer (R)	Esophageal cancer (S)	Cisplatin	Circ_0000337	miR-377-3p/JAK2 axis	[125]
		Paclitaxel	PD-L1	PD-L1/STAT3/miR-21/PTEN/Akt axis	[126]
		Docetaxel	LOC85009	USP5/USF1/ATG5 axis	[127]

Table 1. Cont.

Donor Cell	Recipient Cell	Resistance	Exosomal Components	Molecular Mechanisms	Ref.
Nasopharyngeal carcinoma (R)	Nasopharyngeal carcinoma (S)	Cisplatin Taxol	miR-106a-5p DDX53	miR-106a-5p/ARNT2/AKT axis -	[128] [129]
Nasopharyngeal carcinoma	NPC-side population cells	Cisplatin	circPARD3	miR-579-3p/SIRT1/SSRP1 axis	[130]
Gastrointestinal stromal tumor (R)	Gastrointestinal stromal tumor (S)	imatinib	-	USP32-Rab35 axis	[131]
Prostate cancer (R)	Prostate cancer (S)	Docetaxel	lincROR	lincROR/MYH9/ β -catenin/HIF1a	[132]
Breast cancer (R)	Breast cancer (S)	Tamoxifen	miR-9-5p	ADIPOQ	[133]
		DOX and PTX	miR-378a-3p, miR-378d	EZH2/STAT3 axis, DKK3, NUMB	[134]
Breast cancer stem cell, Breast cancer (R)	Breast cancer (S)	DOX and PTX	miR-155	FOXO-3a	[64]
Triple-negative breast cancer (R)	Tumor associated macrophage	Doxorubicin	miR-770	miR-770/STMN1 axis	[135]
Triple-negative breast cancer (KD)	-	Pirarubicin	CircEGFR	circEGFR/miR-1299/EGFR pathway	[136]
Senescent neutrophils	Breast cancer	Docetaxel	piRNA-17560	FTO/ZEB1 signaling	[137]
Breast cancer stem cell (R)	Breast cancer (S)	Paclitaxelb	ANXA6	YAP1	[138]
Myeloid-derived suppressor cells	Prostate cancer	Castration	circMID1	S100A9/circMID1/miR-506-3p/MID1	[139]
Gastric cancer (R)	Gastric cancer (S)	Cisplatin Doxorubicin	RPS3 microRNA-501-5p	PI3K/Akt/cofilin-1 signaling axis BLID	[140] [141]
Gastric cancer (S)	Gastric cancer (R)	5-FU, cisplatin	miR-107	HMGA2/mTOR/P-gp pathway	[142]
Gastric cancer (KD)	-	Oxaliplatin	miR-374a-5p	Neurod1	[143]
M2 tumor-associated macrophages	Hemangioma stem cells	Propranolol	miR-27a-3p	miR-27a-3p/DKK2 axis	[144]
Liver cancer (R)	Lung cancer	Cisplatin	miR-3679-5p	miR-3679-5R/NEDD4L/c-Myc axis	[145]
Mesenchymal stem cells	Liver cancer (S)	Cisplatin	circRNA-G004213	miR-513b-5p/PRPF39	[146]
	Gastric cancer	Cisplatin/vincristine	miR-301b-3p	miR-301b-3p/TXNIP	[147]
	Breast cancer	Doxorubicin	miR-21-5p	miR-21-5p/S100A6	[148]
Renal cell carcinoma (R)	Renal cell carcinoma (S)	Sunitinib	LncRNA IGFL2-AS1	IGFL2-AS1/hnRNPC/TP53INP2 axis	[149]
Advanced renal cell carcinoma (R)	Renal cell carcinoma (S)	Sunitinib	lncARSR	lncARSR/miR-34, miR-449/AXL, c-MET	[150]
Cancer associated fibroblasts	Myeloid-derived suppressor cells	DDP (ESCC)	miR-21/Non-exo IL-6	IL-6/exo-miR-21-STAT3 axis	[151]
Epithelial ovarian cancer (R)	Epithelial ovarian cancer (S)	Cisplatin	miR-6836	miR-6836/DLG2/Yap1/TEAD1 axis	[152]
Resistant pancreatic cancer stem cell	Pancreatic cancer	Gemcitabine	miR-210	miR-210/mTOR pathway	[153]
Chronic myeloid leukemia (R)	Chronic myeloid leukemia (S)	Imatinib	IFITM3, CD146, CD36	-	[154]

Table 1. Cont.

Donor Cell	Recipient Cell	Resistance	Exosomal Components	Molecular Mechanisms	Ref.
Oral squamous cell carcinoma (R)	Oral squamous cell carcinoma (S)	5-FU	lncRNA APCDD1L-AS1	miR-1224-5p/NSD2 axis	[155]
Neuroblastoma (R)	Neuroblastoma (S)	Doxorubicin	circDLGAP4	circDLGAP4/miR-143/HK2 axis	[92]
Gliomas (R)	Gliomas (S)	Temozolomide	MIF	TIMP3/PI3K/AKT axis	[156]
			circWDR62	Circ-WDR162/miR-370-3p/MGMT	[157]
			Circ_0072083	miR-1252-5p/ALKBH5/NANOG axis	[158]
Glioblastoma stem cell	Normal astrocytes (transform to TAA)	Temozolomide	ALKBH7	ALKBH7/APNG regulation network	[159]
Pancreatic cancer (hypoxic)	Pancreatic cancer (normoxic)	Gemcitabine	circZNF91(hypoxic)	miR-23b-3p/SIRT1/HIF-1 α axis	[90]
Osteosarcoma (R)	Osteosarcoma (S)	Cisplatin	circ_103801	-	[160]
M2 macrophage	Pancreatic cancer	Gemcitabine	miR-222-3p	mTOR/AKT/PI3K pathway and TSC1	[161]
	Colorectal cancer	Oxaliplatin	lncRNA FAL1	lnc-FAL1/Beclin1 and TRIM3	[162]
		multidrug	LINC00355	LINC00355/miR-34b-5p/CRKL axis	[163]
Cancer associated fibroblasts	Malignant lymphoma	Anti-pyrimidine	miR-4717-5p	miR-4717-5p/ENT2 axis	[164]
	Monocytic myeloid-derived suppressor cell	Cisplatin (ESCC)	IL-6 and Exo-miR21	IL-6, exo-miR21-STAT3 signaling	[151]
	Vulvar squamous cell carcinoma	Cisplatin	lncRNA UCA1	lncRNA UCA1/miR-103a/WEE1 axis	[165]
	Non-small cell lung cancer	Cisplatin	miRNA-130a	PUM2-Dependent Packaging	[166]
		Cisplatin	microRNA-20a	microRNA-20a/PTEN/PI3K-AKT pathway	[167]
	Colon cancer	Methotrexate	miR-24-3p	miR-24-3p/CDX2/HEPH axis	[168]
	Bladder cancer	Cisplatin	LINC00355	LINC00355/miR-34b-5p/ABCB1 axis	[169]
		PTX and DOX	miR-148b-3p	miR-148b-3p/PTEN/Wnt/ β -catenin pathway	[170]
	Gastric cancer	Oxaliplatin	DACT3-AS1 (down)	miR-181a-5p/SIRT1 axis	[171]
	Ovarian cancer	-	miR-296-3p	PTEN/AKT and SOCS6/STAT3 pathways	[172]
	Oral squamous cell carcinoma	Cisplatin	miR-876-3p	miR-876-3p/GATA1/IGFBP33	[173]
	Pancreatic ductal adenocarcinoma	Gemcitabine	miR-3173-5p	miR-3173-5p/ACSL4 pathway	[174]
Cancer associated fibroblasts (hypoxic)		Platinum	circBIRC6	circBIRC6/XRCC4/SUMO1	[175]
	Esophageal squamous cell carcinoma	Cisplatin	RIG-I	RIG-I/IFN- β signaling	[176]
	Pancreatic cancer	Gemcitabine	miR-21	HIF-1 α /miR-21 and miR-21/RAS/AKT/ERK axis	[177]
	Breast cancer	Paclitaxel	lncRNA H19	lncRNA H19/miR-497/DNMT1	[178]

“-” no conclusion is given in the article; (R) and (S) stand for drug resistance and sensitivity, respectively. (KD) and (OE) indicate self-knockout and self-overexpression verification, respectively.

3. Drug Efflux and Chemoresistance

3.1. Mechanisms of Drug Efflux in Chemoresistance

The mechanisms involving chemoresistance via drug expulsion have been extensively investigated. Indeed, the increased efflux of chemotherapeutic agents, leading to reduced intracellular drug concentrations, is widely recognized as a primary driver of drug resistance [179]. Drug efflux transporters, also known as drug efflux pumps, are recognized as critical determinants of intracellular drug disposition. These efflux transporters harness the energy derived from ATP hydrolysis to expel anticancer drugs from cells to the extracellular milieu [180], thereby diminishing intracellular drug concentrations and compromising the effectiveness of chemotherapy, resulting in suboptimal therapeutic outcomes [181]. Additionally, they have been shown to be intricately regulated by diverse signaling pathways, including but not limited to the S1PR2-ERK pathway [182], the CHD4/MEK/ERK signaling cascade [183], and multiple ncRNAs [184].

3.2. Exosome-Mediated Drug Expulsion

The straightforward drug efflux can also be facilitated by exosome vesicle shedding. Historically, exosomes were considered “cellular waste bins” for disposing of intracellular debris [185,186], a role that aligns with their function in orchestrating chemotherapy resistance through drug sequestration and enhancement of efflux mechanisms (Figure 5). One study has suggested a mechanistic relationship between chemoresistance to anticancer drugs and vesicular shedding, where the differences in vesicle shedding rates correlate with the expression levels of shedding-related genes and trends in epigenetic doxorubicin resistance. Additionally, thermodynamic binding interactions have been demonstrated to explain the accumulation of drugs in membrane domains from which exosome vesicles originate [187]. Follow-up studies have further demonstrated that a wide variety of chemotherapy agents, such as enzalutamide [188], cisplatin [189], 5-Fu [190], paclitaxel [191], doxorubicin, and pixantrone [192], can be actively released from cells via exosomes. It was also demonstrated that anthracyclines are particularly susceptible to sequestration and expulsion through their preferential export into exosomes [192–194]. Meanwhile, the second mechanism involves the horizontal transfer of drug efflux transporters mediated by exosomes. It is well-established that drug efflux transporters consist of ATP-binding cassette (ABC) transporters (such as P-glycoprotein (MDR1/P-gp), breast cancer resistance protein (BCRP)), lipid transport proteins (such as scavenger receptor class B type I (SR-BI)), G protein-coupled receptors (such as CXCR4 and CXCR7), and other components. Notably, the ABC transporter superfamily has been extensively studied and comprises 50 members organized into seven subfamilies (A to G) in humans. These transporters utilize ATP binding to enable the translocation and expulsion of a wide range of structurally and functionally diverse drug molecules [195]. Functional P-gp is among the proteins receiving particular attention (Table 2). In an early study, Levchenko and collaborators proposed that this protein and its corresponding mRNA intercellular transfer between resistant and sensitive cell lines is the result of a process requiring either direct cell-to-cell contact or the exchange of membrane microparticles [196]. Exosomal P-gp delivery confers drug-resistant phenotype in vitro and in vivo [197,198]. Surprisingly, the P-gp transfer is considerably rapid. A significant increase in surface P-gp expression in sensitive cells was observed as early as 4 h after incubation and reached the maxima at 12 h [199]. In addition, Bebawy et al. also demonstrated that recipient cells exhibited P-gp functionality as early as in 2–4 h, which excludes the possibility of de novo synthesis of P-gp in recipient tumor cells [197]. In addition, other transporters like MRP-1 [200] and BCRP [201] are equally capable of intracellular transfer mediated by exosomes. In heterogeneous tumors, the coexistence of drug-resistant and drug-sensitive clones is likely due to genetic and

phenotypic variations among tumor cells. Lateral interactions mediated by exosomes might facilitate the dissemination of drug resistance among tumor cells.

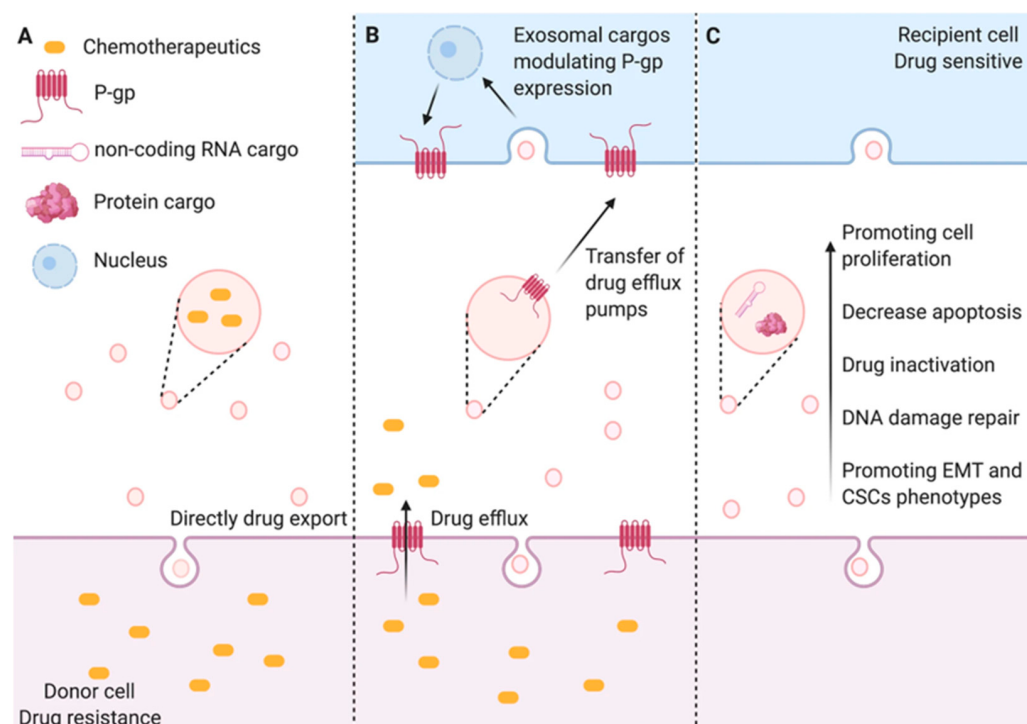


Figure 5. Schematic illustration of exosome-mediated drug efflux. (A) Therapeutic agents may be actively released through exosomal packaging mechanisms. (B) Exosomal vesicles facilitate the horizontal transfer of membrane-associated drug efflux transporters to recipient cells, enhancing chemotherapeutic agent extrusion. Additionally, these extracellular carriers deliver regulatory biomolecules such as microRNAs and functional proteins that upregulate P-glycoprotein (P-gp) expression in target cells. (C) Exosome-mediated cargo transfer promotes multiple pro-survival mechanisms in malignant cells, including enhanced proliferative capacity; resistance to apoptosis; drug metabolism activation; DNA repair facilitation; EMT; and acquisition of stem cell-like property [202].

3.3. Distinction Between Efflux Transporters and Exosome-Mediated Efflux

A compelling question arises: Why has evolution led to the development of two parallel direct efflux systems? A tentative distinction has been drawn between drug efflux mediated by efflux transporters and that facilitated by exosomes. Efflux transporters primarily mediate the expulsion of drugs in the aqueous phase, especially hydrophilic compounds, whereas exosome-mediated efflux is hypothesized to predominantly involve lipophilic drugs present at low concentrations in the cytoplasm [187]. Further investigation is warranted to delve into the precise underlying mechanisms. Another study demonstrated the exosome-mediated drug expulsion mechanism was conducted by Wang and collaborators [203], who also quantified the chemotherapeutic agent content within exosomes. The findings revealed comparable concentrations of paclitaxel in lysates or exosomes across different cancer cell lines, e.g., drug concentration in cell lysates was roughly 27 pmol, while in exosomes, it was about 1.5 pmol per 10^6 trypan blue-labeling cells at 100 nM $C_{\text{medium, total}}$ paclitaxel [203]. As a matter of fact, chemotherapeutic treatment and tumor microenvironment conditions (low pH, hypoxia, and so on) are known to accelerate the biogenesis of exosomes [204–206]. This, in turn, may serve as an impetus for accelerated drug efflux. Interestingly, blocking exosome biogenesis using various exogenous inhibitors, such as GW4869 (an inhibitor that hampers the synthesis of sphingolipid ceramide, which is essential for exosome formation), Omeprazole (an inhibitor of proton pumps involved in

exosome release), Indomethacin (an inhibitor of ATP-binding cassette transporter A3, which is crucial for MVBs and exosome biogenesis), and Lansoprazole (a proton pump inhibitor), results in a decrease in the amount of chemotherapeutic agents within vesicles while simultaneously increasing their content and chemosensitivity (cytotoxicity) in exosome-donor cells [191,192,207]. The combined treatment of 0.5 μ M PEGylated liposomal doxorubicin and GW4869 for acute myeloblastic leukemia U937 cells was sufficient to induce a cytotoxic effect comparable to 1 μ M of either [208]. Phosphorylation-regulated SNAP-23 promotes the release of tumor exosomes by facilitating stable complex formation [209], and the down-regulation of O-GlcNAcylation transferase enhances exosome secretion via facilitating the formation of the SNAP-23-Stx4-VAMP8 complex that increases efflux of intracellular cisplatin [210]. Concurrently, it would be prudent to pursue the development of compounds targeting exosome biogenesis in order to enhance the chemosensitivity of cancer cells.

3.4. Therapeutic Potential of Engineered Exosomes

Recent advances in engineered exosomes have positioned them as a transformative platform for overcoming tumor chemoresistance. By enabling precise delivery of therapeutic miRNAs, small interfering RNA (siRNAs), or chemotherapeutic agents, these nanoscale vesicles enhance drug efficacy in resistant malignancies. Current approaches to miRNA delivery via exosomes broadly fall into two categories: miRNA replacement therapy, which introduces tumor-suppressive miRNA mimics, and miRNA inhibition, which employs anti-miRNA oligonucleotides (AMOs) or inhibitors to silence oncogenic miRNAs (oncomiRs). For example, miR-155 overexpression drives chemoresistance and invasiveness in oral squamous cell carcinoma (OSCC). To counteract this, Kirave et al. engineered exosomes to deliver miR-155 inhibitors into cisplatin-resistant OSCC cells, effectively reversing resistance by upregulating FOXO3a and inducing mesenchymal–epithelial transition (MET) [211]. Similarly, the exosome-mediated delivery of miR-501 inhibitors sensitized DOX-resistant gastric cancer cells to DOX by suppressing miR-501 activity [141]. While exosome-based miRNA therapies show promise, their clinical translation is hindered by insufficient targeting specificity. To address this, recent studies have explored co-loading exosomes with both miRNAs and chemotherapeutic agents to achieve synergistic, tumor-selective effects. As shown in Figure 6, Liang et al. developed EGFR-targeted exosomes by surface-displaying Her2-LAMP2 fusion proteins. These exosomes, co-loaded with miR-21 inhibitors (miR-21i) and 5-fluorouracil (5-FU) (THLG-EXO/5-FU/miR-21i), were internalized via EGFR-mediated endocytosis in 5-FU-resistant HCT-116 colorectal cancer cells (HCT-1165–FR) [212]. In parallel, Ohno et al. demonstrated that GE11 peptide-modified exosomes selectively delivered let-7a miRNA to EGFR-overexpressing breast cancer cells, suppressing tumor growth and restoring 5-FU sensitivity [213]. Shang et al. demonstrated that the systemic delivery of exosomes loaded with miR-199a-3p mimics effectively overcame chemoresistance in DDP-refractory hepatocellular carcinoma (HCC), with bioinformatics and experimental validation revealing its mechanism through target gene regulation. Their findings highlight miR-199a-3p as a promising therapeutic target for reversing DDP resistance in HCC through both in vitro and in vivo models [214].

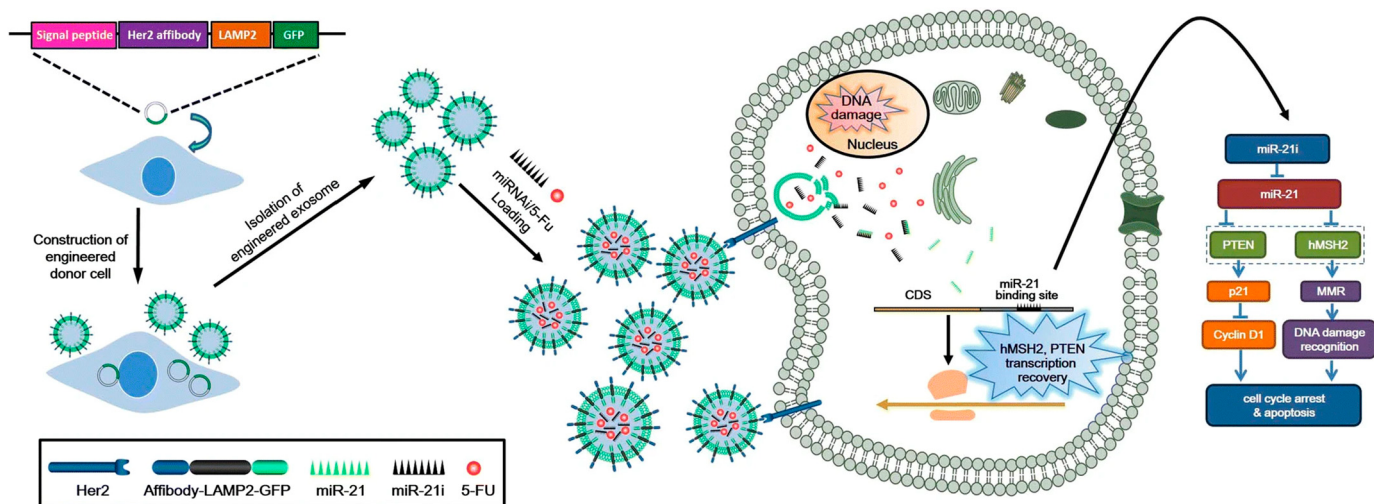


Figure 6. Engineered exosome-based nanocarrier for 5-FU and miR-21i simultaneously delivered to HCT-1165FR human colon cancer cells for enhancing chemotherapy efficacy [212].

Beyond miRNAs, siRNA-loaded exosomes have emerged as potent tools to disrupt chemoresistance pathways. Kamekar et al. pioneered this approach by engineering exosomes to deliver KRASG12D siRNA, which suppressed oncogenic KRAS signaling and shrunk gemcitabine-resistant pancreatic tumors in vivo [215]. In hepatocellular carcinoma, Li et al. leveraged bone marrow mesenchymal stem cell (BM-MSC)-derived exosomes to deliver siRNA targeting Grp78—a key mediator of sorafenib resistance—resensitizing resistant cells to therapy [216]. Similarly, Zhang et al. achieved robust c-Met silencing using exosome-delivered si-c-Met, restoring drug sensitivity in multiple resistant tumor models [217]. Targeting metabolic adaptations, Lin et al. employed iRGD-modified exosomes to deliver siCPT1A into colon cancer cells, inhibiting fatty acid oxidation (FAO) and reversing oxaliplatin resistance by suppressing CPT1A, a rate-limiting FAO enzyme [218]. In addition to their roles in miRNA and siRNA delivery, exosomes have demonstrated potential as versatile carriers for other nucleic acid-based therapeutics, to synergistically enhance chemotherapy efficacy in resistant tumors. For example, Ba et al. identified exosome-mediated transfer of circRNA ciRS-122 as a key mechanism driving chemoresistance in colorectal cancer (CRC), where ciRS-122 sponges miR-122 to upregulate PKM2-driven glycolysis and promote oxaliplatin resistance in recipient cells, with therapeutic inhibition of ciRS-122 reversing metabolic reprogramming and restoring drug sensitivity in preclinical models. This study highlights exosomal circRNAs as critical mediators of intercellular chemoresistance propagation and proposes ciRS-122 as a novel therapeutic target for refractory CRC [56]. In addition, Jiang et al. revealed that heparanase-mediated exosomal transfer of circRNAs, particularly hsa_circ_0042003, drives temozolomide (TMZ) resistance in glioma by promoting chemoresistance propagation from resistant to sensitive cells through in vitro and in vivo models. Their findings highlight targeting heparanase-exosomal circRNA axis as a promising strategy to overcome TMZ resistance in glioma therapy [219].

Collectively, these studies underscore the versatility of engineered exosomes in co-delivering nucleic acids and chemotherapeutics to dismantle chemoresistance mechanisms. However, challenges remain in optimizing tumor targeting, payload stability, and scalable manufacturing. Future efforts integrating advanced surface engineering, biomaterial design, and AI-driven delivery optimization will be pivotal for translating these breakthroughs into clinical practice.

Table 2. Exosome-mediated drug efflux transporters transfer.

Cell Type	Resistant Type	Exosomal Content	Mechanism	Ref
Human breast adenocarcinoma	Doxorubicin	P-gp	Two transfer modalities including P-gp containing microparticles and tunneling nanotubes	[199]
Human osteosarcoma	Doxorubicin	MDR-1/P-gp	Acquisition and dissemination of drug-resistant traits	[220]
Human brain endothelial cell	Doxycycline	Pgp-EGFP	A non-genetic way of intercellular transfer of P-gp occurs in non-cancer cells	[221]
Breast cancer	Docetaxel	P-gp	Mediate docetaxel resistance transfer in MCF-7 cell	[222]
Gastric cancer	Vincristine	CLIC1	Induce the development of resistance to vincristine and related to upregulated P-gp and Bcl-2	[223]
Hormone-refractory prostate cancer	Docetaxel	MDR-1/P-gp	Influence cellular proliferation, invasion, and response to docetaxel	[224]
Breast cancer	Palbociclib		TK1 and CDK9 mRNA expression in plasma-derived exosomes is associated with resistance to palbociclib	[225,226]
Human breast adenocarcinoma and acute lymphoblastic leukemia cell	Doxorubicin	MRP1	MPs shed from cells with a P-gp dominant resistance profile to re-template a pre-existing MRP1 dominant profile in recipient cells	[200]
MDR leukemia and breast cancer	Multidrug	P-gp and MRP1	Change recipient cells' transcriptional environment to reflect donor MDR phenotype	[227]
Human breast cancer cell	Adriamycin	UCH-L1 and P-gp	Transferring the chemoresistance phenotype in a time-dependent manner	[228]
Colorectal Cancer	5-fluorouracil (5-FU)		p-STAT3 transferred by exosomes from 5-FU-resistant cells could induce chemotherapy resistance in recipient cells by reducing caspase cascade activation	[229,230]

4. Conclusions and Future Perspectives

This review systematically elucidates the molecular mechanisms underlying exosome biogenesis and their role in mediating tumor resistance. It covers recent advances in tumor-derived exosomes as critical regulators of microenvironment remodeling, therapeutic resistance, and distant metastasis, revealing their function as “molecular messengers” that drive adaptive survival of tumor cells through the transfer of bioactive cargoes such as proteins, nucleic acids, and metabolites. Compared to previous studies, the add-on value of this review lies in three key contributions: First, it deciphers the regulatory mechanisms of chemotherapy resistance mediated by vesicle formation, secretion, and tumor cell uptake through a dynamic interaction perspective between exosome biogenesis and tumor resistance signaling networks. Second, it comprehensively summarizes current research on exosomal components implicated in chemotherapy resistance, presented via a clear and systematic table. Third, it prospectively explores the therapeutic potential of engineered exosomes for chemoresistant tumors—particularly through the targeted delivery of chemotherapeutic agents or nucleic acid molecules to reverse drug-resistant phenotypes—thereby providing clinically feasible strategies for engineered exosome-based cancer therapies.

Exosome-based drug delivery systems hold multifaceted promise in overcoming cancer resistance. With advancing developments in engineered exosomes, these systems may enhance the precision and efficacy of cancer therapies by specifically targeting drug-resistant cells, thereby minimizing off-target effects and systemic toxicity. Combining engineered exosome-based delivery with existing therapies may yield synergistic effects while addressing multiple resistance mechanisms. The unique ability of exosomes to tra-

verse biological barriers such as the blood–brain barrier further expands their therapeutic potential, particularly for metastatic and hard-to-reach tumors. Despite their considerable promise, practical clinical translation of engineered exosomes for chemoresistant cancers faces significant hurdles. The lack of unified and stable industrial standards remains a major challenge, as current exosome isolation methods suffer from low efficiency, high costs, and inconsistent purity. However, ongoing technological advancements—including bioreactors, 3D scaffolds, and microfluidic devices—offer viable solutions to enhance exosome production. Establishing standardized protocols for exosome preparation and purification is critical to improving therapeutic efficacy and enabling clinical application. Another challenge lies in achieving precise, personalized treatments for cancer patients, complicated by exosomal heterogeneity and the complex in vivo microenvironment, which limit targeted delivery and desired therapeutic outcomes. Current research demonstrates that autologous exosomes, obtained via minimally invasive techniques or surgical samples and expanded under specific culture conditions, exhibit remarkable tumor-targeting capabilities. However, since exosomes carry diverse proteins and immune-modulatory components, their administration may trigger robust host immune responses, potentially leading to rapid clearance. Comprehensive preclinical evaluations—including pharmacokinetic, toxicological, and pharmacodynamic analyses—are therefore essential to mitigate adverse effects. Despite the considerable challenges and difficulties in applying exosomes to clinical cancer therapy, engineered exosomes, as next-generation nanomaterials for advanced drug delivery and chemoresistant cancer treatment, hold potential for clinical translation.

Author Contributions: G.L.: Investigation, Conceptualization, Writing—Original Draft Preparation. J.L.: Writing—Original Draft Preparation, Investigation. S.L.: Writing—Original Draft. Y.Z.: Writing—Review and Editing, Supervision, Funding Acquisition. R.H.: Writing—Reviewing and Editing. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by the National Natural Science Foundation of China (22375144 and 32071384) and the National Key Research and Development Program (2021YFC2102300).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

MVBs	multivesicular bodies
ILVs	intraluminal vesicles
CAFs	cancer-associated fibroblasts
HNSCC	head and neck squamous cell carcinoma
ncRNAs	non-coding RNAs
ABC	ATP-binding cassette
BCRP	breast cancer resistance protein
SR-BI	scavenger receptor class B type I
AMOs	anti-miRNA oligonucleotides
OSCC	oral squamous cell carcinoma
MET	mesenchymal–epithelial transition
5-FU	5-fluorouracil
EMT	epithelial–mesenchymal transition
HCC	hepatocellular carcinoma

miRNA	microRNA
siRNA	small interfering RNA
oncomiRs	oncogenic miRNAs
TMZ	temozolomide

References

1. Thery, C.; Ostrowski, M.; Segura, E. Membrane vesicles as conveyors of immune responses. *Nat. Rev. Immunol.* **2009**, *9*, 581–593. [[CrossRef](#)] [[PubMed](#)]
2. Pisitkun, T.; Shen, R.F.; Knepper, M.A. Identification and proteomic profiling of exosomes in human urine. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 13368–13373. [[CrossRef](#)]
3. Pan, B.T.; Johnstone, R.M. Fate of the transferrin receptor during maturation of sheep reticulocytes in vitro: Selective externalization of the receptor. *Cell* **1983**, *33*, 967–978. [[CrossRef](#)]
4. Pan, B.T.; Teng, K.; Wu, C.; Adam, M.; Johnstone, R.M. Electron microscopic evidence for externalization of the transferrin receptor in vesicular form in sheep reticulocytes. *J. Cell Biol.* **1985**, *101*, 942–948. [[CrossRef](#)]
5. Johnstone, R.M.; Adam, M.; Hammond, J.R.; Orr, L.; Turbide, C. Vesicle formation during reticulocyte maturation. Association of plasma membrane activities with released vesicles (exosomes). *J. Biol. Chem.* **1987**, *262*, 9412–9420. [[CrossRef](#)] [[PubMed](#)]
6. Raposo, G.; Nijman, H.W.; Stoorvogel, W.; Liejendekker, R.; Harding, C.V.; Melief, C.J.; Geuze, H.J. B lymphocytes secrete antigen-presenting vesicles. *J. Exp. Med.* **1996**, *183*, 1161–1172. [[CrossRef](#)] [[PubMed](#)]
7. Blanchard, N.; Lankar, D.; Faure, F.; Regnault, A.; Dumont, C.; Raposo, G.; Hivroz, C. TCR activation of human T cells induces the production of exosomes bearing the TCR/CD3/zeta complex. *J. Immunol.* **2002**, *168*, 3235–3241. [[CrossRef](#)]
8. Lugini, L.; Cecchetti, S.; Huber, V.; Luciani, F.; Macchia, G.; Spadaro, F.; Paris, L.; Abalsamo, L.; Colone, M.; Molinari, A.; et al. Immune Surveillance Properties of Human NK Cell-Derived Exosomes. *J. Immunol.* **2012**, *189*, 2833–2842. [[CrossRef](#)]
9. Thery, C.; Regnault, A.; Garin, J.; Wolfers, J.; Zitvogel, L.; Ricciardi-Castagnoli, P.; Raposo, G.; Amigorena, S. Molecular characterization of dendritic cell-derived exosomes: Selective accumulation of the heat shock protein hsc73. *J. Cell Biol.* **1999**, *147*, 599–610. [[CrossRef](#)]
10. Raposo, G.; Tenza, D.; Mecheri, S.; Peronet, R.; Bonnerot, C.; Desaymard, C. Accumulation of major histocompatibility complex class II molecules in mast cell secretory granules and their release upon degranulation. *Mol. Biol. Cell* **1997**, *8*, 2631–2645. [[CrossRef](#)]
11. van Niel, G.; Raposo, G.; Candalh, C.; Boussac, M.; Hershberg, R.; Cerf-Bensussan, N.; Heyman, M. Intestinal epithelial cells secrete exosome-like vesicles. *Gastroenterology* **2001**, *121*, 337–349. [[CrossRef](#)]
12. Janiszewski, M.; do Carmo, A.O.; Pedro, M.A.; Silva, E.; Knobel, E.; Laurindo, F.R.M. Platelet-derived exosomes of septic individuals possess proapoptotic NAD(P)H oxidase activity: A novel vascular redox pathway. *Crit. Care Med.* **2004**, *32*, 818–825. [[CrossRef](#)]
13. Mears, R.; Craven, R.A.; Hanrahan, S.; Totty, N.; Upton, C.; Young, S.L.; Patel, P.; Selby, P.J.; Banks, R.E. Proteomic analysis of melanoma-derived exosomes by two-dimensional polyacrylamide gel electrophoresis and mass spectrometry. *Proteomics* **2004**, *4*, 4019–4031. [[CrossRef](#)] [[PubMed](#)]
14. Li, Q.-L.; Bu, N.; Yu, Y.-C.; Hua, W.; Xin, X.-Y. Ex vivo experiments of human ovarian cancer ascites-derived exosomes presented by dendritic cells derived from umbilical cord blood for immunotherapy treatment. *Clin. Med. Oncol.* **2008**, *2*, 461–467. [[CrossRef](#)]
15. Bard, M.P.; Hegmans, J.P.; Hemmes, A.; Luiders, T.M.; Willemsen, R.; Severijnen, L.A.A.; van Meerbeeck, J.P.; Burgers, S.A.; Hoogsteden, H.C.; Lambrecht, B.N. Proteomic analysis of exosomes isolated from human malignant pleural effusions. *Am. J. Respir. Cell Mol. Biol.* **2004**, *31*, 114–121. [[CrossRef](#)]
16. Michael, A.; Bajracharya, S.D.; Yuen, P.S.T.; Zhou, H.; Star, R.A.; Illei, G.G.; Alevizos, I. Exosomes from human saliva as a source of microRNA biomarkers. *Oral Dis.* **2010**, *16*, 34–38. [[CrossRef](#)] [[PubMed](#)]
17. Vella, L.J.; Greenwood, D.L.V.; Cappai, R.; Scheerlinck, J.P.Y.; Hill, A.F. Enrichment of prion protein in exosomes derived from ovine cerebral spinal fluid. *Vet. Immunol. Immunopathol.* **2008**, *124*, 385–393. [[CrossRef](#)]
18. Qiu, S.Q.; Duan, X.B.; Geng, X.R.; Xie, J.X.; Gao, H. Antigen-specific activities of CD8⁺T cells in the nasal mucosa of patients with nasal allergy. *Asian Pac. J. Allergy Immunol.* **2012**, *30*, 107–113. [[PubMed](#)]
19. Keller, S.; Rupp, C.; Stoeck, A.; Runz, S.; Fogel, M.; Lugert, S.; Hager, H.D.; Abdel-Bakky, M.S.; Gutwein, P.; Altevogt, P. CD24 is a marker of exosomes secreted into urine and amniotic fluid. *Kidney Int.* **2007**, *72*, 1095–1102. [[CrossRef](#)]
20. Graner, M.W.; Alzate, O.; Dechkovskaia, A.M.; Keene, J.D.; Sampson, J.H.; Mitchell, D.A.; Bigner, D.D. Proteomic and immunologic analyses of brain tumor exosomes. *FASEB J.* **2009**, *23*, 1541–1557. [[CrossRef](#)]
21. Simpson, R.J.; Lim, J.W.E.; Moritz, R.L.; Mathivanan, S. Exosomes: Proteomic insights and diagnostic potential. *Expert Rev. Proteom.* **2009**, *6*, 267–283. [[CrossRef](#)]
22. Jeppesen, D.K.; Fenix, A.M.; Franklin, J.L.; Higginbotham, J.N.; Zhang, Q.; Zimmerman, L.J.; Liebler, D.C.; Ping, J.; Liu, Q.; Evans, R.; et al. Reassessment of Exosome Composition. *Cell* **2019**, *177*, 428–445.e18. [[CrossRef](#)] [[PubMed](#)]

23. Vidal, M.; Sainte-Marie, J.; Philippot, J.R.; Bienvenue, A. Asymmetric distribution of phospholipids in the membrane of vesicles released during in vitro maturation of guinea pig reticulocytes: Evidence precluding a role for “aminophospholipid translocase”. *J. Cell. Physiol.* **1989**, *140*, 455–462. [[CrossRef](#)] [[PubMed](#)]
24. Skog, J.; Wurdinger, T.; van Rijn, S.; Meijer, D.H.; Gainche, L.; Sena-Esteves, M.; Curry, W.T.; Carter, B.S.; Krichevsky, A.M.; Breakefield, X.O. Glioblastoma microvesicles transport RNA and proteins that promote tumour growth and provide diagnostic biomarkers. *Nat. Cell Biol.* **2008**, *10*, 1470–1476. [[CrossRef](#)]
25. Valadi, H.; Ekstrom, K.; Bossios, A.; Sjostrand, M.; Lee, J.J.; Lotvall, J.O. Exosome-mediated transfer of mRNAs and microRNAs is a novel mechanism of genetic exchange between cells. *Nat. Cell Biol.* **2007**, *9*, 654–659. [[CrossRef](#)]
26. Balaj, L.; Lessard, R.; Dai, L.X.; Cho, Y.J.; Pomeroy, S.L.; Breakefield, X.O.; Skog, J. Tumour microvesicles contain retrotransposon elements and amplified oncogene sequences. *Nat. Commun.* **2011**, *2*, 180. [[CrossRef](#)]
27. Williams, C.; Rodriguez-Barrueco, R.; Silva, J.M.; Zhang, W.J.; Hearn, S.; Elemento, O.; Paknejad, N.; Manova-Todorova, K.; Welte, K.; Bromberg, J.; et al. Double-stranded DNA in exosomes: A novel biomarker in cancer detection. *Cell Res.* **2014**, *24*, 766–769.
28. Pan, W.; Miao, Q.; Yin, W.; Li, X.; Ye, W.; Zhang, D.; Deng, L.; Zhang, J.; Chen, M. The role and clinical applications of exosomes in cancer drug resistance. *Cancer Drug Resist.* **2024**, *7*, 43. [[CrossRef](#)]
29. Kowal, J.; Tkach, M.; Théry, C. Biogenesis and secretion of exosomes. *Curr. Opin. Cell Biol.* **2014**, *29*, 116–125. [[CrossRef](#)] [[PubMed](#)]
30. Théry, C.; Witwer, K.W.; Aikawa, E.; Alcaraz, M.J.; Anderson, J.D.; Andriantsitohaina, R.; Antoniou, A.; Arab, T.; Archer, F.; Atkin-Smith, G.K.; et al. Minimal information for studies of extracellular vesicles 2018 (MISEV2018): A position statement of the International Society for Extracellular Vesicles and update of the MISEV2014 guidelines. *J. Extracell. Vesicles* **2018**, *7*, 1535750. [[CrossRef](#)]
31. Gurung, S.; Perocheau, D.; Touramanidou, L.; Baruteau, J. The exosome journey: From biogenesis to uptake and intracellular signalling. *Cell Commun. Signal.* **2021**, *19*, 47. [[CrossRef](#)] [[PubMed](#)]
32. Raposo, G.; Stoorvogel, W. Extracellular vesicles: Exosomes, microvesicles, and friends. *J. Cell Biol.* **2013**, *200*, 373–383. [[CrossRef](#)] [[PubMed](#)]
33. Hoshino, A.; Costa-Silva, B.; Shen, T.-L.; Rodrigues, G.; Hashimoto, A.; Tesic Mark, M.; Molina, H.; Kohsaka, S.; Di Giannatale, A.; Ceder, S.; et al. Tumour exosome integrins determine organotropic metastasis. *Nature* **2015**, *527*, 329–335. [[CrossRef](#)]
34. Arriagada, R.; Bergman, B.; Dunant, A.; Le Chevalier, T.; Pignon, J.P.; Vansteenkiste, J. Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small-cell lung cancer. *N. Engl. J. Med.* **2004**, *350*, 351–360.
35. Douillard, J.Y.; Rosell, R.; De Lena, M.; Carpagnano, F.; Ramlau, R.; González-Larriba, J.L.; Grodzki, T.; Pereira, J.R.; Le Groumellec, A.; Lorusso, V.; et al. Adjuvant vinorelbine plus cisplatin versus observation in patients with completely resected stage IB–IIIA non-small-cell lung cancer (Adjuvant Navelbine International Trialist Association [ANITA]): A randomised controlled trial. *Lancet Oncol.* **2006**, *7*, 719–727. [[CrossRef](#)]
36. Wilting, R.H.; Dannenberg, J.H. Epigenetic mechanisms in tumorigenesis, tumor cell heterogeneity and drug resistance. *Drug Resist. Updates* **2012**, *15*, 21–38. [[CrossRef](#)]
37. Gottesman, M.M. Mechanisms of cancer drug resistance. *Annu. Rev. Med.* **2002**, *53*, 615–627. [[CrossRef](#)]
38. Muralidharan-Chari, V.; Kohan, H.G.; Asimakopoulos, A.G.; Sudha, T.; Sell, S.; Kannan, K.; Boroujerdi, M.; Davis, P.J.; Mousa, S.A. Microvesicle removal of anticancer drugs contributes to drug resistance in human pancreatic cancer cells. *Oncotarget* **2016**, *7*, 50365–50379. [[CrossRef](#)]
39. Xavier, C.P.R.; Belisario, D.C.; Rebelo, R.; Assaraf, Y.G.; Giovannetti, E.; Kopecka, J.; Vasconcelos, M.H. The role of extracellular vesicles in the transfer of drug resistance competences to cancer cells. *Drug Resist. Updates* **2022**, *62*, 100833. [[CrossRef](#)]
40. Zhou, Y.; Tang, W.; Zhuo, H.; Zhu, D.; Rong, D.; Sun, J.; Song, J. Cancer-associated fibroblast exosomes promote chemoresistance to cisplatin in hepatocellular carcinoma through circZFR targeting signal transducers and activators of transcription (STAT3)/nuclear factor- κ B (NF- κ B) pathway. *Bioengineered* **2022**, *13*, 4786–4797. [[CrossRef](#)]
41. Lyu, T.; Wang, Y.; Li, D.; Yang, H.; Qin, B.; Zhang, W.; Li, Z.; Cheng, C.; Zhang, B.; Guo, R.; et al. Exosomes from BM-MSCs promote acute myeloid leukemia cell proliferation, invasion and chemoresistance via upregulation of S100A4. *Exp. Hematol. Oncol.* **2021**, *10*, 24. [[CrossRef](#)] [[PubMed](#)]
42. Zheng, P.; Chen, L.; Yuan, X.; Luo, Q.; Liu, Y.; Xie, G.; Ma, Y.; Shen, L. Exosomal transfer of tumor-associated macrophage-derived miR-21 confers cisplatin resistance in gastric cancer cells. *J. Exp. Clin. Cancer Res. CR* **2017**, *36*, 53. [[CrossRef](#)]
43. Sansone, P.; Savini, C.; Kurelac, I.; Chang, Q.; Amato, L.B.; Strillacci, A.; Stepanova, A.; Iommarini, L.; Mastroleo, C.; Daly, L.; et al. Packaging and transfer of mitochondrial DNA via exosomes regulate escape from dormancy in hormonal therapy-resistant breast cancer. *Proc. Natl. Acad. Sci. USA* **2017**, *114*, e9066–e9075. [[CrossRef](#)] [[PubMed](#)]
44. Li, X.; Li, K.; Li, M.; Lin, X.; Mei, Y.; Huang, X.; Yang, H. Chemoresistance Transmission via Exosome-Transferred MMP14 in Pancreatic Cancer. *Front. Oncol.* **2022**, *12*, 844648. [[CrossRef](#)]

45. Alharbi, M.; Lai, A.; Sharma, S.; Kalita-de Croft, P.; Godbole, N.; Campos, A.; Guanzon, D.; Salas-Burgos, A.; Carrion, F.; Zuñiga, F.A.; et al. Extracellular Vesicle Transmission of Chemoresistance to Ovarian Cancer Cells Is Associated with Hypoxia-Induced Expression of Glycolytic Pathway Proteins, and Prediction of Epithelial Ovarian Cancer Disease Recurrence. *Cancers* **2021**, *13*, 3388. [\[CrossRef\]](#)
46. Wang, J.; Li, T.; Wang, B. Exosomal transfer of miR-25-3p promotes the proliferation and temozolomide resistance of glioblastoma cells by targeting FBXW7. *Int. J. Oncol.* **2021**, *59*, 64. [\[CrossRef\]](#)
47. Mao, L.; Li, J.; Chen, W.X.; Cai, Y.Q.; Yu, D.D.; Zhong, S.L.; Zhao, J.H.; Zhou, J.W.; Tang, J.H. Exosomes decrease sensitivity of breast cancer cells to adriamycin by delivering microRNAs. *Tumour Biol.* **2016**, *37*, 5247–5256. [\[CrossRef\]](#)
48. Zhang, S.; Zhong, J.; Guo, D.; Zhang, S.; Huang, G.; Chen, Y.; Xu, C.; Chen, W.; Zhang, Q.; Zhao, C.; et al. MIAT shuttled by tumor-secreted exosomes promotes paclitaxel resistance in esophageal cancer cells by activating the TAF1/SREBF1 axis. *J. Biochem. Mol. Toxicol.* **2023**, *37*, e23380. [\[CrossRef\]](#)
49. Zhang, F.; Jiang, J.; Qian, H.; Yan, Y.; Xu, W. Exosomal circRNA: Emerging insights into cancer progression and clinical application potential. *J. Hematol. Oncol.* **2023**, *16*, 67. [\[CrossRef\]](#)
50. Lin, Z.; Ji, Y.; Zhou, J.; Li, G.; Wu, Y.; Liu, W.; Li, Z.; Liu, T. Exosomal circRNAs in cancer: Implications for therapy resistance and biomarkers. *Cancer Lett.* **2023**, *566*, 216245. [\[CrossRef\]](#) [\[PubMed\]](#)
51. Azmi, A.S.; Bao, B.; Sarkar, F.H. Exosomes in cancer development, metastasis, and drug resistance: A comprehensive review. *Cancer Metastasis Rev.* **2013**, *32*, 623–642. [\[CrossRef\]](#) [\[PubMed\]](#)
52. Wang, Z.; Li, Y.; Ahmad, A.; Banerjee, S.; Azmi, A.S.; Kong, D.; Sarkar, F.H. Pancreatic cancer: Understanding and overcoming chemoresistance. *Nat. Rev. Gastroenterol. Hepatol.* **2011**, *8*, 27–33. [\[CrossRef\]](#) [\[PubMed\]](#)
53. Junttila, M.R.; de Sauvage, F.J. Influence of tumour micro-environment heterogeneity on therapeutic response. *Nature* **2013**, *501*, 346–354. [\[CrossRef\]](#)
54. Vasan, N.; Baselga, J.; Hyman, D.M. A view on drug resistance in cancer. *Nature* **2019**, *575*, 299–309. [\[CrossRef\]](#)
55. Boelens, M.C.; Wu, T.J.; Nabet, B.Y.; Xu, B.; Qiu, Y.; Yoon, T.; Azzam, D.J.; Twyman-Saint Victor, C.; Wiemann, B.Z.; Ishwaran, H.; et al. Exosome transfer from stromal to breast cancer cells regulates therapy resistance pathways. *Cell* **2014**, *159*, 499–513. [\[CrossRef\]](#)
56. Wang, X.; Zhang, H.; Yang, H.; Bai, M.; Ning, T.; Deng, T.; Liu, R.; Fan, Q.; Zhu, K.; Li, J.; et al. Exosome-delivered circRNA promotes glycolysis to induce chemoresistance through the miR-122-PKM2 axis in colorectal cancer. *Mol. Oncol.* **2020**, *14*, 539–555. [\[CrossRef\]](#)
57. Zhang, G.; Sun, L.; Lu, X.; Chen, Z.; Duerksen-Hughes, P.J.; Hu, H.; Zhu, X.; Yang, J. Cisplatin treatment leads to changes in nuclear protein and microRNA expression. *Mutat. Res.* **2012**, *746*, 66–77. [\[CrossRef\]](#)
58. Guo, X.; Gao, C.; Yang, D.H.; Li, S. Exosomal circular RNAs: A chief culprit in cancer chemotherapy resistance. *Drug Resist. Updates* **2023**, *67*, 100937. [\[CrossRef\]](#)
59. Qin, X.; Guo, H.; Wang, X.; Zhu, X.; Yan, M.; Wang, X.; Xu, Q.; Shi, J.; Lu, E.; Chen, W.; et al. Exosomal miR-196a derived from cancer-associated fibroblasts confers cisplatin resistance in head and neck cancer through targeting CDKN1B and ING5. *Genome Biol.* **2019**, *20*, 12. [\[CrossRef\]](#)
60. Ferreira, J.A.; Peixoto, A.; Neves, M.; Gaiteiro, C.; Reis, C.A.; Assaraf, Y.G.; Santos, L.L. Mechanisms of cisplatin resistance and targeting of cancer stem cells: Adding glycosylation to the equation. *Drug Resist. Updates* **2016**, *24*, 34–54. [\[CrossRef\]](#) [\[PubMed\]](#)
61. Figueroa, J.; Phillips, L.M.; Shahar, T.; Hossain, A.; Gumin, J.; Kim, H.; Bean, A.J.; Calin, G.A.; Fueyo, J.; Walters, E.T.; et al. Exosomes from Glioma-Associated Mesenchymal Stem Cells Increase the Tumorigenicity of Glioma Stem-like Cells via Transfer of miR-1587. *Cancer Res.* **2017**, *77*, 5808–5819. [\[CrossRef\]](#)
62. Hu, Y.; Yan, C.; Mu, L.; Huang, K.; Li, X.; Tao, D.; Wu, Y.; Qin, J. Fibroblast-Derived Exosomes Contribute to Chemoresistance through Priming Cancer Stem Cells in Colorectal Cancer. *PLoS ONE* **2015**, *10*, e0125625. [\[CrossRef\]](#)
63. Jie, Z.; Qianqian, S.; Mengna, W.; Wenjie, Z. The Emerging Roles of Exosomes in the Chemoresistance of Hepatocellular Carcinoma. *Curr. Med. Chem.* **2021**, *28*, 93–109.
64. Santos, J.C.; Lima, N.d.S.; Sarian, L.O.; Matheu, A.; Ribeiro, M.L.; Derchain, S.F.M. Exosome-mediated breast cancer chemoresistance via miR-155 transfer. *Sci. Rep.* **2018**, *8*, 829. [\[CrossRef\]](#)
65. Ren, J.; Ding, L.; Zhang, D.; Shi, G.; Xu, Q.; Shen, S.; Wang, Y.; Wang, T.; Hou, Y. Carcinoma-associated fibroblasts promote the stemness and chemoresistance of colorectal cancer by transferring exosomal lncRNA H19. *Theranostics* **2018**, *8*, 3932–3948. [\[CrossRef\]](#)
66. Asare-Werehene, M.; Nakka, K.; Reunov, A.; Chiu, C.T.; Lee, W.T.; Abedini, M.R.; Wang, P.W.; Shieh, D.B.; Dilworth, F.J.; Carmona, E.; et al. The exosome-mediated autocrine and paracrine actions of plasma gelsolin in ovarian cancer chemoresistance. *Oncogene* **2020**, *39*, 1600–1616. [\[CrossRef\]](#)
67. Safaei, R.; Larson, B.J.; Cheng, T.C.; Gibson, M.A.; Otani, S.; Naerdemann, W.; Howell, S.B. Abnormal lysosomal trafficking and enhanced exosomal export of cisplatin in drug-resistant human ovarian carcinoma cells. *Mol. Cancer Ther.* **2005**, *4*, 1595–1604. [\[CrossRef\]](#) [\[PubMed\]](#)

68. Wang, X.; Qiao, D.; Chen, L.; Xu, M.; Chen, S.; Huang, L.; Wang, F.; Chen, Z.; Cai, J.; Fu, L. Chemotherapeutic drugs stimulate the release and recycling of extracellular vesicles to assist cancer cells in developing an urgent chemoresistance. *Mol. Cancer* **2019**, *18*, 182. [\[CrossRef\]](#)
69. Wang, Z.; He, J.; Bach, D.H.; Huang, Y.H.; Li, Z.; Liu, H.; Lin, P.; Yang, J. Induction of m(6)A methylation in adipocyte exosomal lncRNAs mediates myeloma drug resistance. *J. Exp. Clin. Cancer Res. CR* **2022**, *41*, 4. [\[CrossRef\]](#)
70. Chen, F.; Chen, J.; Yang, L.; Liu, J.; Zhang, X.; Zhang, Y.; Tu, Q.; Yin, D.; Lin, D.; Wong, P.P.; et al. Extracellular vesicle-packaged HIF-1 α -stabilizing lncRNA from tumour-associated macrophages regulates aerobic glycolysis of breast cancer cells. *Nat. Cell Biol.* **2019**, *21*, 498–510. [\[CrossRef\]](#) [\[PubMed\]](#)
71. Wu, S.; Luo, M.; To, K.K.W.; Zhang, J.; Su, C.; Zhang, H.; An, S.; Wang, F.; Chen, D.; Fu, L. Intercellular transfer of exosomal wild type EGFR triggers osimertinib resistance in non-small cell lung cancer. *Mol. Cancer* **2021**, *20*, 17. [\[CrossRef\]](#) [\[PubMed\]](#)
72. Polónia, B.; Xavier, C.P.R.; Kopecka, J.; Riganti, C.; Vasconcelos, M.H. The role of Extracellular Vesicles in glycolytic and lipid metabolic reprogramming of cancer cells: Consequences for drug resistance. *Cytokine Growth Factor Rev.* **2023**, *73*, 150–162. [\[CrossRef\]](#) [\[PubMed\]](#)
73. Vahabi, M.; Comandatore, A.; Franczak, M.A.; Smolenski, R.T.; Peters, G.J.; Morelli, L.; Giovannetti, E. Role of exosomes in transferring chemoresistance through modulation of cancer glycolytic cell metabolism. *Cytokine Growth Factor Rev.* **2023**, *73*, 163–172. [\[CrossRef\]](#)
74. Zeng, A.; Wei, Z.; Yan, W.; Yin, J.; Huang, X.; Zhou, X.; Li, R.; Shen, F.; Wu, W.; Wang, X.; et al. Exosomal transfer of miR-151a enhances chemosensitivity to temozolomide in drug-resistant glioblastoma. *Cancer Lett.* **2018**, *436*, 10–21. [\[CrossRef\]](#)
75. Hui, B.; Zhou, C.; Xu, Y.; Wang, R.; Dong, Y.; Zhou, Y.; Ding, J.; Zhang, X.; Xu, J.; Gu, Y. Exosomes secreted by *Fusobacterium nucleatum*-infected colon cancer cells transmit resistance to oxaliplatin and 5-FU by delivering hsa_circ_0004085. *J. Nanobiotechnol.* **2024**, *22*, 62. [\[CrossRef\]](#)
76. Wang, J.; Hendrix, A.; Hernot, S.; Lemaire, M.; De Bruyne, E.; Van Valckenborgh, E.; Lahoutte, T.; De Wever, O.; Vanderkerken, K.; Menu, E. Bone marrow stromal cell-derived exosomes as communicators in drug resistance in multiple myeloma cells. *Blood* **2014**, *124*, 555–566. [\[CrossRef\]](#)
77. Sun, C.; Huang, X.; Li, J.; Fu, Z.; Hua, Y.; Zeng, T.; He, Y.; Duan, N.; Yang, F.; Liang, Y.; et al. Exosome-Transmitted tRF-16-K8J7K1B Promotes Tamoxifen Resistance by Reducing Drug-Induced Cell Apoptosis in Breast Cancer. *Cancers* **2023**, *15*, 899. [\[CrossRef\]](#)
78. Meng, C.; Yang, Y.; Feng, W.; Ma, P.; Bai, R. Exosomal miR-331-3p derived from chemoresistant osteosarcoma cells induces chemoresistance through autophagy. *J. Orthop. Surg. Res.* **2023**, *18*, 892. [\[CrossRef\]](#)
79. Zhang, K.; Chen, J.; Li, C.; Fang, S.R.; Liu, W.F.; Qian, Y.Y.; Ma, J.Y.; Chang, L.G.; Chen, F.F.; Yang, Z.H.; et al. Exosome-mediated transfer of SNHG7 enhances docetaxel resistance in lung adenocarcinoma. *Cancer Lett.* **2022**, *526*, 142–154. [\[CrossRef\]](#)
80. Balaji, S.; Kim, U.; Muthukkaruppan, V.; Vanniarajan, A. Emerging role of tumor microenvironment derived exosomes in therapeutic resistance and metastasis through epithelial-to-mesenchymal transition. *Life Sci.* **2021**, *280*, 119750. [\[CrossRef\]](#) [\[PubMed\]](#)
81. Deng, J.; Pan, T.; Lv, C.; Cao, L.; Li, L.; Zhou, X.; Li, G.; Li, H.; Vicencio, J.M.; Xu, Y.; et al. Exosomal transfer leads to chemoresistance through oxidative phosphorylation-mediated stemness phenotype in colorectal cancer. *Theranostics* **2023**, *13*, 5057–5074. [\[CrossRef\]](#)
82. Ma, Y.; Yuwen, D.; Chen, J.; Zheng, B.; Gao, J.; Fan, M.; Xue, W.; Wang, Y.; Li, W.; Shu, Y.; et al. Exosomal Transfer Of Cisplatin-Induced miR-425-3p Confers Cisplatin Resistance In NSCLC Through Activating Autophagy. *Int. J. Nanomed.* **2019**, *14*, 8121–8132. [\[CrossRef\]](#)
83. White, E. Deconvoluting the context-dependent role for autophagy in cancer. *Nat. Rev. Cancer* **2012**, *12*, 401–410. [\[CrossRef\]](#) [\[PubMed\]](#)
84. Zhang, H.; Deng, T.; Liu, R.; Ning, T.; Yang, H.; Liu, D.; Zhang, Q.; Lin, D.; Ge, S.; Bai, M.; et al. CAF secreted miR-522 suppresses ferroptosis and promotes acquired chemo-resistance in gastric cancer. *Mol. Cancer* **2020**, *19*, 43. [\[CrossRef\]](#) [\[PubMed\]](#)
85. Zhang, H.; Deng, T.; Liu, R.; Bai, M.; Zhou, L.; Wang, X.; Li, S.; Wang, X.; Yang, H.; Li, J.; et al. Exosome-delivered EGFR regulates liver microenvironment to promote gastric cancer liver metastasis. *Nat. Commun.* **2017**, *8*, 15016. [\[CrossRef\]](#)
86. Fong, M.Y.; Zhou, W.; Liu, L.; Alontaga, A.Y.; Chandra, M.; Ashby, J.; Chow, A.; O'Connor, S.T.F.; Li, S.; Chin, A.R.; et al. Breast-cancer-secreted miR-122 reprograms glucose metabolism in premetastatic niche to promote metastasis. *Nat. Cell Biol.* **2015**, *17*, 183–194. [\[CrossRef\]](#) [\[PubMed\]](#)
87. Yu, S.; Zang, W.; Qiu, Y.; Liao, L.; Zheng, X. Deubiquitinase OTUB2 exacerbates the progression of colorectal cancer by promoting PKM2 activity and glycolysis. *Oncogene* **2022**, *41*, 46–56. [\[CrossRef\]](#)
88. Jing, Y.Y.; Cai, F.F.; Zhang, L.; Han, J.; Yang, L.; Tang, F.; Li, Y.B.; Chang, J.F.; Sun, F.; Yang, X.M.; et al. Epigenetic regulation of the Warburg effect by H2B monoubiquitination. *Cell Death Differ.* **2020**, *27*, 1660–1676. [\[CrossRef\]](#)
89. Petanidis, S.; Domvri, K.; Porpodis, K.; Anestakis, D.; Freitag, L.; Hohenforst-Schmidt, W.; Tsavlis, D.; Zarogoulidis, K. Inhibition of kras-derived exosomes downregulates immunosuppressive BACH2/GATA-3 expression via RIP-3 dependent necroptosis and miR-146/miR-210 modulation. *Biomed. Pharmacother.* **2020**, *122*, 109461. [\[CrossRef\]](#)

90. Zeng, Z.; Zhao, Y.; Chen, Q.; Zhu, S.; Niu, Y.; Ye, Z.; Hu, P.; Chen, D.; Xu, P.; Chen, J.; et al. Hypoxic exosomal HIF-1 α -stabilizing circZNF91 promotes chemoresistance of normoxic pancreatic cancer cells via enhancing glycolysis. *Oncogene* **2021**, *40*, 5505–5517. [\[CrossRef\]](#)
91. Wang, D.; Zhao, C.; Xu, F.; Zhang, A.; Jin, M.; Zhang, K.; Liu, L.; Hua, Q.; Zhao, J.; Liu, J.; et al. Cisplatin-resistant NSCLC cells induced by hypoxia transmit resistance to sensitive cells through exosomal PKM2. *Theranostics* **2021**, *11*, 2860–2875. [\[CrossRef\]](#)
92. Tan, W.Q.; Yuan, L.; Wu, X.Y.; He, C.G.; Zhu, S.C.; Ye, M. Exosome-delivered circular RNA DLGAP4 induces chemoresistance via miR-143-HK2 axis in neuroblastoma. *Cancer Biomark. Sect. A Dis. Markers* **2022**, *34*, 375–384. [\[CrossRef\]](#)
93. Zhuang, L.; Zhang, B.; Liu, X.; Lin, L.; Wang, L.; Hong, Z.; Chen, J. Exosomal miR-21-5p derived from cisplatin-resistant SKOV3 ovarian cancer cells promotes glycolysis and inhibits chemosensitivity of its progenitor SKOV3 cells by targeting PDHA1. *Cell Biol. Int.* **2021**, *45*, 2140–2149. [\[CrossRef\]](#)
94. Nguyen Cao, T.G.; Truong Hoang, Q.; Kang, J.H.; Kang, S.J.; Ravichandran, V.; Rhee, W.J.; Lee, M.; Ko, Y.T.; Shim, M.S. Bioreducible exosomes encapsulating glycolysis inhibitors potentiate mitochondria-targeted sonodynamic cancer therapy via cancer-targeted drug release and cellular energy depletion. *Biomaterials* **2023**, *301*, 122242. [\[CrossRef\]](#)
95. Wu, S.; Yun, J.; Tang, W.; Familiari, G.; Relucanti, M.; Wu, J.; Li, X.; Chen, H.; Chen, R. Therapeutic m6A Eraser ALKBH5 mRNA-Loaded Exosome-Liposome Hybrid Nanoparticles Inhibit Progression of Colorectal Cancer in Preclinical Tumor Models. *ACS Nano* **2023**, *17*, 11838–11854. [\[CrossRef\]](#)
96. Mikamori, M.; Yamada, D.; Eguchi, H.; Hasegawa, S.; Kishimoto, T.; Tomimaru, Y.; Asaoka, T.; Noda, T.; Wada, H.; Kawamoto, K.; et al. MicroRNA-155 Controls Exosome Synthesis and Promotes Gemcitabine Resistance in Pancreatic Ductal Adenocarcinoma. *Sci. Rep.* **2017**, *7*, 42339. [\[CrossRef\]](#)
97. Gu, Y.Y.; Yu, J.; Zhang, J.F.; Wang, C. Suppressing the secretion of exosomal miR-19b by gw4869 could regulate oxaliplatin sensitivity in colorectal cancer. *Neoplasma* **2019**, *66*, 39–45. [\[CrossRef\]](#)
98. Zhang, Y.; Tan, X.; Lu, Y. Exosomal transfer of circ_0006174 contributes to the chemoresistance of doxorubicin in colorectal cancer by depending on the miR-1205/CCND2 axis. *J. Physiol. Biochem.* **2022**, *78*, 39–50. [\[CrossRef\]](#)
99. Qiao, X.X.; Shi, H.B.; Xiao, L. Serum exosomal hsa-circ-0004771 modulates the resistance of colorectal cancer to 5-fluorouracil via regulating miR-653/ZEB2 signaling pathway. *Cancer Cell Int.* **2023**, *23*, 243. [\[CrossRef\]](#)
100. Zhao, K.; Cheng, X.; Ye, Z.; Li, Y.; Peng, W.; Wu, Y.; Xing, C. Exosome-Mediated Transfer of circ_0000338 Enhances 5-Fluorouracil Resistance in Colorectal Cancer through Regulating MicroRNA 217 (miR-217) and miR-485-3p. *Mol. Cell. Biol.* **2021**, *41*, e00517–20. [\[CrossRef\]](#)
101. Ning, T.; Li, J.; He, Y.; Zhang, H.; Wang, X.; Deng, T.; Liu, R.; Li, H.; Bai, M.; Fan, Q.; et al. Exosomal miR-208b related with oxaliplatin resistance promotes Treg expansion in colorectal cancer. *Mol. Ther.* **2021**, *29*, 2723–2736. [\[CrossRef\]](#)
102. Xu, Y.; Qiu, A.; Peng, F.; Tan, X.; Wang, J.; Gong, X. Exosomal transfer of circular RNA FBXW7 ameliorates the chemoresistance to oxaliplatin in colorectal cancer by sponging miR-18b-5p. *Neoplasma* **2021**, *68*, 108–118. [\[CrossRef\]](#)
103. Li, L.; He, D.; Guo, Q.; Zhang, Z.; Ru, D.; Wang, L.; Gong, K.; Liu, F.; Duan, Y.; Li, H. Exosome-liposome hybrid nanoparticle codelivery of TP and miR497 conspicuously overcomes chemoresistant ovarian cancer. *J. Nanobiotechnol.* **2022**, *20*, 50. [\[CrossRef\]](#)
104. Yin, J.; Huang, H.Y.; Long, Y.; Ma, Y.; Kamalibaike, M.; Dawuti, R.; Li, L. circ_C20orf11 enhances DDP resistance by inhibiting miR-527/YWHAZ through the promotion of extracellular vesicle-mediated macrophage M2 polarization in ovarian cancer. *Cancer Biol. Ther.* **2021**, *22*, 440–454. [\[CrossRef\]](#)
105. Liu, H.; Deng, S.; Yao, X.; Liu, Y.; Qian, L.; Wang, Y.; Zhang, T.; Shan, G.; Chen, L.; Zhou, Y. Ascites exosomal lncRNA PLADE enhances platinum sensitivity by inducing R-loops in ovarian cancer. *Oncogene* **2024**, *43*, 714–728. [\[CrossRef\]](#)
106. Hao, X.; Zhang, Y.; Shi, X.; Liu, H.; Zheng, Z.; Han, G.; Rong, D.; Zhang, C.; Tang, W.; Wang, X. CircPAK1 promotes the progression of hepatocellular carcinoma via modulation of YAP nucleus localization by interacting with 14-3-3 ζ . *J. Exp. Clin. Cancer Res. CR* **2022**, *41*, 281. [\[CrossRef\]](#)
107. Xu, J.; Ji, L.; Liang, Y.; Wan, Z.; Zheng, W.; Song, X.; Gorshkov, K.; Sun, Q.; Lin, H.; Zheng, X.; et al. CircRNA-SORE mediates sorafenib resistance in hepatocellular carcinoma by stabilizing YBX1. *Signal Transduct. Target. Ther.* **2020**, *5*, 298. [\[CrossRef\]](#)
108. Gao, Y.; Yin, Z.; Qi, Y.; Peng, H.; Ma, W.; Wang, R.; Li, W. Golgi phosphoprotein 3 promotes angiogenesis and sorafenib resistance in hepatocellular carcinoma via upregulating exosomal miR-494-3p. *Cancer Cell Int.* **2022**, *22*, 35. [\[CrossRef\]](#)
109. Wu, J.; Zhang, Y.; Li, X.; Ren, J.; Chen, L.; Chen, J.; Cao, Y. Exosomes from bone marrow mesenchymal stem cells decrease chemosensitivity of acute myeloid leukemia cells via delivering miR-10a. *Biochem. Biophys. Res. Commun.* **2022**, *622*, 149–156. [\[CrossRef\]](#)
110. Kou, R.; Li, T.; Fu, C.; Jiang, D.; Wang, Y.; Meng, J.; Zhong, R.; Liang, C.; Dong, M. Exosome-shuttled FTO from BM-MSCs contributes to cancer malignancy and chemoresistance in acute myeloid leukemia by inducing m6A-demethylation: A nano-based investigation. *Environ. Res.* **2024**, *244*, 117783. [\[CrossRef\]](#)
111. Liu, X.; Guo, Q.; Gao, G.; Cao, Z.; Guan, Z.; Jia, B.; Wang, W.; Zhang, K.; Zhang, W.; Wang, S.; et al. Exosome-transmitted circCABIN1 promotes temozolomide resistance in glioblastoma via sustaining ErbB downstream signaling. *J. Nanobiotechnol.* **2023**, *21*, 45. [\[CrossRef\]](#)

112. Yang, Z.J.; Zhang, L.L.; Bi, Q.C.; Gan, L.J.; Wei, M.J.; Hong, T.; Tan, R.J.; Lan, X.M.; Liu, L.H.; Han, X.J.; et al. Exosomal connexin 43 regulates the resistance of glioma cells to temozolomide. *Oncol. Rep.* **2021**, *45*, 44. [\[CrossRef\]](#)
113. Wan, X.; Xie, B.; Sun, H.; Gu, W.; Wang, C.; Deng, Q.; Zhou, S. Exosomes derived from M2 type tumor-associated macrophages promote osimertinib resistance in non-small cell lung cancer through MSTRG.292666.16-miR-6836-5p-MAPK8IP3 axis. *Cancer Cell Int.* **2022**, *22*, 83. [\[CrossRef\]](#)
114. Yang, B.; Teng, F.; Chang, L.; Wang, J.; Liu, D.L.; Cui, Y.S.; Li, G.H. Tumor-derived exosomal circRNA_102481 contributes to EGFR-TKIs resistance via the miR-30a-5p/ROR1 axis in non-small cell lung cancer. *Aging* **2021**, *13*, 13264–13286. [\[CrossRef\]](#)
115. Wei, F.; Ma, C.; Zhou, T.; Dong, X.; Luo, Q.; Geng, L.; Ding, L.; Zhang, Y.; Zhang, L.; Li, N.; et al. Correction to: Exosomes derived from gemcitabine resistant cells transfer malignant phenotypic traits via delivery of miRNA-222-3p. *Mol. Cancer* **2021**, *20*, 35. [\[CrossRef\]](#)
116. Song, Z.; Jia, G.; Ma, P.; Cang, S. Exosomal miR-4443 promotes cisplatin resistance in non-small cell lung carcinoma by regulating FSP1 m6A modification-mediated ferroptosis. *Life Sci.* **2021**, *276*, 119399. [\[CrossRef\]](#)
117. Gu, G.; Hu, C.; Hui, K.; Zhang, H.; Chen, T.; Zhang, X.; Jiang, X. Exosomal miR-136-5p Derived from Anlotinib-Resistant NSCLC Cells Confers Anlotinib Resistance in Non-Small Cell Lung Cancer Through Targeting PPP2R2A. *Int. J. Nanomed.* **2021**, *16*, 6329–6343. [\[CrossRef\]](#)
118. Shi, Q.; Ji, T.; Ma, Z.; Tan, Q.; Liang, J. Serum Exosomes-Based Biomarker circ_0008928 Regulates Cisplatin Sensitivity, Tumor Progression, and Glycolysis Metabolism by miR-488/HK2 Axis in Cisplatin-Resistant Nonsmall Cell Lung Carcinoma. *Cancer Biother. Radiopharm.* **2023**, *38*, 558–571. [\[CrossRef\]](#)
119. Liu, S.; Wang, W.; Ning, Y.; Zheng, H.; Zhan, Y.; Wang, H.; Yang, Y.; Luo, J.; Wen, Q.; Zang, H.; et al. Exosome-mediated miR-7-5p delivery enhances the anticancer effect of Everolimus via blocking MNK/eIF4E axis in non-small cell lung cancer. *Cell Death Dis.* **2022**, *13*, 129. [\[CrossRef\]](#)
120. Chen, R.; Qian, Z.; Xu, X.; Zhang, C.; Niu, Y.; Wang, Z.; Sun, J.; Zhang, X.; Yu, Y. Exosomes-transmitted miR-7 reverses gefitinib resistance by targeting YAP in non-small-cell lung cancer. *Pharmacol. Res.* **2021**, *165*, 105442. [\[CrossRef\]](#)
121. Hisakane, K.; Seike, M.; Sugano, T.; Yoshikawa, A.; Matsuda, K.; Takano, N.; Takahashi, S.; Noro, R.; Gemma, A. Exosome-derived miR-210 involved in resistance to osimertinib and epithelial-mesenchymal transition in EGFR mutant non-small cell lung cancer cells. *Thoracic. Cancer* **2021**, *12*, 1690–1698. [\[CrossRef\]](#)
122. Li, M.; Shan, W.; Hua, Y.; Chao, F.; Cui, Y.; Lv, L.; Dou, X.; Bian, X.; Zou, J.; Li, H.; et al. Exosomal miR-92b-3p Promotes Chemoresistance of Small Cell Lung Cancer Through the PTEN/AKT Pathway. *Front. Cell Dev. Biol.* **2021**, *9*, 661602. [\[CrossRef\]](#) [\[PubMed\]](#)
123. Zhu, X.; Shen, H.; Yin, X.; Yang, M.; Wei, H.; Chen, Q.; Feng, F.; Liu, Y.; Xu, W.; Li, Y. Macrophages derived exosomes deliver miR-223 to epithelial ovarian cancer cells to elicit a chemoresistant phenotype. *J. Exp. Clin. Cancer Res. CR* **2019**, *38*, 81. [\[CrossRef\]](#)
124. Au Yeung, C.L.; Co, N.N.; Tsuruga, T.; Yeung, T.L.; Kwan, S.Y.; Leung, C.S.; Li, Y.; Lu, E.S.; Kwan, K.; Wong, K.K.; et al. Exosomal transfer of stroma-derived miR21 confers paclitaxel resistance in ovarian cancer cells through targeting APAF1. *Nat. Commun.* **2016**, *7*, 11150. [\[CrossRef\]](#)
125. Zang, R.; Qiu, X.; Song, Y.; Wang, Y. Exosomes Mediated Transfer of Circ_0000337 Contributes to Cisplatin (CDDP) Resistance of Esophageal Cancer by Regulating JAK2 via miR-377-3p. *Front. Cell Dev. Biol.* **2021**, *9*, 673237. [\[CrossRef\]](#)
126. Wang, H.; Qi, Y.; Lan, Z.; Liu, Q.; Xu, J.; Zhu, M.; Yang, T.; Shi, R.; Gao, S.; Liang, G. Exosomal PD-L1 confers chemoresistance and promotes tumorigenic properties in esophageal cancer cells via upregulating STAT3/miR-21. *Gene Ther.* **2023**, *30*, 88–100. [\[CrossRef\]](#)
127. Yu, Z.; Tang, H.; Chen, S.; Xie, Y.; Shi, L.; Xia, S.; Jiang, M.; Li, J.; Chen, D. Exosomal LOC85009 inhibits docetaxel resistance in lung adenocarcinoma through regulating ATG5-induced autophagy. *Drug Resist. Updates* **2023**, *67*, 100915. [\[CrossRef\]](#) [\[PubMed\]](#)
128. Li, J.; Hu, C.; Chao, H.; Zhang, Y.; Li, Y.; Hou, J.; Huang, L. Exosomal transfer of miR-106a-5p contributes to cisplatin resistance and tumorigenesis in nasopharyngeal carcinoma. *J. Cell. Mol. Med.* **2021**, *25*, 9183–9198. [\[CrossRef\]](#)
129. Yuan, F.; Zhou, Z.F. Exosomes derived from Taxol-resistant nasopharyngeal carcinoma (NPC) cells transferred DDX53 to NPC cells and promoted cancer resistance to Taxol. *Eur. Rev. Med. Pharmacol. Sci.* **2021**, *25*, 127–138.
130. Ai, J.; Tan, G.; Li, W.; Liu, H.; Li, T.; Zhang, G.; Zhou, Z.; Gan, Y. Exosomes loaded with circPARD3 promotes EBV-miR-BART4-induced stemness and cisplatin resistance in nasopharyngeal carcinoma side population cells through the miR-579-3p/SIRT1/SSRP1 axis. *Cell Biol. Toxicol.* **2023**, *39*, 537–556. [\[CrossRef\]](#)
131. Li, C.; Gao, Z.; Cui, Z.; Liu, Z.; Bian, Y.; Sun, H.; Wang, N.; He, Z.; Li, B.; Li, F.; et al. Deubiquitylation of Rab35 by USP32 promotes the transmission of imatinib resistance by enhancing exosome secretion in gastrointestinal stromal tumours. *Oncogene* **2023**, *42*, 894–910. [\[CrossRef\]](#)
132. Jiang, X.; Xu, Y.; Liu, R.; Guo, S. Exosomal lincROR Promotes Docetaxel Resistance in Prostate Cancer through a β -catenin/HIF1 α Positive Feedback Loop. *Mol. Cancer Res.* **2023**, *21*, 472–482. [\[CrossRef\]](#)
133. Liu, J.; Zhu, S.; Tang, W.; Huang, Q.; Mei, Y.; Yang, H. Correction to: Exosomes from tamoxifen-resistant breast cancer cells transmit drug resistance partly by delivering miR-9-5p. *Cancer Cell Int.* **2021**, *21*, 673. [\[CrossRef\]](#)

134. Yang, Q.; Zhao, S.; Shi, Z.; Cao, L.; Liu, J.; Pan, T.; Zhou, D.; Zhang, J. Chemotherapy-elicited exosomal miR-378a-3p and miR-378d promote breast cancer stemness and chemoresistance via the activation of EZH2/STAT3 signaling. *J. Exp. Clin. Cancer Res. CR* **2021**, *40*, 120. [\[CrossRef\]](#)
135. Li, Y.; Liang, Y.; Sang, Y.; Song, X.; Zhang, H.; Liu, Y.; Jiang, L.; Yang, Q. MiR-770 suppresses the chemo-resistance and metastasis of triple negative breast cancer via direct targeting of STMN1. *Cell Death Dis.* **2018**, *9*, 14. [\[CrossRef\]](#)
136. Ma, J.; Chen, C.; Fan, Z.; Zhang, Y.; Ji, J.; Wei, D.; Zhang, F.; Sun, B.; Huang, P.; Ren, L. CircEGFR reduces the sensitivity of pirarubicin and regulates the malignant progression of triple-negative breast cancer via the miR-1299/EGFR axis. *Int. J. Biol. Macromol.* **2023**, *244*, 125295. [\[CrossRef\]](#)
137. Ou, B.; Liu, Y.; Gao, Z.; Xu, J.; Yan, Y.; Li, Y.; Zhang, J. Senescent neutrophils-derived exosomal piRNA-17560 promotes chemoresistance and EMT of breast cancer via FTO-mediated m6A demethylation. *Cell Death Dis.* **2022**, *13*, 905. [\[CrossRef\]](#)
138. Guo, Z.; Guo, A.; Zhou, C. Breast Cancer Stem Cell-Derived ANXA6-Containing Exosomes Sustain Paclitaxel Resistance and Cancer Aggressiveness in Breast Cancer. *Front. Cell Dev. Biol.* **2021**, *9*, 718721. [\[CrossRef\]](#)
139. Gao, F.; Xu, Q.; Tang, Z.; Zhang, N.; Huang, Y.; Li, Z.; Dai, Y.; Yu, Q.; Zhu, J. Exosomes derived from myeloid-derived suppressor cells facilitate castration-resistant prostate cancer progression via S100A9/circMID1/miR-506-3p/MID1. *J. Transl. Med.* **2022**, *20*, 346. [\[CrossRef\]](#)
140. Sun, M.Y.; Xu, B.; Wu, Q.X.; Chen, W.L.; Cai, S.; Zhang, H.; Tang, Q.F. Cisplatin-Resistant Gastric Cancer Cells Promote the Chemoresistance of Cisplatin-Sensitive Cells via the Exosomal RPS3-Mediated PI3K-Akt-Cofilin-1 Signaling Axis. *Front. Cell Dev. Biol.* **2021**, *9*, 618899. [\[CrossRef\]](#)
141. Liu, X.; Lu, Y.; Xu, Y.; Hou, S.; Huang, J.; Wang, B.; Zhao, J.; Xia, S.; Fan, S.; Yu, X.; et al. Exosomal transfer of miR-501 confers doxorubicin resistance and tumorigenesis via targeting of BLID in gastric cancer. *Cancer Lett.* **2019**, *459*, 122–134. [\[CrossRef\]](#)
142. Jiang, L.; Zhang, Y.; Guo, L.; Liu, C.; Wang, P.; Ren, W. Exosomal microRNA-107 reverses chemotherapeutic drug resistance of gastric cancer cells through HMGA2/mTOR/P-gp pathway. *BMC Cancer* **2021**, *21*, 1290. [\[CrossRef\]](#)
143. Ji, R.; Zhang, X.; Gu, H.; Ma, J.; Wen, X.; Zhou, J.; Qian, H.; Xu, W.; Qian, J.; Lin, J. miR-374a-5p: A New Target for Diagnosis and Drug Resistance Therapy in Gastric Cancer. *Mol. Ther. Nucleic Acids* **2019**, *18*, 320–331. [\[CrossRef\]](#)
144. Liu, C.; Zhao, Z.; Guo, S.; Zhang, L.; Fan, X.; Zheng, J. Exosomal miR-27a-3p derived from tumor-associated macrophage suppresses propranolol sensitivity in infantile hemangioma. *Cell. Immunol.* **2021**, *370*, 104442. [\[CrossRef\]](#)
145. Wang, H.; Wang, L.; Pan, H.; Wang, Y.; Shi, M.; Yu, H.; Wang, C.; Pan, X.; Chen, Z. Exosomes Derived From Macrophages Enhance Aerobic Glycolysis and Chemoresistance in Lung Cancer by Stabilizing c-Myc via the Inhibition of NEDD4L. *Front. Cell Dev. Biol.* **2020**, *8*, 620603. [\[CrossRef\]](#)
146. Qin, L.; Zhan, Z.; Wei, C.; Li, X.; Zhang, T.; Li, J. Hsa-circRNA-G004213 promotes cisplatin sensitivity by regulating miR-513b-5p/PRPF39 in liver cancer. *Mol. Med. Rep.* **2021**, *23*, 421. [\[CrossRef\]](#)
147. Zhu, T.; Hu, Z.; Wang, Z.; Ding, H.; Li, R.; Wang, J.; Wang, G. microRNA-301b-3p from mesenchymal stem cells-derived extracellular vesicles inhibits TXNIP to promote multidrug resistance of gastric cancer cells. *Cell Biol. Toxicol.* **2023**, *39*, 1923–1937. [\[CrossRef\]](#)
148. Luo, T.; Liu, Q.; Tan, A.; Duan, L.; Jia, Y.; Nong, L.; Tang, J.; Zhou, W.; Xie, W.; Lu, Y.; et al. Mesenchymal Stem Cell-Secreted Exosome Promotes Chemoresistance in Breast Cancer via Enhancing miR-21-5p-Mediated S100A6 Expression. *Mol. Ther. Oncolytics* **2020**, *19*, 283–293. [\[CrossRef\]](#)
149. Pan, Y.; Lu, X.; Shu, G.; Cen, J.; Lu, J.; Zhou, M.; Huang, K.; Dong, J.; Li, J.; Lin, H.; et al. Extracellular Vesicle-Mediated Transfer of LncRNA IGFL2-AS1 Confers Sunitinib Resistance in Renal Cell Carcinoma. *Cancer Res.* **2023**, *83*, 103–116. [\[CrossRef\]](#)
150. Qu, L.; Ding, J.; Chen, C.; Wu, Z.J.; Liu, B.; Gao, Y.; Chen, W.; Liu, F.; Sun, W.; Li, X.F.; et al. Exosome-Transmitted lncARSR Promotes Sunitinib Resistance in Renal Cancer by Acting as a Competing Endogenous RNA. *Cancer Cell* **2016**, *29*, 653–668. [\[CrossRef\]](#)
151. Zhao, Q.; Huang, L.; Qin, G.; Qiao, Y.; Ren, F.; Shen, C.; Wang, S.; Liu, S.; Lian, J.; Wang, D.; et al. Cancer-associated fibroblasts induce monocytic myeloid-derived suppressor cell generation via IL-6/exosomal miR-21-activated STAT3 signaling to promote cisplatin resistance in esophageal squamous cell carcinoma. *Cancer Lett.* **2021**, *518*, 35–48. [\[CrossRef\]](#)
152. Zou, Y.; Zhao, Z.; Wang, J.; Ma, L.; Liu, Y.; Sun, L.; Song, Y. Extracellular vesicles carrying miR-6836 derived from resistant tumor cells transfer cisplatin resistance of epithelial ovarian cancer via DLG2-YAP1 signaling pathway. *Int. J. Biol. Sci.* **2023**, *19*, 3099–3114. [\[CrossRef\]](#)
153. Yang, Z.; Zhao, N.; Cui, J.; Wu, H.; Xiong, J.; Peng, T. Exosomes derived from cancer stem cells of gemcitabine-resistant pancreatic cancer cells enhance drug resistance by delivering miR-210. *Cell. Oncol.* **2020**, *43*, 123–136. [\[CrossRef\]](#)
154. Hrdinova, T.; Toman, O.; Dresler, J.; Klimentova, J.; Salovska, B.; Pajer, P.; Bartos, O.; Polivkova, V.; Linhartova, J.; Machova Polakova, K.; et al. Exosomes released by imatinib-resistant K562 cells contain specific membrane markers, IFITM3, CD146 and CD36 and increase the survival of imatinib-sensitive cells in the presence of imatinib. *Int. J. Oncol.* **2021**, *58*, 238–250. [\[CrossRef\]](#)

155. Li, S.; Shi, Z.; Fu, S.; Li, Q.; Li, B.; Sang, L.; Wu, D. Exosomal-mediated transfer of APCDD1L-AS1 induces 5-fluorouracil resistance in oral squamous cell carcinoma via miR-1224-5p/nuclear receptor binding SET domain protein 2 (NSD2) axis. *Bioengineered* **2021**, *12*, 7188–7204. [\[CrossRef\]](#)
156. Wei, Q.T.; Liu, B.Y.; Ji, H.Y.; Lan, Y.F.; Tang, W.H.; Zhou, J.; Zhong, X.Y.; Lian, C.L.; Huang, Q.Z.; Wang, C.Y.; et al. Exosome-mediated transfer of MIF confers temozolomide resistance by regulating TIMP3/PI3K/AKT axis in gliomas. *Mol. Ther. Oncolytics* **2021**, *22*, 114–128. [\[CrossRef\]](#)
157. Geng, X.; Zhang, Y.; Lin, X.; Zeng, Z.; Hu, J.; Hao, L.; Xu, J.; Wang, X.; Wang, H.; Li, Q. Exosomal circWDR62 promotes temozolomide resistance and malignant progression through regulation of the miR-370-3p/MGMT axis in glioma. *Cell Death Dis.* **2022**, *13*, 596. [\[CrossRef\]](#)
158. Ding, C.; Yi, X.; Chen, X.; Wu, Z.; You, H.; Chen, X.; Zhang, G.; Sun, Y.; Bu, X.; Wu, X.; et al. Warburg effect-promoted exosomal circ_0072083 releasing up-regulates NANO expression through multiple pathways and enhances temozolomide resistance in glioma. *J. Exp. Clin. Cancer Res. CR* **2021**, *40*, 164. [\[CrossRef\]](#)
159. Liu, X.; Liu, L.; Wu, A.; Huang, S.; Xu, Z.; Zhang, X.; Li, Z.; Li, H.; Dong, J. Transformed astrocytes confer temozolomide resistance on glioblastoma via delivering ALKBH7 to enhance APNG expression after educating by glioblastoma stem cells-derived exosomes. *CNS Neurosci. Ther.* **2024**, *30*, e14599. [\[CrossRef\]](#)
160. Pan, Y.; Lin, Y.; Mi, C. Cisplatin-resistant osteosarcoma cell-derived exosomes confer cisplatin resistance to recipient cells in an exosomal circ_103801-dependent manner. *Cell Biol. Int.* **2021**, *45*, 858–868. [\[CrossRef\]](#)
161. Guo, Y.; Wu, H.; Xiong, J.; Gou, S.; Cui, J.; Peng, T. miR-222-3p-containing macrophage-derived extracellular vesicles confer gemcitabine resistance via TSC1-mediated mTOR/AKT/PI3K pathway in pancreatic cancer. *Cell Biol. Toxicol.* **2023**, *39*, 1203–1214. [\[CrossRef\]](#)
162. Zhu, S.; Mao, J.; Zhang, X.; Wang, P.; Zhou, Y.; Tong, J.; Peng, H.; Yang, B.; Fu, Q. CAF-derived exosomal lncRNA FAL1 promotes chemoresistance to oxaliplatin by regulating autophagy in colorectal cancer. *Dig. Liver Dis.* **2023**, *56*, 330–342. [\[CrossRef\]](#)
163. Hu, J.H.; Tang, H.N.; Wang, Y.H. Cancer-associated fibroblast exosome LINC00355 promotes epithelial-mesenchymal transition and chemoresistance in colorectal cancer through the miR-34b-5p/CRKL axis. *Cancer Gene Ther.* **2024**, *31*, 259–272. [\[CrossRef\]](#)
164. Kunou, S.; Shimada, K.; Takai, M.; Sakamoto, A.; Aoki, T.; Hikita, T.; Kagaya, Y.; Iwamoto, E.; Sanada, M.; Shimada, S.; et al. Exosomes secreted from cancer-associated fibroblasts elicit anti-pyrimidine drug resistance through modulation of its transporter in malignant lymphoma. *Oncogene* **2021**, *40*, 3989–4003. [\[CrossRef\]](#)
165. Gao, Q.; Fang, X.; Chen, Y.; Li, Z.; Wang, M. Exosomal lncRNA UCA1 from cancer-associated fibroblasts enhances chemoresistance in vulvar squamous cell carcinoma cells. *J. Obstet. Gynaecol. Res.* **2021**, *47*, 73–87. [\[CrossRef\]](#)
166. Zhang, T.; Zhang, P.; Li, H.X. CAFs-Derived Exosomal miRNA-130a Confers Cisplatin Resistance of NSCLC Cells Through PUM2-Dependent Packaging. *Int. J. Nanomed.* **2021**, *16*, 561–577. [\[CrossRef\]](#) [\[PubMed\]](#)
167. Shi, L.; Zhu, W.; Huang, Y.; Zhuo, L.; Wang, S.; Chen, S.; Zhang, B.; Ke, B. Cancer-associated fibroblast-derived exosomal microRNA-20a suppresses the PTEN/PI3K-AKT pathway to promote the progression and chemoresistance of non-small cell lung cancer. *Clin. Transl. Med.* **2022**, *12*, e989. [\[CrossRef\]](#)
168. Zhang, H.W.; Shi, Y.; Liu, J.B.; Wang, H.M.; Wang, P.Y.; Wu, Z.J.; Li, L.; Gu, L.P.; Cao, P.S.; Wang, G.R.; et al. Cancer-associated fibroblast-derived exosomal microRNA-24-3p enhances colon cancer cell resistance to MTX by down-regulating CDX2/HEPH axis. *J. Cell. Mol. Med.* **2021**, *25*, 3699–3713. [\[CrossRef\]](#)
169. Luo, G.; Zhang, Y.; Wu, Z.; Zhang, L.; Liang, C.; Chen, X. Exosomal LINC00355 derived from cancer-associated fibroblasts promotes bladder cancer cell resistance to cisplatin by regulating miR-34b-5p/ABCB1 axis. *Acta Biochim. Biophys. Sin.* **2021**, *53*, 558–566. [\[CrossRef\]](#) [\[PubMed\]](#)
170. Shan, G.; Zhou, X.; Gu, J.; Zhou, D.; Cheng, W.; Wu, H.; Wang, Y.; Tang, T.; Wang, X. Correction to: Downregulated exosomal microRNA-148b-3p in cancer associated fibroblasts enhance chemosensitivity of bladder cancer cells by downregulating the Wnt/ β -catenin pathway and upregulating PTEN. *Cell Oncol.* **2021**, *44*, 959. [\[CrossRef\]](#) [\[PubMed\]](#)
171. Qu, X.; Liu, B.; Wang, L.; Liu, L.; Zhao, W.; Liu, C.; Ding, J.; Zhao, S.; Xu, B.; Yu, H.; et al. Loss of cancer-associated fibroblast-derived exosomal DACT3-AS1 promotes malignant transformation and ferroptosis-mediated oxaliplatin resistance in gastric cancer. *Drug Resist. Updates* **2023**, *68*, 100936. [\[CrossRef\]](#)
172. Sun, L.; Ke, M.; Yin, M.; Zeng, Y.; Ji, Y.; Hu, Y.; Fu, S.; Zhang, C. Extracellular vesicle-encapsulated microRNA-296-3p from cancer-associated fibroblasts promotes ovarian cancer development through regulation of the PTEN/AKT and SOCS6/STAT3 pathways. *Cancer Sci.* **2024**, *115*, 155–169. [\[CrossRef\]](#)
173. Kang, S.H.; Oh, S.Y.; Lee, K.Y.; Lee, H.J.; Kim, M.S.; Kwon, T.G.; Kim, J.W.; Lee, S.T.; Choi, S.Y.; Hong, S.H. Differential effect of cancer-associated fibroblast-derived extracellular vesicles on cisplatin resistance in oral squamous cell carcinoma via miR-876-3p. *Theranostics* **2024**, *14*, 460–479. [\[CrossRef\]](#)
174. Qi, R.; Bai, Y.; Li, K.; Liu, N.; Xu, Y.; Dal, E.; Wang, Y.; Lin, R.; Wang, H.; Liu, Z.; et al. Cancer-associated fibroblasts suppress ferroptosis and induce gemcitabine resistance in pancreatic cancer cells by secreting exosome-derived ACSL4-targeting miRNAs. *Drug Resist. Updates* **2023**, *68*, 100960. [\[CrossRef\]](#)

175. Zheng, S.; Tian, Q.; Yuan, Y.; Sun, S.; Li, T.; Xia, R.; He, R.; Luo, Y.; Lin, Q.; Fu, Z.; et al. Extracellular vesicle-packaged circBIRC6 from cancer-associated fibroblasts induce platinum resistance via SUMOylation modulation in pancreatic cancer. *J. Exp. Clin. Cancer Res.* **2023**, *42*, 324. [\[CrossRef\]](#)
176. Cui, Y.; Zhang, S.; Hu, X.; Gao, F. Tumor-associated fibroblasts derived exosomes induce the proliferation and cisplatin resistance in esophageal squamous cell carcinoma cells through RIG-I/IFN- β signaling. *Bioengineered* **2022**, *13*, 12462–12474. [\[CrossRef\]](#)
177. Deng, K.; Zou, F.; Xu, J.; Xu, D.; Luo, Z. Cancer-associated fibroblasts promote stemness maintenance and gemcitabine resistance via HIF-1 α /miR-21 axis under hypoxic conditions in pancreatic cancer. *Mol. Carcinog.* **2024**, *63*, 524–537. [\[CrossRef\]](#)
178. Tao, S.; Wang, J.; Li, F.; Shi, B.; Ren, Q.; Zhuang, Y.; Qian, X. Extracellular vesicles released by hypoxia-induced tumor-associated fibroblasts impart chemoresistance to breast cancer cells via long noncoding RNA H19 delivery. *Faseb J.* **2024**, *38*, e23165. [\[CrossRef\]](#)
179. Wang, X.; Zhang, H.; Chen, X. Drug resistance and combating drug resistance in cancer. *Cancer Drug Resist.* **2019**, *2*, 141–160. [\[CrossRef\]](#)
180. Giddings, E.L.; Champagne, D.P.; Wu, M.H.; Laffin, J.M.; Thornton, T.M.; Valenca-Pereira, F.; Culp-Hill, R.; Fortner, K.A.; Romero, N.; East, J.; et al. Mitochondrial ATP fuels ABC transporter-mediated drug efflux in cancer chemoresistance. *Nat. Commun.* **2021**, *12*, 2804. [\[CrossRef\]](#)
181. Frank, N.Y.; Margaryan, A.; Huang, Y.; Schatton, T.; Waaga-Gasser, A.M.; Gasser, M.; Sayegh, M.H.; Sadee, W.; Frank, M.H. ABCB5-mediated doxorubicin transport and chemoresistance in human malignant melanoma. *Cancer Res.* **2005**, *65*, 4320–4333. [\[CrossRef\]](#)
182. Yang, C.; Yuan, H.; Gu, J.; Xu, D.; Wang, M.; Qiao, J.; Yang, X.; Zhang, J.; Yao, M.; Gu, J.; et al. ABCA8-mediated efflux of taurocholic acid contributes to gemcitabine insensitivity in human pancreatic cancer via the S1PR2-ERK pathway. *Cell Death Discov.* **2021**, *7*, 6. [\[CrossRef\]](#)
183. Wu, J.; Zhou, Z.; Li, J.; Liu, H.; Zhang, H.; Zhang, J.; Huang, W.; He, Y.; Zhu, S.; Huo, M.; et al. CHD4 promotes acquired chemoresistance and tumor progression by activating the MEK/ERK axis. *Drug Resist. Updates* **2023**, *66*, 100913. [\[CrossRef\]](#)
184. Khalaf, B.H.; Suleiman, A.A.; Suwaid, M.A. Exploring the Regulatory Roles of miR-21, miR-15, and miR-let-7 in ABC Transporter-Mediated Chemoresistance: Implications for Breast Cancer Etiology and Treatment. *Mol. Biotechnol.* **2023**, *67*, 149–159. [\[CrossRef\]](#)
185. Chen, Y.-F.; Luh, F.; Ho, Y.-S.; Yen, Y. Exosomes: A review of biologic function, diagnostic and targeted therapy applications, and clinical trials. *J. Biomed. Sci.* **2024**, *31*, 67. [\[CrossRef\]](#)
186. Meng, W.; Hao, Y.; He, C.; Li, L.; Zhu, G. Exosome-orchestrated hypoxic tumor microenvironment. *Mol. Cancer* **2019**, *18*, 57. [\[CrossRef\]](#)
187. Shedden, K.; Xie, X.T.; Chandaroy, P.; Chang, Y.T.; Rosania, G.R. Expulsion of small molecules in vesicles shed by cancer cells: Association with gene expression and chemosensitivity profiles. *Cancer Res.* **2003**, *63*, 4331–4337.
188. Peak, T.; Panigrahi, G.; Praharaj, P.; Chavez, J.; Chyr, J.; Singh, R.; Vander Griend, D.; Bitting, R.; Hemal, A.; Deep, G. PD65-01 do exosomes contribute to the development of enzalutamide-resistant prostate cancer? *J. Urol.* **2018**, *199*, e1224. [\[CrossRef\]](#)
189. Federici, C.; Petrucci, F.; Caimi, S.; Cesolini, A.; Logozzi, M.; Borghi, M.; D'Ilio, S.; Lugini, L.; Violante, N.; Azzarito, T.; et al. Exosome release and low pH belong to a framework of resistance of human melanoma cells to cisplatin. *PLoS ONE* **2014**, *9*, e88193. [\[CrossRef\]](#)
190. Li, R.; Dong, C.; Jiang, K.; Sun, R.; Zhou, Y.; Yin, Z.; Lv, J.; Zhang, J.; Wang, Q.; Wang, L. Rab27B enhances drug resistance in hepatocellular carcinoma by promoting exosome-mediated drug efflux. *Carcinogenesis* **2020**, *41*, 1583–1591. [\[CrossRef\]](#)
191. Wang, J.; Yeung, B.Z.; Wientjes, M.G.; Cui, M.; Peer, C.J.; Lu, Z.; Figg, W.D.; Woo, S.; Au, J.L. A Quantitative Pharmacology Model of Exosome-Mediated Drug Efflux and Perturbation-Induced Synergy. *Pharmaceutics* **2021**, *13*, 997. [\[CrossRef\]](#)
192. Koch, R.; Aung, T.; Vogel, D.; Chapuy, B.; Wenzel, D.; Becker, S.; Sinzig, U.; Venkataramani, V.; von Mach, T.; Jacob, R.; et al. Nuclear Trapping through Inhibition of Exosomal Export by Indomethacin Increases Cytostatic Efficacy of Doxorubicin and Pixantrone. *Clin. Cancer Res.* **2016**, *22*, 395–404. [\[CrossRef\]](#)
193. Mattioli, R.; Ilari, A.; Colotti, B.; Mosca, L.; Fazi, F.; Colotti, G. Doxorubicin and other anthracyclines in cancers: Activity, chemoresistance and its overcoming. *Mol. Aspects Med.* **2023**, *93*, 101205. [\[CrossRef\]](#)
194. Chapuy, B.; Koch, R.; Radunski, U.; Corsham, S.; Cheong, N.; Inagaki, N.; Ban, N.; Wenzel, D.; Reinhardt, D.; Zapf, A.; et al. Intracellular ABC transporter A3 confers multidrug resistance in leukemia cells by lysosomal drug sequestration. *Leukemia* **2008**, *22*, 1576–1586. [\[CrossRef\]](#)
195. Rees, D.C.; Johnson, E.; Lewinson, O. ABC transporters: The power to change. *Nat. Rev. Mol. Cell Biol.* **2009**, *10*, 218–227. [\[CrossRef\]](#)
196. Levchenko, A.; Mehta, B.M.; Niu, X.; Kang, G.; Villafania, L.; Way, D.; Polycarpe, D.; Sadelain, M.; Larson, S.M. Intercellular transfer of P-glycoprotein mediates acquired multidrug resistance in tumor cells. *Proc. Natl. Acad. Sci. USA* **2005**, *102*, 1933–1938. [\[CrossRef\]](#)
197. Bebawy, M.; Combes, V.; Lee, E.; Jaiswal, R.; Gong, J.; Bonhoure, A.; Grau, G.E. Membrane microparticles mediate transfer of P-glycoprotein to drug sensitive cancer cells. *Leukemia* **2009**, *23*, 1643–1649. [\[CrossRef\]](#)

198. Wang, X.; Xu, C.; Hua, Y.; Sun, L.; Cheng, K.; Jia, Z.; Han, Y.; Dong, J.; Cui, Y.; Yang, Z. Exosomes play an important role in the process of psoralen reverse multidrug resistance of breast cancer. *J. Exp. Clin. Cancer Res.* **2016**, *35*, 186. [\[CrossRef\]](#)
199. Pasquier, J.; Galas, L.; Boulangé-Lecomte, C.; Rioult, D.; Bultelle, F.; Magal, P.; Webb, G.; Le Foll, F. Different modalities of intercellular membrane exchanges mediate cell-to-cell p-glycoprotein transfers in MCF-7 breast cancer cells. *J. Biol. Chem.* **2012**, *287*, 7374–7387. [\[CrossRef\]](#)
200. Lu, J.F.; Luk, F.; Gong, J.; Jaiswal, R.; Grau, G.E.; Bebawy, M. Microparticles mediate MRP1 intercellular transfer and the re-templating of intrinsic resistance pathways. *Pharmacol. Res.* **2013**, *76*, 77–83. [\[CrossRef\]](#)
201. Kong, J.N.; He, Q.; Wang, G.; Dasgupta, S.; Dinkins, M.B.; Zhu, G.; Kim, A.; Spassieva, S.; Bieberich, E. Guggulsterone and bexarotene induce secretion of exosome-associated breast cancer resistance protein and reduce doxorubicin resistance in MDA-MB-231 cells. *Int. J. Cancer* **2015**, *137*, 1610–1620. [\[CrossRef\]](#)
202. Dong, X.; Bai, X.; Ni, J.; Zhang, H.; Duan, W.; Graham, P.; Li, Y. Exosomes and breast cancer drug resistance. *Cell Death Dis.* **2020**, *11*, 987. [\[CrossRef\]](#)
203. Wang, J.; Yeung, B.Z.; Cui, M.; Peer, C.J.; Lu, Z.; Figg, W.D.; Guillaume Wientjes, M.; Woo, S.; Au, J.L. Exosome is a mechanism of intercellular drug transfer: Application of quantitative pharmacology. *J. Control. Release* **2017**, *268*, 147–158. [\[CrossRef\]](#)
204. Debbi, L.; Guo, S.; Safina, D.; Levenberg, S. Boosting extracellular vesicle secretion. *Biotechnol. Adv.* **2022**, *59*, 107983. [\[CrossRef\]](#)
205. Aubertin, K.; Silva, A.K.; Luciani, N.; Espinosa, A.; Djemat, A.; Charue, D.; Gallet, F.; Blanc-Brude, O.; Wilhelm, C. Massive release of extracellular vesicles from cancer cells after photodynamic treatment or chemotherapy. *Sci. Rep.* **2016**, *6*, 35376. [\[CrossRef\]](#)
206. Dorayappan, K.D.P.; Wanner, R.A.; Wallbillich, J.J.; Saini, U.; Zingarelli, R.A.; Suárez, A.A.; Cohn, D.E.; Selvendiran, K. Hypoxia-induced exosomes contribute to a more aggressive and chemoresistant ovarian cancer phenotype: A novel mechanism linking STAT3/Rab proteins. *Oncogene* **2018**, *37*, 3806–3821. [\[CrossRef\]](#)
207. Khoo, X.H.; Paterson, I.C.; Goh, B.H.; Lee, W.L. Cisplatin-Resistance in Oral Squamous Cell Carcinoma: Regulation by Tumor Cell-Derived Extracellular Vesicles. *Cancers* **2019**, *11*, 1166. [\[CrossRef\]](#)
208. Hekmatirad, S.; Moloudizargari, M.; Moghadamnia, A.A.; Kazemi, S.; Mohammadnia-Afrouzi, M.; Baeeri, M.; Moradkhani, F.; Asghari, M.H. Inhibition of Exosome Release Sensitizes U937 Cells to PEGylated Liposomal Doxorubicin. *Front. Immunol.* **2021**, *12*, 692654. [\[CrossRef\]](#)
209. Yang, L.; Peng, X.; Li, Y.; Zhang, X.; Ma, Y.; Wu, C.; Fan, Q.; Wei, S.; Li, H.; Liu, J. Long non-coding RNA HOTAIR promotes exosome secretion by regulating RAB35 and SNAP23 in hepatocellular carcinoma. *Mol. Cancer* **2019**, *18*, 78. [\[CrossRef\]](#)
210. Qian, L.; Yang, X.; Li, S.; Zhao, H.; Gao, Y.; Zhao, S.; Lv, X.; Zhang, X.; Li, L.; Zhai, L.; et al. Reduced O-GlcNAcylation of SNAP-23 promotes cisplatin resistance by inducing exosome secretion in ovarian cancer. *Cell Death Discov.* **2021**, *7*, 112. [\[CrossRef\]](#)
211. Kirave, P.; Gondaliya, P.; Kulkarni, B.; Rawal, R.; Kalia, K. Exosome mediated miR-155 delivery confers cisplatin chemoresistance in oral cancer cells via epithelial-mesenchymal transition. *Oncotarget* **2020**, *11*, 1157–1171. [\[CrossRef\]](#)
212. Liang, G.; Zhu, Y.; Ali, D.J.; Tian, T.; Xu, H.; Si, K.; Sun, B.; Chen, B.; Xiao, Z. Engineered exosomes for targeted co-delivery of miR-21 inhibitor and chemotherapeutics to reverse drug resistance in colon cancer. *J. Nanobiotechnol.* **2020**, *18*, 10. [\[CrossRef\]](#)
213. Ohno, S.-i.; Takanashi, M.; Sudo, K.; Ueda, S.; Ishikawa, A.; Matsuyama, N.; Fujita, K.; Mizutani, T.; Ohgi, T.; Ochiya, T.; et al. Systemically Injected Exosomes Targeted to EGFR Deliver Antitumor MicroRNA to Breast Cancer Cells. *Mol. Ther.* **2013**, *21*, 185–191. [\[CrossRef\]](#)
214. Rezaei, R.; Baghaei, K.; Amani, D.; Piccin, A.; Hashemi, S.M.; Asadzadeh Aghdaei, H.; Zali, M.R. Exosome-mediated delivery of functionally active miRNA-375-3p mimic regulate epithelial mesenchymal transition (EMT) of colon cancer cells. *Life Sci.* **2021**, *269*, 119035. [\[CrossRef\]](#)
215. Kamekar, S.; LeBleu, V.S.; Sugimoto, H.; Yang, S.; Ruivo, C.F.; Melo, S.A.; Lee, J.J.; Kalluri, R. Exosomes facilitate therapeutic targeting of oncogenic KRAS in pancreatic cancer. *Nature* **2017**, *546*, 498–503. [\[CrossRef\]](#)
216. Li, H.; Yang, C.; Shi, Y.; Zhao, L. Exosomes derived from siRNA against GRP78 modified bone-marrow-derived mesenchymal stem cells suppress Sorafenib resistance in hepatocellular carcinoma. *J. Nanobiotechnol.* **2018**, *16*, 103. [\[CrossRef\]](#)
217. Zhang, Q.; Haiyang, Z.; Tao, N.; Dongying, L.; Ting, D.; Rui, L.; Ming, B.; Kegan, Z.; Jialu, L.; Qian, F.; et al. Exosome-Delivered c-Met siRNA Could Reverse Chemoresistance to Cisplatin in Gastric Cancer. *Int. J. Nanomed.* **2020**, *15*, 2323–2335. [\[CrossRef\]](#)
218. Lin, D.; Zhang, H.; Liu, R.; Deng, T.; Ning, T.; Bai, M.; Yang, Y.; Zhu, K.; Wang, J.; Duan, J.; et al. iRGD-modified exosomes effectively deliver CPT1A siRNA to colon cancer cells, reversing oxaliplatin resistance by regulating fatty acid oxidation. *Mol. Oncol.* **2021**, *15*, 3430–3446. [\[CrossRef\]](#)
219. Si, J.; Li, W.; Li, X.; Cao, L.; Chen, Z.; Jiang, Z. Heparanase confers temozolomide resistance by regulation of exosome secretion and circular RNA composition in glioma. *Cancer Sci.* **2021**, *112*, 3491–3506. [\[CrossRef\]](#)
220. Torreggiani, E.; Roncuzzi, L.; Perut, F.; Zini, N.; Baldini, N. Multimodal transfer of MDR by exosomes in human osteosarcoma. *Int. J. Oncol.* **2016**, *49*, 189–196. [\[CrossRef\]](#)
221. Noack, A.; Noack, S.; Buettner, M.; Naim, H.Y.; Löscher, W. Intercellular transfer of P-glycoprotein in human blood-brain barrier endothelial cells is increased by histone deacetylase inhibitors. *Sci. Rep.* **2016**, *6*, 29253. [\[CrossRef\]](#)

222. Lv, M.M.; Zhu, X.Y.; Chen, W.X.; Zhong, S.L.; Hu, Q.; Ma, T.F.; Zhang, J.; Chen, L.; Tang, J.H.; Zhao, J.H. Exosomes mediate drug resistance transfer in MCF-7 breast cancer cells and a probable mechanism is delivery of P-glycoprotein. *Tumour Biol.* **2014**, *35*, 10773–10779. [[CrossRef](#)]
223. Zhao, K.; Wang, Z.; Li, X.; Liu, J.L.; Tian, L.; Chen, J.Q. Exosome-mediated transfer of CLIC1 contributes to the vincristine-resistance in gastric cancer. *Mol. Cell. Biochem.* **2019**, *462*, 97–105. [[CrossRef](#)] [[PubMed](#)]
224. Corcoran, C.; Rani, S.; O'Brien, K.; O'Neill, A.; Principe, M.; Sheikh, R.; Webb, G.; McDermott, R.; Watson, W.; Crown, J.; et al. Docetaxel-resistance in prostate cancer: Evaluating associated phenotypic changes and potential for resistance transfer via exosomes. *PLoS ONE* **2012**, *7*, e50999. [[CrossRef](#)] [[PubMed](#)]
225. Del Re, M.; Bertolini, I.; Crucitta, S.; Fontanelli, L.; Rofi, E.; De Angelis, C.; Diodati, L.; Cavallero, D.; Gianfilippo, G.; Salvadori, B.; et al. Overexpression of TK1 and CDK9 in plasma-derived exosomes is associated with clinical resistance to CDK4/6 inhibitors in metastatic breast cancer patients. *Breast Cancer Res. Treat.* **2019**, *178*, 57–62. [[CrossRef](#)] [[PubMed](#)]
226. Pokharel, D.; Padula, M.P.; Lu, J.F.; Jaiswal, R.; Djordjevic, S.P.; Bebawy, M. The Role of CD44 and ERM Proteins in Expression and Functionality of P-glycoprotein in Breast Cancer Cells. *Molecules* **2016**, *21*, 290. [[CrossRef](#)]
227. Jaiswal, R.; Gong, J.; Sambasivam, S.; Combes, V.; Mathys, J.M.; Davey, R.; Grau, G.E.; Bebawy, M. Microparticle-associated nucleic acids mediate trait dominance in cancer. *Faseb J.* **2012**, *26*, 420–429. [[CrossRef](#)]
228. Ning, K.; Wang, T.; Sun, X.; Zhang, P.; Chen, Y.; Jin, J.; Hua, D. UCH-L1-containing exosomes mediate chemotherapeutic resistance transfer in breast cancer. *J. Surg. Oncol.* **2017**, *115*, 932–940. [[CrossRef](#)]
229. Zhang, Q.; Liu, R.-X.; Chan, K.-W.; Hu, J.; Zhang, J.; Wei, L.; Tan, H.; Yang, X.; Liu, H. Exosomal transfer of p-STAT3 promotes acquired 5-FU resistance in colorectal cancer cells. *J. Exp. Clin. Cancer Res.* **2019**, *38*, 320. [[CrossRef](#)]
230. Goler-Baron, V.; Assaraf, Y.G. Structure and function of ABCG2-rich extracellular vesicles mediating multidrug resistance. *PLoS ONE* **2011**, *6*, e16007. [[CrossRef](#)]

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