Review

Exosomes: The Elixir or the Trojan Horse Exosome Biologic Dual-Face

Armin Khosravipour , Mahna Mansoori , Hamideh Aboutalebi , Fahimeh Hashemi , Shayan Vafaei *

Posted Date: 25 February 2026

doi: 10.20944/preprints202602.1440.v1

Keywords: exosomes; extracellular vesicles; nano drug delivery; regenerative medicine; tumor microenvironment; neurodegenerative disease

 doi:10.20944/preprints202602.1440.v1

Review

Exosomes: The Elixir or the Trojan Horse Exosome Biologic Dual-Face

Armin Khosravipour [1], Mahna Mansoori [2], Hamideh Aboutalebi [3], Fahime Hashemi [4, 5] and Shayan Vafaei [6,*]

1. Department of Anatomy and Cell Biology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Department of Medicine, Medicine School, Islamic Azad University, Kerman Branch, Kerman, Iran
3. Department of Anatomy and Cell Biology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
4. Department of Nursing, Nursing and Midwifery School, Islamic Azad University, Kerman Branch, Kerman, Iran
5. Department of Nursing, Faculty of Nursing and Midwifery, Mashhad Medical Sciences, Islamic Azad University, Mashhad, Iran
6. Department of Anatomy and Cell Biology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

* Correspondence: Vafaeish@mums.ac.ir; Tel.: +989156168086

Abstract

Background: Exosomes are nanosized extracellular vesicles that range from 30 to 150 nm and have a bilayer lipid membrane which encapsulates proteins, lipids, and nucleic acids, first identified in the 1960s and expanded in application from disease diagnostics to targeted therapeutics. They are intercellular communicators with roles in physiological regulation and pathological progression. Results: Exosomes applications in gene therapy, drug delivery, tissue regeneration, and disease diagnostics activate signaling pathways such as Wnt/β-catenin, PI3K/Akt, etc., deliver anti-aging molecules, and promote angiogenesis refers to their properties such as biocompatibility, cross the blood-brain barrier, serving as vectors and selective cargo delivery. Altogether, these effects promote tissue regeneration, as well as its therapeutic potential in dermatology, orthopedics, cardiology, neurology, and wound healing. However the same mechanisms that promote regeneration can also drive tumor progression, induce drug resistance, suppress immune responses, and mediate the pathogenic factors spread. It means that exosome's dual nature presents challenges. On the therapeutic side, exosomes can promote tumor growth, drug resistance, and immune suppression. In contrast, the transmission of viral or pathogenic proteins, tumor progression, and so on, underscores their "Trojan horse" potential.Conclusion: Exosomes embody a biological paradox as mentioned. It is essential for developing safe and effective exosome based therapies to understanding of this duality deeper for harnessing their therapeutic potential while mitigating associated risks.

Keywords: exosomes; extracellular vesicles; nano drug delivery; regenerative medicine; tumor microenvironment; neurodegenerative disease

1. Introduction

Exosomes contain a rich collection of diverse molecules that play a key role as molecular messengers in intercellular communication and physiological processes. Exosomes are usually 30 to 150 nm in diameter and are surrounded by a membrane-like structure. This membrane-like structure protects the cargo from enzymatic degradation and provides stability to exosomes in biological fluids such as cerebrospinal fluid, blood, and saliva (Kalluri and LeBleu 2020, Vafaei, Mansoori et al. 2022, Zhang, Yan et al. 2024). On the other hand, the membrane of exosomes contains proteins similar to the cell membrane structure, such as tetraspanins (CD9, CD63 and CD81), glycoproteins, membrane

 doi:10.20944/preprints202602.1440.v1

proteins, heat shock proteins (HSPs), inner membrane transport proteins, fusion proteins, adhesion molecules, antigen-presenting molecules, and cell-specific receptors (Vader, Mol et al. 2016, Mehdizadeh, Mamaghani et al. 2025). The cargo of exosomes contains cytoskeletal proteins, growth factors, cytokines, and a variety of nucleic acids that contribute to their vital role in gene regulation and cell signaling (Mehdizadeh, Mamaghani et al. 2025). Figure 1 shows exosomes briefly.

2. The Beneficial Potential of Exosomes

Exosomes, because of their biological roles and therapeutic potential, have become a major subject of interest in recent years. These nanoscale vesicles, act as mediators of intercellular communication, and thus they can influence a variety of physiological and pathological processes in cells (Meldolesi 2018, Li, Li et al. 2022). They also have potential applications in regenerative medicine, treatment of inflammatory conditions and drug delivery. Some studies even suggest their usefulness in imaging and cellular waste management (Li, Li et al. 2022).

In the following sections, we will highlight these diverse roles, with particular emphasis on their contributions to gene transfer, cell signaling, and therapeutic interventions.

2.1. Exosomes in Intercellular Communication

Exosomes facilitate intercellular communication through several mechanisms, including surface binding, fusion with the plasma membrane, endocytosis, and receptor-mediated uptake. Exosomes can bind to recipient cells via adhesion molecules such as integrins and tetraspanins and initiate signaling cascades. The direct fusion of exosomes with the plasma membrane allows the delivery of cargo into the cytoplasm of recipient cells. Exosomes are also internalized by recipient cells through clathrin-dependent or independent endocytosis, macropinocytosis, or phagocytosis. Interactions between exosomal ligands (glycoproteins) and cell surface receptors (MARCO) facilitate this uptake. Through these interactions functional biomolecules such as miRNAs and proteins transfer to the cells. Biomolecules can reprogram recipient cells by modulating gene expression and activating signaling pathways (Meldolesi 2018, Liu and Wang 2023, Chimal-Vega, Maldonado-Arvizu et al. 2025).

It should be noted that external and internal environmental factors can influence exosome biogenesis, release, and cargo composition, thereby modulating their role in intercellular communication. For instance, exposure to environmental pollutants such as airborne particulate matter (PM2.5) has been shown to alter exosomal miRNA profiles, contributing to lung cancer progression and precancerous lesions in experimental models. (Eckhardt, Baccarelli and Wu 2022, Bahri, Mansoori et al. 2024).

In addition to external environmental factors, internal stresses or cellular microenvironment are also important in shaping exosome-mediated signaling. Factors such as pH, temperature, oxidative stress, and hypoxia can significantly influence exosome biogenesis, release, and uptake. Hypoxia can modify exosomal miRNA and protein profiles, which can impact cellular responses to stress. (Sutter, Rouillard et al. 2021, Liu and Wang 2023).

2.2. Exosomes as Gene Delivery Vectors

Exosomes, which carry a wide range of genetic materials (such as miRNAs, siRNAs, lncRNAs, mRNAs, and DNA), have revolutionized the field of gene therapy due to their unique biological properties (Zhang, Liu et al. 2022).

Their lipid bilayer structure protects fragile genetic material from being broken down by enzymes in body fluids. Additionally, exosomes can cross tough biological barriers like the BBB, which is a major challenge for traditional drug delivery systems (Dubey, Chen et al. 2023, Osaid, Haider et al. 2023).

Moreover, due to their endogenous origin, exosomes can evade immune detection and clearance, significantly improving their circulation time and therapeutic efficacy (Dubey, Chen et al. 2023, Wallen, Aqil et al. 2023). This superior biocompatibility and minimal immunogenicity represent

 doi:10.20944/preprints202602.1440.v1

a key advantage of exosomes over other delivery systems (Li, Wang and Chen 2025, Saka, Dora et al. 2025). These advantages of exosomes over other delivery systems, such as viral vectors and liposomes, are summarized in Table 1.

Table 1. Comparative Overview of Gene Delivery Systems: Exosomes, Viral Vectors, and Liposomes.

Feature	Exosomes	Viral Vectors	Liposomal Systems
Immunogenicity	Very low (immune-evasive)	High (strong immune response)	Moderate (may activate complement)
Genomic Integration	None (safe, non-integrative)	Common (may integrate into the genome)	None
Toxicity	Low (natural, biocompatible)	Moderate to high (inflammatory)	Variable (depends on lipids)
Safety	High (minimal side effects)	Moderate (risk of mutagenesis)	High (generally safe)
Loading Capacity	Moderate (good for nucleic acids/proteins)	Limited (restricted by viral genome size)	High (larger vesicles allow more cargo)
BBB Penetration	Yes (can cross BBB naturally)	Rare (usually cannot cross the BBB)	Limited (improvable with modifications)
Circulation Half-life	Long (48–72 hours)	Variable (often short due to clearance)	Moderate (24–48 hours)
Engineering Flexibility	High (easily modified)	Moderate (limited modifications)	High (surface can be functionalized)
Diagnostic Use	Yes (biomarkers for liquid biopsy)	Limited	Limited

These properties have been effectively utilized in therapeutic applications. For instance, in Parkinson's disease models, MSC-derived exosomes loaded with α-synuclein siRNA achieved potent

 doi:10.20944/preprints202602.1440.v1

gene silencing without triggering inflammatory responses, demonstrating their safety advantage (Geng, Long et al. 2023).

Furthermore, exosomes exhibit remarkable stability in circulation. Studies have shown that exosomal miRNAs, such as miR-423-3p, remain detectable in plasma for extended periods. This stability enables both therapeutic applications and disease monitoring (Boukouris and Mathivanan 2015, Li, Zheng et al. 2015, Guo, Wang et al. 2021).

The therapeutic potential of exosomes has been significantly improved due to recent advances in exosome engineering. Viral transduction methods that use lentiviral or adenoviral vectors are now able to pack therapeutic nucleic acids into exosomes efficiently. For example, lentiviral delivery of pre-miR-214 into mesenchymal stem cells (MSCs) resulted in exosomes enriched with miR-214, which demonstrated neuroprotective effects in cerebral injury models (Wu, Wu et al. 2024). Viral transduction is not the only way to load exosomes with cargoes. Exosomes can also be loaded with chemical and physical methods, such as electroporation and incubation, which can include siRNAs, mRNAs, and even CRISPR/Cas9 components. Surface modification techniques have further enhanced the targeting precision of exosomes (Xu, Yang et al. 2020, Zeng, Guo et al. 2023, Kim, Park et al. 2024). These engineering strategies address the historical challenge of low loading efficiency while preserving the natural delivery efficiency of exosomes (Xu, Yang et al. 2020, Zeng, Guo et al. 2023).

In oncology, exosomes serve dual diagnostic and therapeutic roles. Tumor-derived exosomes carry molecular signatures such as miR-21 and miR-1246, which serve as biomarkers for early cancer detection in liquid biopsies (Hannafon, Trigoso et al. 2016, Choi, Park et al. 2020). Engineered exosomes, on the other hand, deliver targeted therapies like KRAS siRNA in pancreatic cancer and PLK-1 siRNA in bladder cancer, demonstrating potent antitumor effects in preclinical models (Greco, Franzen et al. 2016, Kamerkar, LeBleu et al. 2017, Pofali, Mondal and Londhe 2020). See Table 2 for specific examples of exosome applications in cancer therapy and diagnosis.

Table 2. Exosome applications in cancer therapy and diagnosis.

Disease	Genetic Cargo	Exosome Source	Application	Results/Efficacy	Reference
Breast Cancer	miR-21, miR-1246	MCF-7 cells; Patient plasma	Diagnostic (Biomarker)	Elevated levels detected in patient plasma	(Hannafon, Trigoso et al. 2016)
	let-7a	HEK293T (GE11 modified)	Therapeutic	1000-fold increase in let-7a, 5-fold decrease in HMGA2	(Ohno, Takanashi et al. 2013)

 doi:10.20944/preprints202602.1440.v1

	BCL-2 siRNA	NK cell-derived	Therapeutic	Enhanced apoptosis	(Kaban, Hinterleitner et al. 2021)
Colorectal Cancer	miR-23a, miR-1246	Patient serum	Diagnostic	Increased levels in early stages	(Ogata-Kawata, Izumiya et al. 2014)
	miR-375-3p	Tumor-derived	Therapeutic	Reversed EMT, inhibited invasion	(Rezaei, Baghaei et al. 2021)
	CPT1A siRNA	iRGD-engineered	Therapeutic	Reversed oxaliplatin resistance	(Lin, Zhang et al. 2021)
	FGL1/TGF-β1 siRNA	cRGD-modified	Therapeutic	Enhanced T-cell infiltration	(Pei, Zhang et al. 2021)
Glioblastoma	miR-21	Patient serum	Diagnostic	Correlated with tumor progression	(Santangelo, Imbrucè et al. 2018)
	miR-21 inhibitor	T7-peptide engineered	Therapeutic	Reduced tumor size	(Kim, Kim et al. 2020)
	PTEN mRNA	Cellular nanoporation	Therapeutic	Median survival increased by 45 days	(Yang, Shi et al. 2020)

 doi:10.20944/preprints202602.1440.v1

Lung Cancer	KRAS siRNA	iRGD-engineered exosomes	Therapeutic	Tumor growth inhibition in A549 models	(Zhou, Yuan et al. 2019)
	SOX2 siRNA	HEK293T (Tuy-p-1 modified)	Therapeutic	Reduced cancer stemness	(Bai, Duan et al. 2020)
	survivin siRNA	EGFR aptamer-engineered	Therapeutic	Tumor regression	(Li, Yang et al. 2021)
Ovarian Cancer	miR-21, miR-200 family	Patient serum	Diagnostic	Early detection and prognosis	(Taylor and Gercel-Taylor 2008)
	PARP-1 CRISPR/Cas 9	Tumor-derived	Therapeutic	Complete inhibition of PARP-1	(Kim, Yang et al. 2017)
Pancreatic Cancer	KRASG12D siRNA	MSC-derived exosomes	Therapeutic	Tumor growth suppression in PDAC models	(Kamerkar, LeBleu et al. 2017)
	galectin-9 siRNA + Oxaliplatin	BM-MSC-derived exosomes	Therapeutic	A twofold increase in tumor inhibition	(Zhou, Zhou et al. 2021)
Prostate Cancer	miR-205	BM-MSC-derived exosomes	Therapeutic	Downregulation of RHPN2; inhibited proliferation	(Jiang, Mo et al. 2019)
	SIRT6 siRNA	Engineered exosomes	Therapeutic	Suppressed metastasis	(Han, Xie et al. 2021)

 doi:10.20944/preprints202602.1440.v1

Bladder Cancer	PLK-1 siRNA	HEK293T-derived exosomes; MSC-derived	Therapeutic	Induced apoptosis and tumor inhibition	(Greco, Franzen et al. 2016)
	lncRNA PTENP1	HEK293A-derived	Therapeutic	Inhibited tumor growth	(Zheng, Du et al. 2018)
Liver Cancer (HCC)	miR-26a	Engineered HEK293T (Apo-A1-CD63)	Therapeutic	Inhibited migration and proliferation via downregulating CCND2, CCNE2, and CDK6	(Liang, Shu et al. 2018)
Uveal Melanoma	miR-146a	Vitreous/patient serum	Diagnostic	Associated with metastasis	(Ragusa, Barbagallo et al. 2015)

2.3. Exosomes in Cellular Rewiring and Recycling

Exosomes play a key role in cellular rewiring and metabolic recycling processes by facilitating the removal of dysfunctional organelles and proteins via autophagic pathways, thereby maintaining cellular homeostasis (Baixauli, López-Otín and Mittelbrunn 2014, Desdín-Micó and Mittelbrunn 2017). They are not only involved in intercellular communication but also serve as vehicles for the selective removal of damaged mitochondrial fragments, misfolded and ubiquitinated proteins, and stress-related molecules like heat shock proteins. Such a process ensures that cells discard toxic substances without disrupting a proper balance in protein quality control (Soria, Pampliega et al. 2017, Takahashi, Okada et al. 2017). In addition, exosomes contribute to the exchange of metabolites and signaling molecules between cells. This exchange is essential for both energy metabolism and adaptation to stressful conditions. For instance, the transfer of key metabolic enzymes and substrates via exosomes can restore ATP production in energy-deprived cells, a process that is especially important in hypoxic environments like those found in tumors (Göran Ronquist 2019, Stahl and Raposo 2019). In cancer, tumor-derived exosomes are known to affect the tumor microenvironment by delivering immunosuppressive factors such as PD-L1 and TGF-β, thereby promoting metabolic reprogramming that aids the survival and proliferation of cancer cells (Yang, Wang et al. 2020).

Studies have shown that surface integrins on exosomes often play a role in tissue-specific docking and uptake during this targeted delivery function (Kuang, Wu and Li 2025). In addition to cancer, the process of exosome secretion is an ongoing process that enables tissues to exchange metabolites under normal conditions. For example, exosomes enriched in glycolytic enzymes are

 doi:10.20944/preprints202602.1440.v1

released and targeted in muscles after exercise to enhance glucose metabolism in the liver. This delivery effectively rewires cellular function to support tissue renewal and maintain overall homeostasis (Wang, Zhu et al. 2020, Yang, Wang et al. 2020).

2.4. Exosomes in the Nervous System

Within the nervous system, exosomes regulate synaptic function, neuroinflammation, and cellular homeostasis. However, under pathological conditions, they can also spread neurodegenerative processes by transporting misfolded proteins such as Aβ[1], tau, and α-synuclein (Fan, Chen and Zhang 2022, Daksh, Mathew et al. 2025). Recent studies have design exosomes can carry drugs or therapeutic molecules that can cross the blood-brain barrier, enhance neuroregeneration, and modulate pathological pathways (Kalluri and LeBleu 2020, Khan, Khan et al. 2022).

The term "exosome repurposing" describes the deliberate engineering and redirecting of exosomes for therapeutic benefit. This may be done by surface modification, cargo loading, or preconditioning of donor cells. Exosome targeting has been achieved by placing ligands or antibodies that bind to neuronal receptors on exosome membranes, improving targeting. Furthermore, therapeutic molecules such as siRNA, miRNAs, anti-inflammatory agents, or antioxidants can be loaded into exosomes via electroporation or co-incubation (Fu, Wang et al. 2020, Sadeghi, Tehrani et al. 2023). Preconditioning of neural stem cells or MSCs[2] can also stimulate the release of exosomes containing neuroprotective factors (Serrenho, Ferreira and Baltazar 2024). These molecules have the capacity to modulate immune responses, block neuronal apoptosis, promote myelination, and activate regenerative signaling pathways like PI3K/Akt and Wnt/β-catenin, thus enabling neural circuit recovery after injury or disease (Khan, Jeong et al. 2023).

In AD[3], engineered exosomes have been used to ameliorate Aβ aggregation, γ-secretase and phosphorylated tau through the exosomes containing other enzymatic agents, or gene-silencing RNAs. These approaches are not only effective but surpass traditional therapies in overcoming the BBB and minimizing systemic toxicity (Fan, Chen and Zhang 2022, Khan, Jeong et al. 2023, Daksh, Mathew et al. 2025). Lastly, exosomes derived from microglia or astrocytes have been used to carry HSPs and miR-124, which improve synaptic resilience to counteract tau hyperphosphorylation (Smalheiser 2007, Sharma, Tanwar et al. 2024).

In PD [4], where α-synuclein aggregation and neuroinflammatory processes drive neurodegeneration, exosomes offer a dual strategy. Engineerable vesicles can deliver siRNA to reduce α-synuclein levels, while also carrying anti-inflammatory miRNAs to mitigate proinflammatory glial activation. These approaches have led to enhanced survival of dopaminergic neurons, with concomitant improvements in motor function in relevant preclinical models (Fan, Chen and Zhang 2022, Geng, Long et al. 2023). Interestingly, MSC-derived exosomes have also been shown to reduce glial scar and stimulate mitochondrial biogenesis in dopaminergic neurons, demonstrating their Regenerative potential (Li, Chen et al. 2024).

TBI[5] is another area where exosome therapy offers potential benefit. Exosomes from human umbilical cord MSCs have been shown to enhance neurorestoration by inhibiting ferroptosis and activating antioxidant pathways (for example, TUBB6/Nrf2), which then translates into improved spatial memory and functional recovery in animal studies even after a delayed therapy post-injury (Che, Wang et al. 2024). Additionally, these vesicles can also initiate the angiogenesis process by the delivery of miR-21-3p and miR-214, induce endothelial tube formation, and enhancement of

[1] amyloid-β

[2] mesenchymal stem cells

[3] Alzheimer's disease

[4] Parkinson's disease

[5] Traumatic Brain Injury

 doi:10.20944/preprints202602.1440.v1

neurovascular niche remodeling and so supporting long-term tissue repair (Yang, Ye et al. 2017, Fan, Chen and Zhang 2022).

Exosomes possess diagnostic capabilities in addition to therapeutic applications. The biological cargo of exosomes can provide insight into the pathological condition of the donor cell, which provides the opportunity for early identification of neurological disorders using a liquid biopsy. Current work is underway to include disease-specific exosomal markers (such as Aβ and phosphorylated tau in AD or α-synuclein in PD) into diagnostic pipelines for real-time disease assessment and personalized medicine (Fan, Chen and Zhang 2022, Wu, Shang et al. 2024).

2.5. Exosome-Mediated Tissue Regeneration and Rejuvenation

Exosomes rejuvenating properties result from the transfer of biological materials such as telomerase and sirtuins, which put the brake on cellular senescence and neutralize oxidative stress, a primary driver of aging (Hajialiasgary Najafabadi, Soheilifar and Masoudi-Khoram 2024, Liu, Sheng and Sun 2024). Exosomes also epigenetically reprogram recipient cells via microRNAs, restoring youthful gene expression profiles (Hajialiasgary Najafabadi, Soheilifar and Masoudi-Khoram 2024, Liu, Sheng and Sun 2024, Rasti, Afrisham et al. 2024). In tissue regeneration, exosomes activate major signaling pathways such as Wnt/β-catenin and PI3K/AKT to promote cell proliferation, while their anti-inflammatory cargo minimizes fibrosis (Qian, Pi et al. 2021, Ren, Chen et al. 2022, Yan, Guo et al. 2025). Exosomes also mediate angiogenesis, through VEGF and angiopoietin-1, especially in ischemic processes (Chen, Huang et al. 2020, Lu, Cheng et al. 2020).

Taken together, these properties form the biological basis for a wide and growing range of clinical applications from dermatology and orthopedics to cardiology and neurology, to reproductive medicine, and complex wound healing (Malekpour, Hazrati et al. 2022, Szwedowicz, Łapińska et al. 2022, Wu, Li et al. 2022, Wang, Wang et al. 2025). These mechanisms, detailed in Table 3, underlie their broad therapeutic potential across various medical fields.

The transition from mechanism to clinical application has already shown exciting results. In dermatology, exosome therapies improve skin quality and reduce visible aging signs, while orthopedic applications accelerate musculoskeletal injury healing. Cardiovascular studies report improved outcomes following myocardial damage, and neurological applications show potential for addressing neurodegenerative conditions (Chen, Huang et al. 2020, Lin, Anderson et al. 2020, Sreeraj, AnuKiruthika et al. 2024). These diverse applications, summarized in Table 4.

Table 3. Mechanisms of Exosome-Mediated Rejuvenation and Regeneration.

Category	Mechanism	Signaling Pathways	Biological Effects	References
Skin Rejuvenation	Downregulation of MMPs (MMP-1, MMP-3)	MAPK/AP-1, TGF-β/Smad	Prevents collagen/elastin degradation, reduces wrinkles	(Kim, mi Yoo et al. 2017, Choi, Cho et al. 2019, Hu, Li et al. 2019, Deng, Yu et al. 2020, Gao, Wang et al. 2021, Gao, Yuan et al. 2023, Yan, Huang et al. 2023)
	Increased collagen/elastin production	TGF-β, EGF, SIRT1, Nrf2	Improves skin elasticity and thickness	(Kim, mi Yoo et al. 2017, Oh, Lee et al. 2018, Choi, Cho et al. 2019, Hu, Li et al. 2019, Deng, Yu et al. 2020, Gao, Wang et al. 2021, Wu, Zhang et al. 2021, Gao, Yuan et al. 2023, Gao, Zhang et al. 2023)

 doi:10.20944/preprints202602.1440.v1

	Activation of signaling pathways	MAPK/AP-1, TGF-β/Smad, Nrf2/ARE, SIRT1	Enhances cell proliferation, reduces oxidative stress	(Oh, Lee et al. 2018, Hu, Li et al. 2019, Deng, Yu et al. 2020, Wang, Jian et al. 2020, Gao, Wang et al. 2021, Wu, Zhang et al. 2021, Gao, Yuan et al. 2023, Yan, Huang et al. 2023)
	Oxidative stress reduction	Antioxidant enzymes (e.g., SOD, catalase), miR-1246, 14-3-3ζ	Reduces ROS, prevents DNA damage	(Deng, Yu et al. 2020, Wang, Jian et al. 2020, Gao, Wang et al. 2021, Wu, Zhang et al. 2021, Gao, Yuan et al. 2023, Yan, Huang et al. 2023)
	Macrophage polarization (M1 → M2)	TLR4/NF-κB, STAT3, PI3K/AKT	Reduces inflammation, promotes tissue repair	(Ti, Hao et al. 2015, Dalirfardouei, Jamialahmadi et al. 2019, He, Dong et al. 2019, Liu, Yu et al. 2020)
	Angiogenesis stimulation	VEGF, PI3K/AKT, Wnt/β-catenin		(Tao, Guo et al. 2017, Qiu, Liu et al. 2020, Yang, Chen et al. 2020, Hu, Tao et al. 2021)
Tissue Regeneration	Wnt/β-catenin pathway activation	Wnt ligands, β-catenin	Promotes cell proliferation in the heart, kidney, lung, and brain	(Zhang, Wu et al. 2015, Cui, He et al. 2017, Jia, Zhu et al. 2020, Qian, Pi et al. 2021, Sha, Shen et al. 2021, Zhang, Geng et al. 2021)
	Anti-inflammatory/fibrosis effects	TGF-β1, IL-6 inhibitors, miR-146a	Improves tissue microenvironment, reduces fibrosis	(Xia, Zeng et al. 2019, Xu, Zhang et al. 2019, Mao, Jacob et al. 2021, Ning, Chen et al. 2021, Lee, Lötvall and Cho 2023, Shen and Lane 2023, Harrell, Djonov et al. 2024)
	microRNA/protein transfer	miR-21-5p, miR-150-5p, miR-199a	Modulates gene expression, enhances repair	(Luther, Haar et al. 2018, Lou, Chen et al. 2020, Huang, Chen et al. 2021, Li, Zhang et al. 2021)
	Angiogenesis stimulation	VEGF, HIF-1α, miR-31	Promotes new blood vessel formation	(Liao, Ning et al. 2019, Chen, Huang et al. 2020, Lu, Cheng et al. 2020, Sun, Shen et al. 2020)
	Paracrine/autocrine signaling	Growth factors (IGF-1, PDGF), cytokines	Activates repair pathways, enhances cell survival	(Ma, Liang et al. 2021, Wang, Zhu et al. 2021, Jiang, Chen et al. 2022)
	Cell proliferation/survival	miR-34a, miR-124, S100A6	Facilitates tissue reconstruction	(Barile, Cervio et al. 2018, Chen, Tang et al. 2019, Sun, Zhu et al. 2020, Lee, Lee et al. 2021)

 doi:10.20944/preprints202602.1440.v1

Table 4. Clinical Applications of Exosome-Based Therapies.

Therapeutic Area	Condition	Intervention	Study Phase	Key Findings	Status	Clinical Trial Code	Study Type
Dermatology	Skin Aging	Microfat + Exosome vs PRF	Phase I	Increase in collagen, wrinkle reduction	Completed	IRCT20240402061398N1	Randomized Controlled Trial
	Acne Scars	Fractional CO_2 Laser + Adipose Exosomes	Phase I/II	Significant scar size reduction	Recruiting	IRCT20200127046282N52	Single-blind RCT
	Melasma	UC-MSC Exosomes + 1565nm Laser	Phase II	Basement membrane repair	Recruiting	NCT06677931	Quadruple-blind RCT
Hair Restoration	Androgenetic Alopecia	Plant-derived Exosomes	Phase I/II	Increase in hair density	Completed	NCT06930326	Double-blind RCT
Dentistry	Dental Pulp Regeneration	Fibrin Hydrogel + DPSC Exosomes	Phase I	Radiographic evidence of pulp regeneration	Recruiting	IRCT20230513058168N1	Double-blind RCT
Reproductive	Thin Endometrium	Engineered UC-MSC Exosomes vs PRP	Phase I/II	Increased endometrial thickness	Recruiting	NCT06896747	Non-randomized Clinical Trial
Orthopedics	Meniscal Injury	SF-MSC Exosomes vs SF-MSCs	Phase I/II	Increase in cartilage thickness	Active	NCT05261360	Open-label RCT
	Acute Ankle Sprain	Zhishang Ointment (TCM) vs Diclofenac	Post-marketing	Improved AOFAS score, pain reduction	Recruiting	ITMCTR2025000218	Comparative Study

 doi:10.20944/preprints202602.1440.v1

Wound Healing	Diabetic Foot Ulcers	MSC Exosomes + Nutritional Therapy	Phase II	Faster healing rate	Recruiting	NCT05243368	Factorial RCT
	Chronic Wounds	DermGEN™ (Exosome-based) vs Standard Care	RCT	Faster healing, fewer complications	Not Recruiting	NCT05251480	Parallel RCT
Urology	Erectile Dysfunction	Adipose-derived Exosomes	Observational	Improved IIEF score	Recruiting	NCT06605508	Cohort Study
Neurology	Acute Ischemic Stroke	SNE-101 (EV Therapy)	Phase I	Safety and tolerability	Not Yet Recruiting	NCT06995625	Dose-escalation Clinical Trial
COVID-19	Hyperinflammation	MSC Exosomes IV	Phase II	Reduced cytokine storm	Unknown	NCT05216562	Triple-blind RCT

3. The Janus-Faced Nature of Exosomes

Exosomes once considered mere cellular debris are now recognized as master regulators of intercellular communication. These nanosized vesicles shuttle bioactive cargo-proteins, lipids, and nucleic acids-between cells orchestrating processes vital to development, immunity and tissue repair but yet this very ability to transmit molecular messages also equips exosomes with a darker potential so that they can propagate disease, fuel tumor progression, and undermine therapeutic interventions and these conditions like a double-edged sword exosomes exemplify nature's paradox, their physiological precision in maintaining homeostasis is mirrored by their capacity to amplify pathology. This review unpacks the duality of exosomes, exploring how their role as both healers and harbingers of disease hinges on context, cargo, and cellular recipient.

3.1. Multifaceted Roles of Exosomes in Cancer Progression and Immunomodulation

Exosomes as extracellular vesicles are integral to cell-cell communication, growth, differentiation, and survival and their influence on the TME[6] is a key factor in promoting cell metastasis and notably exosomes also convey information about the surrounding cellular conditions, mediating changes within the microenvironment (Kim, Kim and Cho 2019, LeBleu and Kalluri 2020) so that in cancerous states exosomes contribute to shaping the TME, inducing alterations in vascularization, cell polarity, and immune system modulation and they are implicated in both EMT[7]

[6] tumor microenvironment

[7] epithelial-to-mesenchymal transition

 doi:10.20944/preprints202602.1440.v1

and MET[8] (Rajagopal and Harikumar 2018). While exosomes are known to promote tumorigenesis, metastasis, and chemoresistance, their potential for therapeutic intervention is also recognized; for instance, dendritic cell-derived exosomes (dexosomes) can be engineered to stimulate antitumor immune responses (Mashouri, Yousefi et al. 2019, Kalluri and LeBleu 2020).

Exosomes contribute to tumor development through various mechanisms including the modulation of protein function via PTMs[9] such as ubiquitination so that dysregulation of ubiquitination and deubiquitination pathways often influenced by exosomal content can directly promote tumor development (Sun, Liu and Yang 2020) and beyond PTMs specific exosomal contents also contribute to tumor progression; for example Wnt5b found within exosomes has been associated with squamous cell carcinomas of the head and neck, invasive breast cancer, and lung and pancreatic cancer (Harada, Yamamoto et al. 2017). Other significant PTMs include glycosylation where extracellular vesicles from ovarian cancer (for instance) are notably rich in mannose and sialic acid residues (Escrevente, Keller et al. 2011) and similarly exosomal Src-phosphorylation has been shown to enhance angiogenesis in myeloid leukemia contribute with tumor development (Mineo, Garfield et al. 2012).

Exosomes particularly those carrying nucleic acids, are implicated in modulating both innate and adaptive immune responses (Kalluri and LeBleu 2020) also they can stimulate the anticancer activities of CD4+ T cells (Raposo, Nijman et al. 1996). Exosomes derived from various cell types can carry molecules that mediate immune responses to tumor formation; for instance they can influence the function of Th17 cells which are known to secrete both anticancer factors and promote angiogenesis (Bilska, Pawłowska et al. 2020). Exosomal content is highly influenced by the cytokine milieu and can modulate immune responses; for example in nasopharyngeal carcinoma (NPC) exosomes have been observed to hinder T cell proliferation and Th1/Th17 differentiation correlating with decreased levels of IL-2, IFN-γ, and IL-17 and simultaneously these exosomes promote the stimulation and activation of regulatory T(Treg) cells often by increasing levels of IL-1β, IL-6, and IL-10 (Ye, Li et al. 2014). An elevated Treg/Th17 ratio, a common characteristic of primary and metastatic tumor environments is often facilitated by exosomes. These vesicles released by macrophages transfer miR-29a-3p and miR-21-5p to T helper (CD4+) cells (Zhou, Li et al. 2018) furthermore exosomal transfer of miRNA let-7d has been shown to reduce Th1 proliferation and IFN-γ secretion (Okoye, Coomes et al. 2014). Exosomes play a significant role in immune suppression by carrying PD-L1[10] that which has been shown in animal studies to directly inhibit the anti-cancer function of CD8+ T cells and thereby promote immune suppression, tumor progression, and altered response to immunotherapy (Theodoraki, Yerneni et al. 2018).

3.2. the Tme and Exosome-Mediated Effects

The TME is a critical determinant in most cancer conditions (Camuzard, Santucci-Darmanin et al. 2020) characterized by features such as hypoxia, increased lactate, extracellular acidosis and nutrient deprivation (Ma, Wang et al. 2021); where various cell types including mesenchymal stem cells, fibroblasts, endothelial cells, and immune cells secrete growth factors and cytokines (Ye, Wu et al. 2014) whose intricate network of interactions critically influences tumor progression, with macrophages, among the most abundant immune cells within tumors existing as M1 (anti-tumorigenic) and M2 (pro-tumorigenic) phenotypes (Moraes, Kar et al. 2017) typically shifting towards M2 polarization in cancerous conditions (Yang, Guo et al. 2021). One of the molecular signaling pathways in this condition that plays an oncogenic role is the signal transducer and activator of transcription 3 (STAT3) pathway (Mohan, Rangappa et al. 2021) so that STAT3 activation contributes to cell growth, metastasis, EMT and chemoresistance (Lee, Kim et al. 2017, Liu, Liao et al. 2021). Recent experimental studies have established a crucial link between exosomes, STAT3 and

[8] mesenchymal-to-epithelial transition

[9] post translational modifications

[10] programmed death-ligand 1

 doi:10.20944/preprints202602.1440.v1

macrophage polarity so that exosomes containing high levels of interleukin-6 (IL-6) and miR-155-3p can drive this process that IL-6 activates STAT3 which in turn upregulates miR-155-3p expression and this miR-155-3p then induces autophagy, a process that further enhances STAT3 phosphorylation and ultimately promotes tumorigenesis furthermore exosome-induced autophagy contributes to M2 macrophage polarization exacerbating tumor progression and drug resistance (Xu, Zhang et al. 2021).

3.3. Exosomes and Angiogenesis

Exosomes secreted from tumor cells play a crucial role in inducing angiogenesis and consequently cancer progression with exosomal miR-210-3p specifically identified as a key pro-angiogenic factor whose increased expression in tumor cells correlates with elevated microvessel density (MVD) and higher tumor grade, mechanistically stimulating angiogenesis by suppressing ephrin A3 expression which in turn activates the PI3K/Akt pathway (Wang, Wang et al. 2020).

Beyond general intercellular communication, exosomes enhance specific pro-tumorigenic conditions such as increased angiogenesis in tumor cells; for instance in NPC cells elevated angiogenesis is linked to their high migratory capacity furthermore this high migratory capacity can be attributed to exosomal miR-23a that by binding to the 3'-UTR of TSGA10 and reducing its expression, miR-23a promotes both angiogenesis and metastasis in these cells (Bao, You et al. 2018).

3.4. Exosomes and Metabolic Reprogramming

Exosomes also carry miR-3679-5p whose elevated levels enhance c-Myc stability by downregulating NEDD4L thereby inducing glycolysis and promoting cancer cell proliferation (Wang, Wang et al. 2020) that this highlights how exosomes can reprogram cellular metabolism towards glycolysis favoring cancer cell growth and contributing to drug resistance (Wang, Wang et al. 2019). Key drivers of cancer cell proliferation include accelerated cell cycle progression, inhibited apoptosis and metabolic shifts like increased glycolysis that the rapid energy demands of proliferating cancer cells cannot be met solely by the slower process of oxidative phosphorylation making glycolysis a crucial alternative for sustained growth (Dai, Wang et al. 2017).

The STAT3 signaling pathway is an oncogenic pathway because it prevents cell cycle arrest, apoptosis and promotes cell growth and metastasis (Lee, Kim et al. 2017) furthermore STAT3 can play a role in EMT and enhance cancer invasion also overexpression of STAT3 can lead to chemoresistance (Wang, Tao et al. 2020, Liu, Liao et al. 2021).

Exosomes can reprogram macrophages into CAMs[11] through alterations in their polarization state that this process is facilitated by the exosomes' rich gp130 content which enables them to induce the STAT3 signaling pathway via upregulation of IL-6 (Ham, Lima et al. 2018) furthermore STAT3-containing exosomes can suppress the immune system and facilitate cancer progression by creating an imbalance between T cells and tumor-associated macrophages (Zhou, Li et al. 2018) also STAT3-containing exosomes can induce the expression of cyclin D1, MMP-2, and MMP-9 which are important factors in cancer cell proliferation and invasion (Yu, Zhang et al. 2019) moreover conditions like hypoxia can promote self-renewal conditions by helping to increase STAT3 expression (Ren, Sun et al. 2019).

In addition to the above pathways, exosomes can also lead to cancer cell resistance through other pathways such as the Wnt/β-catenin axis; for example the presence of exosomal miRNA-92a-3p leads to the inhibition of mitochondrial apoptosis and the induction of cancer cell resistance (Hu, Wang et al. 2019).

Another role of exosomes can be examined in regulating the levels of ROS[12], as ROS generally induces apoptosis in cancer cells, and their modulation by exosomes can exhibit different behaviors;

[11] cancer-associated macrophages

[12] reactive oxygen species

 doi:10.20944/preprints202602.1440.v1

for instance in pancreatic cancer the presence of miRNA-155 in exosomes reduces DCK expression which in turn increases superoxide dismutase and catalase; this reduction in ROS levels increases cancer cell growth and is effective in their resistance to chemotherapy (Patel, Khan et al. 2017).

Exosomes secreted by cancer cells can be absorbed by immune cells and affect their behavior; for example exosomes derived from pancreatic cancer cells can be absorbed by lymphocytes to induce the p38 MAPK signaling pathway and mediate apoptosis through endoplasmic reticulum stress so that this process leads to immune system suppression and paves the way for cancer progression (Shen, Huang et al. 2020) and finally exosomes can suppress apoptosis and enhance growth by stimulating ERK[13] (Wang, Wang et al. 2019).

3.5. Exosomes and Disease Transmission

Exosomes inherent capacity for cell communication and transfering, positions them as potential vehicles for disease transmission so that over the past decade exosomes have been implicated in the spread of disease-associated proteins like prions and beta-amyloid peptides (Rajendran, Honsho et al. 2006, Alenquer and Amorim 2015).

The exosome biogenesis and secretion pathway offers a conducive environment for viral dissemination so that viruses such as HIV,[14] HCV[15], and EBV[16] can directly or indirectly enter MVBs[17] and be subsequently released within exosomes or alternatively viral genetic material such as viral RNAs or related proteins may be packaged into exosomes during their formation with some viruses including HSV[18] and CMV[19] even known to accumulate within MVBs before their exosomal release (Nour, Li et al. 2013, Janas, Janas et al. 2015) furthermore specific mechanisms govern the packaging of viral components where RNA-binding proteins such as hnRNPA2B1 are crucial for transferring viral RNAs into exosomes by binding to specific motifs (Villarroya-Beltri, Gutiérrez-Vázquez et al. 2013) and for viral membrane proteins ubiquitination and the recruitment of the ESCRT machinery represent common packaging mechanisms (Stuffers, Sem Wegner et al. 2009).

Once loaded with viral components exosomes facilitate the spread of the viral genome through intercellular transfer so that these virus-laden exosomes possess remarkable immune evasion capabilities that their origin from host cells often prevents an immediate immune response and their small size coupled with the expression of immune-inhibitory factors like CD47 (which suppresses macrophages) allows them to escape immune surveillance (Dreux, Garaigorta et al. 2012, Ramakrishnaiah, Thumann et al. 2013). Importantly while exosomes containing viral proteins or RNA can initiate infection upon cytoplasmic entry, exosomes carrying viral antigens can also modulate host immune responses by triggering signaling cascades upon receptor binding (Kalamvoki, Du and Roizman 2014).

The striking similarities between exosomes and viruses have led some researchers to hypothesize that exosomes might represent an "ancient virus" (Koenig 2015) because of both share fundamental features including a lipid bilayer structure and analogous mechanisms for secretion, cellular uptake, and RNA molecule transport (Votteler and Sundquist 2013) that these suggest a commonality with enveloped viruses in terms of biogenesis, biophysical characteristics, and cellular sorting pathways (Meckes and Raab-Traub 2011) furthermore exosomes role in cell-to-cell communication and genomic transfer (e.g., mRNA and miRNAs) reinforces this proposed evolutionary link. The shared particle and antigen sorting mechanisms observed in HIV-1 and

[13] extracellular signal-regulated kinase

[14] Human Immunodeficiency Virus

[15] Hepatitis C Virus

[16] Epstein-Barr Virus

[17] MultiVesicular Bodies

[18] Herpes Simplex Virus

[19] CytoMegaloVirus

 doi:10.20944/preprints202602.1440.v1

exosomes further support the ancient virus hypothesis (Izquierdo-Useros, Lorizate et al. 2012) and beyond structural and functional parallels, exosomes can also actively contribute to viral infection by carrying viral antigens and facilitating their transfer, particularly to CD4+ T cells (van Dongen, Masoumi et al. 2016) that the presence of exosomal structural proteins like CD63 and Alix, which are also involved in viral formation and spread, further highlights this intricate relationship (French, Antonyak and Cerione 2017). Table 5 describes signaling pathways contributing to the dual role of exosomes in brief.

Table 5. signaling pathways contributing to the dual role of exosomes. Dark cells contribiute to the dark side and bright cells contribute to the good side of exosomes.

Role	Molecular Pathway	Reference
Cancer Progression & Metastasis	TGF-β/ SMAD signaling	(Hao, Baker and ten Dijke 2019)
Tumor Microenvironment Modulation	Wnt/β-catenin pathway	(Novoa Díaz, Martín and Gentili 2022)
	PI3K/AKT/mTOR pathway	(Jiang, Zhang et al. 2025)
Angiogenesis Promotion	VEGF/VEGFR signaling	(Liu, Gao et al. 2025)
	Notch signaling	(Xiong, Hu et al. 2024)
Metabolic Reprogramming	c-Myc/Myc target genes	(Pan, Wang et al. 2016)
Disease Agent Transmission	Intercellular transfer of viral RNA/protein	(Khadka, Spiers et al. 2023)
Precision Gene & Drug Delivery	Endocytosis and Membrane Fusion	(Liang, Duan et al. 2021)
Intercellular Communication & Signaling	MAPK/ERK pathway	(Dong, Tamari et al. 2024)
	Notch/Delta pathway	(McGough and Vincent 2016)
Cellular Repair & Regeneration	Wnt/β-catenin pathway	(Li, Xu et al. 2023)
	PI3K/AKT pathway	(Li, Qin et al. 2023)
Neurological Therapeutic Applications	BDNF/TrkB signaling	(Wang, Hu et al. 2024)
	CREB pathway	(Ye, Chang et al. 2022)
Tissue Rejuvenation & Healing	TGF-β/SMAD pathway	(Liang, Zhou et al. 2024)

 doi:10.20944/preprints202602.1440.v1

	EGF/EGFR pathway	(Li, Tang et al. 2021)
Biomarker Discovery & Diagnostics	miRNA profiling in exosomes	(Zhu, Gao et al. 2024)

4. Conclusion: The Dual Role of Exosomes in Health and Disease

Overall, exosomes, as natural and efficient carriers of intercellular communication, play a pivotal role in maintaining homeostasis and proper bodily function. By precisely and effectively delivering proteins, lipids, and various types of RNA, they contribute to improving physiological conditions and optimizing cellular processes. In other words, **they make good conditions better** however, this very inherent capacity for transfer and communication transforms them into a powerful tool for the dissemination of pathogenic agents. From the spread of disease-related proteins like prions and beta-amyloid peptides to facilitating the spread of viruses and their escape from immune responses, exosomes can actively contribute to disease progression and by transporting viral components and pathogenic proteins they not only aid in the spread of infection but also through their ability to evade immune surveillance **they make bad conditions worse**. This striking duality in exosome function makes them a key component in understanding disease pathogenesis as well as in designing new therapeutic approaches.

All authors participated in drafting and revising the manuscript.

Conflict of interest: The authors declare that there is no conflict of interest.

References

Alenquer, M. and M. J. Amorim (2015). "Exosome Biogenesis, Regulation, and Function in Viral Infection." Viruses **7**(9): 5066-5083.

Bahri, F., M. Mansoori, S. Vafaei, S. Fooladi, Y. Mir, M. Mehrabani, Y. Hozhabri, M. H. Nematollahi and S. Iravani (2024). "A comprehensive review on ginger-derived exosome-like nanoparticles as feasible therapeutic nano-agents against diseases." Materials Advances **5**(5): 1846-1867.

Bai, J., J. Duan, R. Liu, Y. Du, Q. Luo, Y. Cui, Z. Su, J. Xu, Y. Xie and W. Lu (2020). "Engineered targeting tLyp-1 exosomes as gene therapy vectors for efficient delivery of siRNA into lung cancer cells." Asian journal of pharmaceutical sciences **15**(4): 461-471.

Baixauli, F., C. López-Otín and M. Mittelbrunn (2014). "Exosomes and autophagy: coordinated mechanisms for the maintenance of cellular fitness." Front Immunol **5**: 403.

Bao, L., B. You, S. Shi, Y. Shan, Q. Zhang, H. Yue, J. Zhang, W. Zhang, Y. Shi and Y. Liu (2018). "Metastasis-associated miR-23a from nasopharyngeal carcinoma-derived exosomes mediates angiogenesis by repressing a novel target gene TSGA10." Oncogene **37**(21): 2873-2889.

Barile, L., E. Cervio, V. Lionetti, G. Milano, A. Ciullo, V. Biemmi, S. Bolis, C. Altomare, M. Matteucci and D. Di Silvestre (2018). "Cardioprotection by cardiac progenitor cell-secreted exosomes: role of pregnancy-associated plasma protein-A." Cardiovascular research **114**(7): 992-1005.

Bilska, M., A. Pawłowska, E. Zakrzewska, A. Chudzik, D. Suszczyk, M. Gogacz and I. Wertel (2020). "Th17 cells and IL-17 as novel immune targets in ovarian cancer therapy." Journal of Oncology **2020**(1): 8797683.

Boukouris, S. and S. Mathivanan (2015). "Exosomes in bodily fluids are a highly stable resource of disease biomarkers." PROTEOMICS–Clinical Applications **9**(3-4): 358-367.

Camuzard, O., S. Santucci-Darmanin, G. F. Carle and V. Pierrefite-Carle (2020). "Autophagy in the crosstalk between tumor and microenvironment." Cancer Letters **490**: 143-153.

Che, J., H. Wang, J. Dong, Y. Wu, H. Zhang, L. Fu and J. Zhang (2024). "Human umbilical cord mesenchymal stem cell-derived exosomes attenuate neuroinflammation and oxidative stress through the NRF2/NF-κB/NLRP3 pathway." CNS Neurosci Ther **30**(3): e14454.

 doi:10.20944/preprints202602.1440.v1

Chen, Q., M. Huang, J. Wu, Q. Jiang and X. Zheng (2020). "Exosomes isolated from the plasma of remote ischemic conditioning rats improved cardiac function and angiogenesis after myocardial infarction through targeting Hsp70." Aging (Albany NY) **12**(4): 3682.

Chen, S., Y. Tang, Y. Liu, P. Zhang, L. Lv, X. Zhang, L. Jia and Y. Zhou (2019). "Exosomes derived from miR-375-overexpressing human adipose mesenchymal stem cells promote bone regeneration." Cell Proliferation **52**(5): e12669.

Chimal-Vega, B., J. E. Maldonado-Arvizu, A. D. Hernández Avalos, J. F. Díaz-Villanueva, L. P. Avila-Barrientos and V. G. García González (2025). "Inter-Tissue Communication Mechanisms via Exosomes and Their Implications in Metabolic Diseases: Opportunities for Pharmacological Regulation." Future Pharmacology **5**(1): 11.

Choi, J. S., W. L. Cho, Y. J. Choi, J. D. Kim, H.-A. Park, S. Y. Kim, J. H. Park, D.-G. Jo and Y. W. Cho (2019). "Functional recovery in photo-damaged human dermal fibroblasts by human adipose-derived stem cell extracellular vesicles." Journal of extracellular vesicles **8**(1): 1565885.

Choi, J. U., I. K. Park, Y. K. Lee and S. R. Hwang (2020). "The Biological Function and Therapeutic Potential of Exosomes in Cancer: Exosomes as Efficient Nanocommunicators for Cancer Therapy." Int J Mol Sci **21**(19).

Cui, X., Z. He, Z. Liang, Z. Chen, H. Wang and J. Zhang (2017). "Exosomes from adipose-derived mesenchymal stem cells protect the myocardium against ischemia/reperfusion injury through Wnt/β-catenin signaling pathway." Journal of cardiovascular pharmacology **70**(4): 225-231.

Dai, X., L. Wang, A. Deivasigamni, C. Y. Looi, C. Karthikeyan, P. Trivedi, A. Chinnathambi, S. A. Alharbi, F. Arfuso, A. Dharmarajan, B. C. Goh, K. M. Hui, A. P. Kumar, M. R. Mustafa and G. Sethi (2017). "A novel benzimidazole derivative, MBIC inhibits tumor growth and promotes apoptosis via activation of ROS-dependent JNK signaling pathway in hepatocellular carcinoma." Oncotarget **8**(8): 12831-12842.

Daksh, R., M. S. Mathew, A. M. Bosco, C. Sojan, A. A. Tom, S. L. Bojja and M. Nampoothiri (2025). "The role of exosomes in diagnosis, pathophysiology, and management of Alzheimer's Disease." Biochemical and Biophysical Research Communications **754**: 151526.

Dalirfardouei, R., K. Jamialahmadi, A. H. Jafarian and E. Mahdipour (2019). "Promising effects of exosomes isolated from menstrual blood-derived mesenchymal stem cell on wound-healing process in diabetic mouse model." Journal of Tissue Engineering and Regenerative Medicine **13**(4): 555-568.

Deng, M., T. Z. Yu, D. Li, X. Wang, G. Zhou, W. Liu, Y. Cao, W. Xia, W. Li and W. J. Zhang (2020). "Human umbilical cord mesenchymal stem cell-derived and dermal fibroblast-derived extracellular vesicles protect dermal fibroblasts from ultraviolet radiation-induced photoaging in vitro." Photochemical & Photobiological Sciences **19**(3): 406-414.

Desdín-Micó, G. and M. Mittelbrunn (2017). "Role of exosomes in the protection of cellular homeostasis." Cell adhesion & migration **11**(2): 127-134.

Dong, Y., K. Tamari, M. Kishigami, S. Katsuki, K. Minami, S. Tatekawa, S. Shimizu, M. Koizumi and K. Ogawa (2024). "Irradiated cell-derived exosomes enhance cell proliferation and radioresistance via the MAPK/erk pathway." Cancer Genomics & Proteomics **21**(1): 12-17.

Dreux, M., U. Garaigorta, B. Boyd, E. Décembre, J. Chung, C. Whitten-Bauer, S. Wieland and F. V. Chisari (2012). "Short-range exosomal transfer of viral RNA from infected cells to plasmacytoid dendritic cells triggers innate immunity." Cell Host Microbe **12**(4): 558-570.

Dubey, S., Z. Chen, A. Talis, A. Molotkov, A. Ali, A. Mintz and F. Momen-Heravi (2023). "An exosome-based gene delivery platform for cell-specific CRISPR/Cas9 genome editing." bioRxiv: 2023.2006.2009.542202.

Eckhardt, C. M., A. A. Baccarelli and H. Wu (2022). "Environmental Exposures and Extracellular Vesicles: Indicators of Systemic Effects and Human Disease." Curr Environ Health Rep **9**(3): 465-476.

Escrevente, C., S. Keller, P. Altevogt and J. Costa (2011). "Interaction and uptake of exosomes by ovarian cancer cells." BMC cancer **11**: 1-10.

Fan, Y., Z. Chen and M. Zhang (2022). "Role of exosomes in the pathogenesis, diagnosis, and treatment of central nervous system diseases." Journal of Translational Medicine **20**(1): 291.

French, K. C., M. A. Antonyak and R. A. Cerione (2017). Extracellular vesicle docking at the cellular port: Extracellular vesicle binding and uptake. Seminars in cell & developmental biology, Elsevier.

 doi:10.20944/preprints202602.1440.v1

Fu, S., Y. Wang, X. Xia and J. C. Zheng (2020). "Exosome engineering: Current progress in cargo loading and targeted delivery." NanoImpact **20**: 100261.

Gao, W., X. Wang, Y. Si, J. Pang, H. Liu, S. Li, Q. Ding and Y. Wang (2021). "Exosome derived from ADSCs attenuates ultraviolet B-mediated photoaging in human dermal fibroblasts." Photochemistry and photobiology **97**(4): 795-804.

Gao, W., L.-m. Yuan, Y. Zhang, F.-z. Huang, F. Gao, J. Li, F. Xu, H. Wang and Y.-s. Wang (2023). "miR-1246-overexpressing exosomes suppress UVB-induced photoaging via regulation of TGF-β/Smad and attenuation of MAPK/AP-1 pathway." Photochemical & Photobiological Sciences **22**(1): 135-146.

Gao, W., Y. Zhang, L. Yuan, F. Huang and Y. S. Wang (2023). "Long Non-coding RNA H19-Overexpressing Exosomes Ameliorate UVB-Induced Photoaging by Upregulating SIRT1 Via Sponging miR-138." Photochem Photobiol **99**(6): 1456-1467.

Geng, Y., X. Long, Y. Zhang, Y. Wang, G. You, W. Guo, G. Zhuang, Y. Zhang, X. Cheng, Z. Yuan and J. Zan (2023). "FTO-targeted siRNA delivery by MSC-derived exosomes synergistically alleviates dopaminergic neuronal death in Parkinson's disease via m6A-dependent regulation of ATM mRNA." Journal of Translational Medicine **21**(1): 652.

Göran Ronquist, K. (2019). "Extracellular vesicles and energy metabolism." Clinica Chimica Acta **488**: 116-121.

Greco, K. A., C. A. Franzen, K. E. Foreman, R. C. Flanigan, P. C. Kuo and G. N. Gupta (2016). "PLK-1 silencing in bladder cancer by siRNA delivered with exosomes." Urology **91**: 241. e241-241. e247.

Guo, T., Y. Wang, J. Jia, X. Mao, E. Stankiewicz, G. Scandura, E. Burke, L. Xu, J. Marzec, C. R. Davies, J. J. Lu, P. Rajan, A. Grey, K. Tipples, J. Hines, S. Kudahetti, T. Oliver, T. Powles, C. Alifrangis, M. Kohli, G. Shaw, W. Wang, N. Feng, J. Shamash, D. Berney, L. Wang and Y.-J. Lu (2021). "The Identification of Plasma Exosomal miR-423-3p as a Potential Predictive Biomarker for Prostate Cancer Castration-Resistance Development by Plasma Exosomal miRNA Sequencing." Frontiers in Cell and Developmental Biology **8**.

Hajialiasgary Najafabadi, A., M. H. Soheilifar and N. Masoudi-Khoram (2024). "Exosomes in skin photoaging: biological functions and therapeutic opportunity." Cell Commun Signal **22**(1): 32.

Ham, S., L. G. Lima, E. P. Z. Chai, A. Muller, R. J. Lobb, S. Krumeich, S. W. Wen, A. P. Wiegmans and A. Möller (2018). "Breast Cancer-Derived Exosomes Alter Macrophage Polarization via gp130/STAT3 Signaling." Front Immunol **9**: 871.

Han, Q., Q. R. Xie, F. Li, Y. Cheng, T. Wu, Y. Zhang, X. Lu, A. S. Wong, J. Sha and W. Xia (2021). "Targeted inhibition of SIRT6 via engineered exosomes impairs tumorigenesis and metastasis in prostate cancer." Theranostics **11**(13): 6526.

Hannafon, B. N., Y. D. Trigoso, C. L. Calloway, Y. D. Zhao, D. H. Lum, A. L. Welm, Z. J. Zhao, K. E. Blick, W. C. Dooley and W. Ding (2016). "Plasma exosome microRNAs are indicative of breast cancer." Breast cancer research **18**: 1-14.

Hao, Y., D. Baker and P. ten Dijke (2019). "TGF-β-Mediated Epithelial-Mesenchymal Transition and Cancer Metastasis." International Journal of Molecular Sciences **20**(11): 2767.

Harada, T., H. Yamamoto, S. Kishida, M. Kishida, C. Awada, T. Takao and A. Kikuchi (2017). "Wnt5b-associated exosomes promote cancer cell migration and proliferation." Cancer science **108**(1): 42-52.

Harrell, C. R., V. Djonov, A. Volarevic, A. Arsenijevic and V. Volarevic (2024). "Molecular mechanisms responsible for the therapeutic potential of mesenchymal stem cell-derived exosomes in the treatment of lung fibrosis." International Journal of Molecular Sciences **25**(8): 4378.

He, X., Z. Dong, Y. Cao, H. Wang, S. Liu, L. Liao, Y. Jin, L. Yuan and B. Li (2019). "MSC-derived exosome promotes M2 polarization and enhances cutaneous wound healing." Stem cells international **2019**(1): 7132708.

Hu, J. L., W. Wang, X. L. Lan, Z. C. Zeng, Y. S. Liang, Y. R. Yan, F. Y. Song, F. F. Wang, X. H. Zhu, W. J. Liao, W. T. Liao, Y. Q. Ding and L. Liang (2019). "CAFs secreted exosomes promote metastasis and chemotherapy resistance by enhancing cell stemness and epithelial-mesenchymal transition in colorectal cancer." Mol Cancer **18**(1): 91.

Hu, S., Z. Li, J. Cores, K. Huang, T. Su, P.-U. Dinh and K. Cheng (2019). "Needle-free injection of exosomes derived from human dermal fibroblast spheroids ameliorates skin photoaging." ACS nano **13**(10): 11273-11282.

 doi:10.20944/preprints202602.1440.v1

Hu, Y., R. Tao, L. Chen, Y. Xiong, H. Xue, L. Hu, C. Yan, X. Xie, Z. Lin and A. C. Panayi (2021). "Exosomes derived from pioglitazone-pretreated MSCs accelerate diabetic wound healing through enhancing angiogenesis." Journal of nanobiotechnology **19**(1): 150.

Huang, Y., L. Chen, Z. Feng, W. Chen, S. Yan, R. Yang, J. Xiao, J. Gao, D. Zhang and X. Ke (2021). "EPC-derived exosomal miR-1246 and miR-1290 regulate phenotypic changes of fibroblasts to endothelial cells to exert protective effects on myocardial infarction by targeting ELF5 and SP1." Frontiers in cell and developmental biology **9**: 647763.

Izquierdo-Useros, N., M. Lorizate, M. C. Puertas, M. T. Rodriguez-Plata, N. Zangger, E. Erikson, M. Pino, I. Erkizia, B. Glass, B. Clotet, O. T. Keppler, A. Telenti, H. G. Kräusslich and J. Martinez-Picado (2012). "Siglec-1 is a novel dendritic cell receptor that mediates HIV-1 trans-infection through recognition of viral membrane gangliosides." PLoS Biol **10**(12): e1001448.

Janas, T., M. M. Janas, K. Sapoń and T. Janas (2015). "Mechanisms of RNA loading into exosomes." FEBS Lett **589**(13): 1391-1398.

Jia, Z., H. Zhu, H. Sun, Y. Hua, G. Zhang, J. Jiang and X. Wang (2020). "Adipose mesenchymal stem cell-derived exosomal microRNA-1236 reduces resistance of breast cancer cells to cisplatin by suppressing SLC9A1 and the Wnt/β-catenin signaling." Cancer Management and Research: 8733-8744.

Jiang, M., K. Zhang, Z. Zhang, X. Zeng, Z. Huang, P. Qin, Z. Xie, X. Cai, M. Ashrafizadeh and Y. Tian (2025). "PI3K/AKT/mTOR Axis in Cancer: From Pathogenesis to Treatment." MedComm **6**(8): e70295.

Jiang, S., H. Chen, K. He and J. Wang (2022). "Human bone marrow mesenchymal stem cells-derived exosomes attenuated prostate cancer progression via the miR-99b-5p/IGF1R axis." Bioengineered **13**(2): 2004-2016.

Jiang, S., C. Mo, S. Guo, J. Zhuang, B. Huang and X. Mao (2019). "Human bone marrow mesenchymal stem cells-derived microRNA-205-containing exosomes impede the progression of prostate cancer through suppression of RHPN2." Journal of Experimental & Clinical Cancer Research **38**: 1-16.

Kaban, K., C. Hinterleitner, Y. Zhou, E. Salva, A. G. Kantarci, H. R. Salih and M. Maerklin (2021). "Therapeutic silencing of BCL-2 using NK cell-derived exosomes as a novel therapeutic approach in breast cancer." Cancers **13**(10): 2397.

Kalamvoki, M., T. Du and B. Roizman (2014). "Cells infected with herpes simplex virus 1 export to uninfected cells exosomes containing STING, viral mRNAs, and microRNAs." Proc Natl Acad Sci U S A **111**(46): E4991-4996.

Kalluri, R. and V. S. LeBleu (2020). "The biology, function, and biomedical applications of exosomes." science **367**(6478): eaau6977.

Kamerkar, S., V. S. LeBleu, H. Sugimoto, S. Yang, C. F. Ruivo, S. A. Melo, J. J. Lee and R. Kalluri (2017). "Exosomes facilitate therapeutic targeting of oncogenic KRAS in pancreatic cancer." Nature **546**(7659): 498-503.

Khadka, A., J. G. Spiers, L. Cheng and A. F. Hill (2023). "Extracellular vesicles with diagnostic and therapeutic potential for prion diseases." Cell and Tissue Research **392**(1): 247-267.

Khan, M. I., E. S. Jeong, M. Z. Khan, J. H. Shin and J. D. Kim (2023). "Stem cells-derived exosomes alleviate neurodegeneration and Alzheimer's pathogenesis by ameliorating neuroinflamation, and regulating the associated molecular pathways." Sci Rep **13**(1): 15731.

Khan, S. U., M. I. Khan, M. U. Khan, N. M. Khan, S. Bungau and S. S. u. Hassan (2022). "Applications of extracellular vesicles in nervous system disorders: An overview of recent advances." Bioengineering **10**(1): 51.

Kim, G., M. Kim, Y. Lee, J. W. Byun, D. W. Hwang and M. Lee (2020). "Systemic delivery of microRNA-21 antisense oligonucleotides to the brain using T7-peptide decorated exosomes." Journal of Controlled Release **317**: 273-281.

Kim, H., D. W. Kim and J.-Y. Cho (2019). "Exploring the key communicator role of exosomes in cancer microenvironment through proteomics." Proteome science **17**(1): 5.

Kim, H. I., J. Park, Y. Zhu, X. Wang, Y. Han and D. Zhang (2024). "Recent advances in extracellular vesicles for therapeutic cargo delivery." Experimental & Molecular Medicine **56**(4): 836-849.

Kim, S. M., Y. Yang, S. J. Oh, Y. Hong, M. Seo and M. Jang (2017). "Cancer-derived exosomes as a delivery platform of CRISPR/Cas9 confer cancer cell tropism-dependent targeting." Journal of Controlled Release **266**: 8-16.

 doi:10.20944/preprints202602.1440.v1

Kim, Y.-J., S. mi Yoo, H. H. Park, H. J. Lim, Y.-L. Kim, S. Lee, K.-W. Seo and K.-S. Kang (2017). "Exosomes derived from human umbilical cord blood mesenchymal stem cells stimulates rejuvenation of human skin." Biochemical and Biophysical Research Communications **493**(2): 1102-1108.

Koenig, M. (2015). "Phosphoribosylphosphate and phosphoribosylnicotinate pairing with phosphoribosylamine at the origin of the RNA world." Journal of Theoretical Biology **379**: 94-97.

Kuang, L., L. Wu and Y. Li (2025). "Extracellular vesicles in tumor immunity: mechanisms and novel insights." Molecular Cancer **24**(1): 45.

LeBleu, V. S. and R. Kalluri (2020). "Exosomes as a multicomponent biomarker platform in cancer." Trends in cancer **6**(9): 767-774.

Lee, J. H., C. Kim, S. H. Baek, J. H. Ko, S. G. Lee, W. M. Yang, J. Y. Um, G. Sethi and K. S. Ahn (2017). "Capsazepine inhibits JAK/STAT3 signaling, tumor growth, and cell survival in prostate cancer." Oncotarget **8**(11): 17700-17711.

Lee, J. H., J. Lötvall and B. S. Cho (2023). "The anti-inflammatory effects of adipose tissue mesenchymal stem cell exosomes in a mouse model of inflammatory bowel disease." International Journal of Molecular Sciences **24**(23): 16877.

Lee, K. S., J. Lee, H. K. Kim, S. H. Yeom, C. H. Woo, Y. J. Jung, Y. E. Yun, S. Y. Park, J. Han and E. Kim (2021). "Extracellular vesicles from adipose tissue-derived stem cells alleviate osteoporosis through osteoprotegerin and miR-21-5p." Journal of extracellular vesicles **10**(12): e12152.

Li, B., Y. Chen, Y. Zhou, X. Feng, G. Gu, S. Han, N. Cheng, Y. Sun, Y. Zhang, J. Cheng, Q. Zhang, W. Zhang and J. Liu (2024). "Neural stem cell-derived exosomes promote mitochondrial biogenesis and restore abnormal protein distribution in a mouse model of Alzheimer's disease." Neural Regen Res **19**(7): 1593-1601.

Li, B., H. Tang, X. Bian, K. Ma, J. Chang, X. Fu and C. Zhang (2021). "Calcium silicate accelerates cutaneous wound healing with enhanced re-epithelialization through EGF/EGFR/ERK-mediated promotion of epidermal stem cell functions." Burns & Trauma **9**.

Li, C., T. Qin, Y. Jin, J. Hu, F. Yuan, Y. Cao and C. Duan (2023). "Cerebrospinal fluid-derived extracellular vesicles after spinal cord injury promote vascular regeneration via PI3K/AKT signaling pathway." Journal of Orthopaedic Translation **39**: 124-134.

Li, F., Z. Xu, Z. Xie, X. Sun, C. Li, Y. Chen, J. Xu and G. Pi (2023). "Adipose mesenchymal stem cells-derived exosomes alleviate osteoarthritis by transporting microRNA-376c-3p and targeting the WNT-beta-catenin signaling axis." Apoptosis **28**(3): 362-378.

Li, J., J. Wang and Z. Chen (2025). "Emerging role of exosomes in cancer therapy: progress and challenges." Mol Cancer **24**(1): 13.

Li, T., X. Li, G. Han, M. Liang, Z. Yang, C. Zhang, S. Huang, S. Tai and S. Yu (2022). "The Therapeutic Potential and Clinical Significance of Exosomes as Carriers of Drug Delivery System." Pharmaceutics **15**(1).

Li, Y., J. Zhang, J. Shi, K. Liu, X. Wang, Y. Jia, T. He, K. Shen, Y. Wang and J. Liu (2021). "Exosomes derived from human adipose mesenchymal stem cells attenuate hypertrophic scar fibrosis by miR-192-5p/IL-17RA/Smad axis." Stem Cell Research & Therapy **12**(1): 221.

Li, Y., Q. Zheng, C. Bao, S. Li, W. Guo, J. Zhao, D. Chen, J. Gu, X. He and S. Huang (2015). "Circular RNA is enriched and stable in exosomes: a promising biomarker for cancer diagnosis." Cell research **25**(8): 981-984.

Li, Z., L. Yang, H. Wang, D. W. Binzel, T. M. Williams and P. Guo (2021). "Non-small-cell lung cancer regression by siRNA delivered through exosomes that display EGFR RNA aptamer." Nucleic acid therapeutics **31**(5): 364-374.

Liang, G., K. Shu, Z. Yanliang, F. Shuying, F. Wenpo and S. and Gao (2018). "Engineered exosome-mediated delivery of functionally active miR-26a and its enhanced suppression effect in HepG2 cells." International Journal of Nanomedicine **13**(null): 585-599.

Liang, Q., D. Zhou, X. Ge, P. Song, W. Chu, J. Xu and Y. Shen (2024). "Exosomes from adipose-derived mesenchymal stem cell improve diabetic wound healing and inhibit fibrosis via miR-128-1-5p/TGF-β1/Smad axis." Molecular and Cellular Endocrinology **588**: 112213.

Liang, Y., L. Duan, J. Lu and J. Xia (2021). "Engineering exosomes for targeted drug delivery." Theranostics **11**(7): 3183.

 doi:10.20944/preprints202602.1440.v1

Liao, W., Y. Ning, H.-J. Xu, W.-Z. Zou, J. Hu, X.-Z. Liu, Y. Yang and Z.-H. Li (2019). "BMSC-derived exosomes carrying microRNA-122-5p promote proliferation of osteoblasts in osteonecrosis of the femoral head." Clinical Science **133**(18): 1955-1975.

Lin, D., H. Zhang, R. Liu, T. Deng, T. Ning, M. Bai, Y. Yang, K. Zhu, J. Wang and J. Duan (2021). "iRGD-modified exosomes effectively deliver CPT1A siRNA to colon cancer cells, reversing oxaliplatin resistance by regulating fatty acid oxidation." Molecular oncology **15**(12): 3430-3446.

Lin, Y., J. D. Anderson, L. M. A. Rahnama, S. V. Gu and A. A. Knowlton (2020). "Exosomes in disease and regeneration: biological functions, diagnostics, and beneficial effects." Am J Physiol Heart Circ Physiol **319**(6): H1162-h1180.

Liu, J., F. Gao, D. Wang, R. Zhou and C. Huang (2025). "Effects and mechanisms of exosomes in microenvironment angiogenesis in breast cancer: An updated review." Oncology Research **33**(6): 1323.

Liu, W., M. Yu, D. Xie, L. Wang, C. Ye, Q. Zhu, F. Liu and L. Yang (2020). "Melatonin-stimulated MSC-derived exosomes improve diabetic wound healing through regulating macrophage M1 and M2 polarization by targeting the PTEN/AKT pathway." Stem cell research & therapy **11**(1): 259.

Liu, Y.-J. and C. Wang (2023). "A review of the regulatory mechanisms of extracellular vesicles-mediated intercellular communication." Cell Communication and Signaling **21**(1): 77.

Liu, Y., S. Liao, S. Bennett, H. Tang, D. Song, D. Wood, X. Zhan and J. Xu (2021). "STAT3 and its targeting inhibitors in osteosarcoma." Cell Prolif **54**(2): e12974.

Liu, Y., Z. Sheng and L. Sun (2024). "Exosomes derived from hTERT-immortalized cells delay cellular senescence of human fibroblasts." Experimental Gerontology **194**: 112508.

Lou, G., L. Chen, C. Xia, W. Wang, J. Qi, A. Li, L. Zhao, Z. Chen, M. Zheng and Y. Liu (2020). "MiR-199a-modified exosomes from adipose tissue-derived mesenchymal stem cells improve hepatocellular carcinoma chemosensitivity through mTOR pathway." Journal of Experimental & Clinical Cancer Research **39**(1): 4.

Lu, G.-d., P. Cheng, T. Liu and Z. Wang (2020). "BMSC-derived exosomal miR-29a promotes angiogenesis and osteogenesis." Frontiers in cell and developmental biology **8**: 608521.

Luther, K. M., L. Haar, M. McGuinness, Y. Wang, T. L. Lynch IV, A. Phan, Y. Song, Z. Shen, G. Gardner and G. Kuffel (2018). "Exosomal miR-21a-5p mediates cardioprotection by mesenchymal stem cells." Journal of molecular and cellular cardiology **119**: 125-137.

Ma, R., Z. Liang, X. Shi, L. Xu, X. Li, J. Wu, L. Zhao and G. Liu (2021). "Exosomal miR-486-5p derived from human placental microvascular endothelial cells regulates proliferation and invasion of trophoblasts via targeting IGF1." Human Cell **34**(5): 1310-1323.

Ma, Z., L. Z. Wang, J.-T. Cheng, W. S. T. Lam, X. Ma, X. Xiang, A. L.-A. Wong, B. C. Goh, Q. Gong and G. Sethi (2021). "Targeting hypoxia-inducible factor-1-mediated metastasis for cancer therapy." Antioxidants & redox signaling **34**(18): 1484-1497.

Malekpour, K., A. Hazrati, M. Zahar, A. Markov, A. O. Zekiy, J. G. Navashenaq, L. Roshangar and M. Ahmadi (2022). "The potential use of mesenchymal stem cells and their derived exosomes for orthopedic diseases treatment." Stem cell reviews and reports **18**(3): 933-951.

Mao, Y., V. Jacob, A. Singal, S. Lei, M. S. Park, M. R. Lima, C. Li, S. Dhall, M. Sathyamoorthy and J. Kohn (2021). "Exosomes secreted from amniotic membrane contribute to its anti-fibrotic activity." International journal of molecular sciences **22**(4): 2055.

Mashouri, L., H. Yousefi, A. R. Aref, A. m. Ahadi, F. Molaei and S. K. Alahari (2019). "Exosomes: composition, biogenesis, and mechanisms in cancer metastasis and drug resistance." Molecular cancer **18**: 1-14.

McGough, I. J. and J.-P. Vincent (2016). "Exosomes in developmental signalling." Development **143**(14): 2482-2493.

Meckes, D. G., Jr. and N. Raab-Traub (2011). "Microvesicles and viral infection." J Virol **85**(24): 12844-12854.

Mehdizadeh, S., M. Mamaghani, S. Hassanikia, Y. Pilehvar and Y. N. Ertas (2025). "Exosome-powered neuropharmaceutics: unlocking the blood-brain barrier for next-gen therapies." Journal of Nanobiotechnology **23**(1): 329.

Meldolesi, J. (2018). "Exosomes and Ectosomes in Intercellular Communication." Current Biology **28**(8): R435-R444.

 doi:10.20944/preprints202602.1440.v1

Mineo, M., S. H. Garfield, S. Taverna, A. Flugy, G. De Leo, R. Alessandro and E. C. Kohn (2012). "Exosomes released by K562 chronic myeloid leukemia cells promote angiogenesis in a Src-dependent fashion." Angiogenesis **15**: 33-45.

Mohan, C. D., S. Rangappa, S. C. Nayak, G. Sethi and K. S. Rangappa (2021). "Paradoxical functions of long noncoding RNAs in modulating STAT3 signaling pathway in hepatocellular carcinoma." Biochimica et Biophysica Acta (BBA)-Reviews on Cancer **1876**(1): 188574.

Moraes, L. A., S. Kar, S. L. Foo, T. Gu, Y. Q. Toh, P. B. Ampomah, K. Sachaphibulkij, G. Yap, O. Zharkova and H. M. Lukman (2017). "Annexin-A1 enhances breast cancer growth and migration by promoting alternative macrophage polarization in the tumour microenvironment." Scientific reports **7**(1): 17925.

Ning, H., H. Chen, J. Deng, C. Xiao, M. Xu, L. Shan, C. Yang and Z. Zhang (2021). "Exosomes secreted by FNDC5-BMMSCs protect myocardial infarction by anti-inflammation and macrophage polarization via NF-κB signaling pathway and Nrf2/HO-1 axis." Stem Cell Research & Therapy **12**(1): 519.

Nour, A. M., Y. Li, J. Wolenski and Y. Modis (2013). "Viral membrane fusion and nucleocapsid delivery into the cytoplasm are distinct events in some flaviviruses." PLoS Pathog **9**(9): e1003585.

Novoa Díaz, M. B., M. J. Martín and C. Gentili (2022). "Tumor microenvironment involvement in colorectal cancer progression via Wnt/β-catenin pathway: Providing understanding of the complex mechanisms of chemoresistance." World J Gastroenterol **28**(26): 3027-3046.

Ogata-Kawata, H., M. Izumiya, D. Kurioka, Y. Honma, Y. Yamada, K. Furuta, T. Gunji, H. Ohta, H. Okamoto and H. Sonoda (2014). "Circulating exosomal microRNAs as biomarkers of colon cancer." PloS one **9**(4): e92921.

Oh, M., J. Lee, Y. J. Kim, W. J. Rhee and J. H. Park (2018). "Exosomes derived from human induced pluripotent stem cells ameliorate the aging of skin fibroblasts." International journal of molecular sciences **19**(6): 1715.

Ohno, S.-i., M. Takanashi, K. Sudo, S. Ueda, A. Ishikawa, N. Matsuyama, K. Fujita, T. Mizutani, T. Ohgi and T. Ochiya (2013). "Systemically injected exosomes targeted to EGFR deliver antitumor microRNA to breast cancer cells." Molecular therapy **21**(1): 185-191.

Okoye, I. S., S. M. Coomes, V. S. Pelly, S. Czieso, V. Papayannopoulos, T. Tolmachova, M. C. Seabra and M. S. Wilson (2014). "MicroRNA-containing T-regulatory-cell-derived exosomes suppress pathogenic T helper 1 cells." Immunity **41**(1): 89-103.

Osaid, Z., M. Haider, R. Hamoudi and R. Harati (2023). "Exosomes Interactions with the Blood-Brain Barrier: Implications for Cerebral Disorders and Therapeutics." Int J Mol Sci **24**(21).

Pan, C., X. Wang, K. Shi, Y. Zheng, J. Li, Y. Chen, L. Jin and Z. Pan (2016). "MiR-122 reverses the doxorubicin-resistance in hepatocellular carcinoma cells through regulating the tumor metabolism." PloS one **11**(5): e0152090.

Patel, G. K., M. A. Khan, A. Bhardwaj, S. K. Srivastava, H. Zubair, M. C. Patton, S. Singh, M. Khushman and A. P. Singh (2017). "Exosomes confer chemoresistance to pancreatic cancer cells by promoting ROS detoxification and miR-155-mediated suppression of key gemcitabine-metabolising enzyme, DCK." Br J Cancer **116**(5): 609-619.

Pei, X., X. Zhang, L. Zhang, M. Yuan, L. Sun, F. Yu, B. Wang, J. Zhao, H. He and V. C. Yang (2021). "Targeted exosomes for co-delivery of siFGL1 and siTGF-β1 trigger combined cancer immunotherapy by remodeling immunosuppressive tumor microenvironment." Chemical Engineering Journal **421**: 129774.

Pofali, P., A. Mondal and V. Londhe (2020). "Exosome as a Natural Gene Delivery Vector for Cancer Treatment." Curr Cancer Drug Targets **20**(11): 821-830.

Qian, L., L. Pi, B.-R. Fang and X.-X. Meng (2021). "Adipose mesenchymal stem cell-derived exosomes accelerate skin wound healing via the lncRNA H19/miR-19b/SOX9 axis." Laboratory Investigation **101**(9): 1254-1266.

Qiu, X., J. Liu, C. Zheng, Y. Su, L. Bao, B. Zhu, S. Liu, L. Wang, X. Wang and Y. Wang (2020). "Exosomes released from educated mesenchymal stem cells accelerate cutaneous wound healing via promoting angiogenesis." Cell Proliferation **53**(8): e12830.

Ragusa, M., C. Barbagallo, L. Statello, R. Caltabiano, A. Russo, L. Puzzo, T. Avitabile, A. Longo, M. D. Toro and D. Barbagallo (2015). "miRNA profiling in vitreous humor, vitreal exosomes and serum from uveal melanoma patients: Pathological and diagnostic implications." Cancer biology & therapy **16**(9): 1387-1396.

 doi:10.20944/preprints202602.1440.v1

Rajagopal, C. and K. Harikumar (2018). "The origin and functions of exosomes in cancer." Frontiers in oncology **8**: 66.

Rajendran, L., M. Honsho, T. R. Zahn, P. Keller, K. D. Geiger, P. Verkade and K. Simons (2006). "Alzheimer's disease beta-amyloid peptides are released in association with exosomes." Proc Natl Acad Sci U S A **103**(30): 11172-11177.

Ramakrishnaiah, V., C. Thumann, I. Fofana, F. Habersetzer, Q. Pan, P. E. de Ruiter, R. Willemsen, J. A. Demmers, V. Stalin Raj, G. Jenster, J. Kwekkeboom, H. W. Tilanus, B. L. Haagmans, T. F. Baumert and L. J. van der Laan (2013). "Exosome-mediated transmission of hepatitis C virus between human hepatoma Huh7.5 cells." Proc Natl Acad Sci U S A **110**(32): 13109-13113.

Raposo, G., H. W. Nijman, W. Stoorvogel, R. Liejendekker, C. V. Harding, C. Melief and H. J. Geuze (1996). "B lymphocytes secrete antigen-presenting vesicles." The Journal of experimental medicine **183**(3): 1161-1172.

Rasti, Z., R. Afrisham, E. Bahrami Vahdat, Z. Kashanikhatib, S. H. Mousavi and S. Alizadeh (2024). "The Influence of Circulating Exosomes Derived From Younger and Older Donors on Hypoxia-Inducible Factor 1 Alpha Gene Expression and P21 Protein in Cord Blood Hematopoietic Stem Cells." J Hematol **13**(5): 192-199.

Ren, R., H. Sun, C. Ma, J. Liu and H. Wang (2019). "Colon cancer cells secrete exosomes to promote self-proliferation by shortening mitosis duration and activation of STAT3 in a hypoxic environment." Cell Biosci **9**: 62.

Ren, S., J. Chen, J. Guo, Y. Liu, H. Xiong, B. Jing, X. Yang, G. Li, Y. Kang and C. Wang (2022). "Exosomes from adipose stem cells promote diabetic wound healing through the eHSP90/LRP1/AKT axis." Cells **11**(20): 3229.

Rezaei, R., K. Baghaei, D. Amani, A. Piccin, S. M. Hashemi, H. A. Aghdaei and M. R. Zali (2021). "Exosome-mediated delivery of functionally active miRNA-375-3p mimic regulate epithelial mesenchymal transition (EMT) of colon cancer cells." Life sciences **269**: 119035.

Sadeghi, S., F. R. Tehrani, S. Tahmasebi, A. Shafiee and S. M. Hashemi (2023). "Exosome engineering in cell therapy and drug delivery." Inflammopharmacology **31**(1): 145-169.

Saka, O. M., D. D. Dora, G. Kibar and A. Tevlek (2025). "Expanding the role of exosomes in drug, biomolecule, and nanoparticle delivery." Life Sci **368**: 123499.

Santangelo, A., P. Imbrucè, B. Gardenghi, L. Belli, R. Agushi, A. Tamanini, S. Munari, A. M. Bossi, I. Scambi, D. Benati, R. Mariotti, G. Di Gennaro, A. Sbarbati, A. Eccher, G. K. Ricciardi, E. M. Ciceri, F. Sala, G. Pinna, G. Lippi, G. Cabrini and M. C. Dechecchi (2018). "A microRNA signature from serum exosomes of patients with glioma as complementary diagnostic biomarker." Journal of Neuro-Oncology **136**(1): 51-62.

Serrenho, I., S. A. Ferreira and G. Baltazar (2024). "Preconditioning of MSCs for Acute Neurological Conditions: From Cellular to Functional Impact—A Systematic Review." Cells **13**(10): 845.

Sha, S., X. Shen, Y. Cao and L. Qu (2021). "Mesenchymal stem cells-derived extracellular vesicles ameliorate Alzheimer's disease in rat models via the microRNA-29c-3p/BACE1 axis and the Wnt/β-catenin pathway." Aging (Albany NY) **13**(11): 15285.

Sharma, M., A. K. Tanwar, P. K. Purohit, P. Pal, D. Kumar, S. Vaidya, S. K. Prajapati, A. Kumar, N. Dhama and S. Kumar (2024). "Regulatory roles of microRNAs in modulating mitochondrial dynamics, amyloid beta fibrillation, microglial activation, and cholinergic signaling: implications for alzheimer's disease pathogenesis." Neuroscience & Biobehavioral Reviews: 105685.

Shen, H. and R. A. Lane (2023). "Extracellular vesicles from primed adipose-derived stem cells enhance Achilles tendon repair by reducing inflammation and promoting intrinsic healing." Stem Cells **41**(6): 617-627.

Shen, T., Z. Huang, C. Shi, X. Pu, X. Xu, Z. Wu, G. Ding and L. Cao (2020). "Pancreatic cancer-derived exosomes induce apoptosis of T lymphocytes through the p38 MAPK-mediated endoplasmic reticulum stress." Faseb j **34**(6): 8442-8458.

Smalheiser, N. R. (2007). "Exosomal transfer of proteins and RNAs at synapses in the nervous system." Biology direct **2**: 1-15.

Soria, F. N., O. Pampliega, M. Bourdenx, W. G. Meissner, E. Bezard and B. Dehay (2017). "Exosomes, an unmasked culprit in neurodegenerative diseases." Frontiers in neuroscience **11**: 26.

 doi:10.20944/preprints202602.1440.v1

Sreeraj, H., R. AnuKiruthika, K. S. Tamilselvi and D. Subha (2024). "Exosomes for skin treatment: Therapeutic and cosmetic applications." Nano TransMed **3**: 100048.

Stahl, P. D. and G. Raposo (2019). "Extracellular vesicles: exosomes and microvesicles, integrators of homeostasis." Physiology **34**(3): 169-177.

Stuffers, S., C. Sem Wegner, H. Stenmark and A. Brech (2009). "Multivesicular endosome biogenesis in the absence of ESCRTs." Traffic **10**(7): 925-937.

Sun, J., H. Shen, L. Shao, X. Teng, Y. Chen, X. Liu, Z. Yang and Z. Shen (2020). "HIF-1α overexpression in mesenchymal stem cell-derived exosomes mediates cardioprotection in myocardial infarction by enhanced angiogenesis." Stem cell research & therapy **11**(1): 373.

Sun, L., W. Zhu, P. Zhao, Q. Wang, B. Fan, Y. Zhu, Y. Lu, Q. Chen, J. Zhang and F. Zhang (2020). "Long noncoding RNA UCA1 from hypoxia-conditioned hMSC-derived exosomes: a novel molecular target for cardioprotection through miR-873-5p/XIAP axis." Cell death & disease **11**(8): 696.

Sun, T., Z. Liu and Q. Yang (2020). "The role of ubiquitination and deubiquitination in cancer metabolism." Molecular cancer **19**(1): 146.

Sutter, P. A., M. E. Rouillard, S. A. Alshawi and S. J. Crocker (2021). "Extracellular matrix influences astrocytic extracellular vesicle function in wound repair." Brain Research **1763**: 147462.

Szwedowicz, U., Z. Łapińska, A. Gajewska-Naryniecka and A. Choromańska (2022). "Exosomes and Other Extracellular Vesicles with High Therapeutic Potential: Their Applications in Oncology, Neurology, and Dermatology." Molecules **27**(4): 1303.

Takahashi, A., R. Okada, K. Nagao, Y. Kawamata, A. Hanyu, S. Yoshimoto, M. Takasugi, S. Watanabe, M. T. Kanemaki, C. Obuse and E. Hara (2017). "Exosomes maintain cellular homeostasis by excreting harmful DNA from cells." Nature Communications **8**(1): 15287.

Tao, S.-C., S.-C. Guo, M. Li, Q.-F. Ke, Y.-P. Guo and C.-Q. Zhang (2017). "Chitosan wound dressings incorporating exosomes derived from microRNA-126-overexpressing synovium mesenchymal stem cells provide sustained release of exosomes and heal full-thickness skin defects in a diabetic rat model." Stem cells translational medicine **6**(3): 736-747.

Taylor, D. D. and C. Gercel-Taylor (2008). RETRACTED: MicroRNA signatures of tumor-derived exosomes as diagnostic biomarkers of ovarian cancer, Elsevier.

Theodoraki, M.-N., S. S. Yerneni, T. K. Hoffmann, W. E. Gooding and T. L. Whiteside (2018). "Clinical significance of PD-L1+ exosomes in plasma of head and neck cancer patients." Clinical cancer research **24**(4): 896-905.

Ti, D., H. Hao, C. Tong, J. Liu, L. Dong, J. Zheng, Y. Zhao, H. Liu, X. Fu and W. Han (2015). "LPS-preconditioned mesenchymal stromal cells modify macrophage polarization for resolution of chronic inflammation via exosome-shuttled let-7b." Journal of translational medicine **13**(1): 308.

Vader, P., E. A. Mol, G. Pasterkamp and R. M. Schiffelers (2016). "Extracellular vesicles for drug delivery." Advanced drug delivery reviews **106**: 148-156.

Vafaei, S., M. Mansoori, F. Hashemi and M. Basiri (2022). "Exosome odyssey to original line in dental regeneration." Journal of Oral Biosciences **64**(3): 271-278.

van Dongen, H. M., N. Masoumi, K. W. Witwer and D. M. Pegtel (2016). "Extracellular Vesicles Exploit Viral Entry Routes for Cargo Delivery." Microbiol Mol Biol Rev **80**(2): 369-386.

Villarroya-Beltri, C., C. Gutiérrez-Vázquez, F. Sánchez-Cabo, D. Pérez-Hernández, J. Vázquez, N. Martin-Cofreces, D. J. Martinez-Herrera, A. Pascual-Montano, M. Mittelbrunn and F. Sánchez-Madrid (2013). "Sumoylated hnRNPA2B1 controls the sorting of miRNAs into exosomes through binding to specific motifs." Nat Commun **4**: 2980.

Votteler, J. and W. I. Sundquist (2013). "Virus budding and the ESCRT pathway." Cell host & microbe **14**(3): 232-241.

Wallen, M., F. Aqil, W. Spencer and R. C. Gupta (2023). "Exosomes as an Emerging Plasmid Delivery Vehicle for Gene Therapy." Pharmaceutics **15**(7).

Wang, B., X. Wang, D. Hou, Q. Huang, W. Zhan, C. Chen, J. Liu, R. You, J. Xie, P. Chen and H. Huang (2019). "Exosomes derived from acute myeloid leukemia cells promote chemoresistance by enhancing glycolysis-mediated vascular remodeling." J Cell Physiol **234**(7): 10602-10614.

 doi:10.20944/preprints202602.1440.v1

Wang, B., Y. Wang, Z. Yan, Y. Sun and C. Su (2019). "Colorectal cancer cell-derived exosomes promote proliferation and decrease apoptosis by activating the ERK pathway." Int J Clin Exp Pathol **12**(7): 2485-2495.

Wang, C.-C., X.-M. Hu, Y.-F. Long, H.-R. Huang, Y. He, Z.-R. Xu and Z.-Q. Qi (2024). "Treatment of Parkinson's disease model with human umbilical cord mesenchymal stem cell-derived exosomes loaded with BDNF." Life sciences **356**: 123014.

Wang, H., Z. Tao, M. Feng, X. Li, Z. Deng, G. Zhao, H. Yin, T. Pan, G. Chen, Z. Feng, Y. Li and Y. Zhou (2020). "Dual PLK1 and STAT3 inhibition promotes glioblastoma cells apoptosis through MYC." Biochem Biophys Res Commun **533**(3): 368-375.

Wang, H., L. Wang, H. Pan, Y. Wang, M. Shi, H. Yu, C. Wang, X. Pan and Z. Chen (2020). "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 **8**: 620603.

Wang, H., L. Wang, X. Zhou, X. Luo, K. Liu, E. Jiang, Y. Chen, Z. Shao and Z. Shang (2020). "OSCC exosomes regulate miR-210-3p targeting EFNA3 to promote oral cancer angiogenesis through the PI3K/AKT pathway." BioMed research international **2020**(1): 2125656.

Wang, J., D. Wang, Y. Zhang, P. Sun, L. Yi, A. Han, W. Zhao, Y. Zhang and H. Ma (2025). "Extracellular vesicles in reproductive biology and disorders: a comprehensive review." Frontiers in Endocrinology **Volume 16 - 2025**.

Wang, T., Z. Jian, A. Baskys, J. Yang, J. Li, H. Guo, Y. Hei, P. Xian, Z. He and Z. Li (2020). "MSC-derived exosomes protect against oxidative stress-induced skin injury via adaptive regulation of the NRF2 defense system." Biomaterials **257**: 120264.

Wang, W., N. Zhu, T. Yan, Y.-N. Shi, J. Chen, C.-J. Zhang, X.-J. Xie, D.-F. Liao and L. Qin (2020). "The crosstalk: exosomes and lipid metabolism." Cell Communication and Signaling **18**(1): 119.

Wang, X., Y. Zhu, C. Wu, W. Liu, Y. He and Q. Yang (2021). "Adipose-derived mesenchymal stem cells-derived exosomes carry microRNA-671 to alleviate myocardial infarction through inactivating the TGFBR2/Smad2 axis." Inflammation **44**(5): 1815-1830.

Wu, P., B. Zhang, X. Han, Y. Sun, Z. Sun, L. Li, X. Zhou, Q. Jin, P. Fu and W. Xu (2021). "HucMSC exosome-delivered 14-3-3ζ alleviates ultraviolet radiation-induced photodamage via SIRT1 pathway modulation." Aging (Albany NY) **13**(8): 11542.

Wu, Q., J. H. Wu, Z. Y. Ye, W. She, W. J. Peng, H. X. Zhang, C. Qi, T. Tian, X. Y. Hou and J. Gao (2024). "Exosomes from Hypoxia-treated Mesenchymal Stem Cells: Promoting Neuroprotection in Ischemic Stroke Through miR-214-3p/PTEN Mechanism." Mol Neurobiol **61**(10): 7611-7626.

Wu, R., H. Li, C. Sun, J. Liu, D. Chen, H. Yu, Z. Huang, S. Lin, Y. Chen and Q. Zheng (2022). "Exosome-based strategy for degenerative disease in orthopedics: recent progress and perspectives." Journal of Orthopaedic Translation **36**: 8-17.

Wu, S., X. Shang, M. Guo, L. Su and J. Wang (2024). "Exosomes in the Diagnosis of Neuropsychiatric Diseases: A Review." Biology (Basel) **13**(6).

Xia, C., Z. Zeng, B. Fang, M. Tao, C. Gu, L. Zheng, Y. Wang, Y. Shi, C. Fang and S. Mei (2019). "Mesenchymal stem cell-derived exosomes ameliorate intervertebral disc degeneration via anti-oxidant and anti-inflammatory effects." Free Radical Biology and Medicine **143**: 1-15.

Xiong, Z., Y. Hu, M. Jiang, B. Liu, W. Jin, H. Chen, L. Yang and X. Han (2024). "Hypoxic bone marrow mesenchymal stem cell exosomes promote angiogenesis and enhance endometrial injury repair through the miR-424-5p-mediated DLL4/Notch signaling pathway." PeerJ **12**: e16953.

Xu, J., J. Zhang, Z. Zhang, Z. Gao, Y. Qi, W. Qiu, Z. Pan, Q. Guo, B. Li and S. Zhao (2021). "Hypoxic glioma-derived exosomes promote M2-like macrophage polarization by enhancing autophagy induction." Cell Death & Disease **12**(4): 373.

Xu, M., Q. Yang, X. Sun and Y. Wang (2020). "Recent advancements in the loading and modification of therapeutic exosomes." Frontiers in Bioengineering and Biotechnology **8**: 586130.

Xu, R., F. Zhang, R. Chai, W. Zhou, M. Hu, B. Liu, X. Chen, M. Liu, Q. Xu and N. Liu (2019). "Exosomes derived from pro-inflammatory bone marrow-derived mesenchymal stem cells reduce inflammation and myocardial injury via mediating macrophage polarization." Journal of cellular and molecular medicine **23**(11): 7617-7631.

 doi:10.20944/preprints202602.1440.v1

Yan, T., L. Huang, Y. Yan, Y. Zhong, H. Xie and X. Wang (2023). "Bone marrow mesenchymal stem cell-derived exosome miR-29b-3p alleviates UV irradiation-induced photoaging in skin fibroblast." Photodermatol Photoimmunol Photomed **39**(3): 235-245.

Yan, X., Y.-X. Guo, Y.-X. Liu and C. Liu (2025). "Mesenchymal stem cell-derived exosomes and the Wnt/β-catenin pathway: Unifying mechanisms of multi-organ regeneration and the path to precision clinical translation." World Journal of Stem Cells **17**(6): 106902.

Yang, E., X. Wang, Z. Gong, M. Yu, H. Wu and D. Zhang (2020). "Exosome-mediated metabolic reprogramming: the emerging role in tumor microenvironment remodeling and its influence on cancer progression." Signal Transduction and Targeted Therapy **5**(1): 242.

Yang, J., Z. Chen, D. Pan, H. Li and J. Shen (2020). "Umbilical cord-derived mesenchymal stem cell-derived exosomes combined pluronic F127 hydrogel promote chronic diabetic wound healing and complete skin regeneration." International journal of nanomedicine: 5911-5926.

Yang, Y., Z. Guo, W. Chen, X. Wang, M. Cao, X. Han, K. Zhang, B. Teng, J. Cao and W. Wu (2021). "M2 macrophage-derived exosomes promote angiogenesis and growth of pancreatic ductal adenocarcinoma by targeting E2F2." Molecular Therapy **29**(3): 1226-1238.

Yang, Y., Y. Ye, X. Su, J. He, W. Bai and X. He (2017). "MSCs-derived exosomes and neuroinflammation, neurogenesis and therapy of traumatic brain injury." Frontiers in cellular neuroscience **11**: 55.

Yang, Z., J. Shi, J. Xie, Y. Wang, J. Sun, T. Liu, Y. Zhao, X. Zhao, X. Wang and Y. Ma (2020). "Large-scale generation of functional mRNA-encapsulating exosomes via cellular nanoporation." Nature biomedical engineering **4**(1): 69-83.

Ye, J., D. Wu, P. Wu, Z. Chen and J. Huang (2014). "The cancer stem cell niche: cross talk between cancer stem cells and their microenvironment." Tumor Biology **35**: 3945-3951.

Ye, S.-b., Z.-L. Li, D.-h. Luo, B.-j. Huang, Y.-S. Chen, X.-s. Zhang, J. Cui, Y.-x. Zeng and J. Li (2014). "Tumor-derived exosomes promote tumor progression and T-cell dysfunction through the regulation of enriched exosomal microRNAs in human nasopharyngeal carcinoma." Oncotarget **5**(14): 5439.

Ye, Y.-C., Z.-H. Chang, P. Wang, Y.-W. Wang, J. Liang, C. Chen, J.-J. Wang, H.-T. Sun, Y. Wang and X.-H. Li (2022). "Infarct-preconditioning exosomes of umbilical cord mesenchymal stem cells promoted vascular remodeling and neurological recovery after stroke in rats." Stem Cell Research & Therapy **13**(1): 378.

Yu, X., Q. Zhang, X. Zhang, Q. Han, H. Li, Y. Mao, X. Wang, H. Guo, D. M. Irwin, G. Niu and H. Tan (2019). "Exosomes from Macrophages Exposed to Apoptotic Breast Cancer Cells Promote Breast Cancer Proliferation and Metastasis." J Cancer **10**(13): 2892-2906.

Zeng, H., S. Guo, X. Ren, Z. Wu, S. Liu and X. Yao (2023). "Current Strategies for Exosome Cargo Loading and Targeting Delivery." Cells **12**(10).

Zhang, B., X. Wu, X. Zhang, Y. Sun, Y. Yan, H. Shi, Y. Zhu, L. Wu, Z. Pan and W. Zhu (2015). "Human umbilical cord mesenchymal stem cell exosomes enhance angiogenesis through the Wnt4/β-catenin pathway." Stem cells translational medicine **4**(5): 513-522.

Zhang, E., X. Geng, S. Shan, P. Li, S. Li, W. Li, M. Yu, C. Peng, S. Wang and H. Shao (2021). "Exosomes derived from bone marrow mesenchymal stem cells reverse epithelial-mesenchymal transition potentially via attenuating Wnt/β-catenin signaling to alleviate silica-induced pulmonary fibrosis." Toxicology mechanisms and methods **31**(9): 655-666.

Zhang, H., J. Yan, Q. Ma, L. Lin, Y. Pilehvar, N. Zarghami, L. Liang, K. Xu, X. Zhang and K. Yan (2024). "Sodium alginate hydrogels co-encapsulated with cell free fat extract-loaded core-shell nanofibers and menstrual blood stem cells derived exosomes for acceleration of articular cartilage regeneration." International Journal of Biological Macromolecules **280**: 135851.

Zhang, Y., Q. Liu, X. Zhang, H. Huang, S. Tang, Y. Chai, Z. Xu, M. Li, X. Chen, J. Liu and C. Yang (2022). "Recent advances in exosome-mediated nucleic acid delivery for cancer therapy." J Nanobiotechnology **20**(1): 279.

Zheng, R., M. Du, X. Wang, W. Xu, J. Liang, W. Wang, Q. Lv, C. Qin, H. Chu and M. Wang (2018). "Exosome–transmitted long non-coding RNA PTENP1 suppresses bladder cancer progression." Molecular cancer **17**: 1-13.

 doi:10.20944/preprints202602.1440.v1

Zhou, J., X. Li, X. Wu, T. Zhang, Q. Zhu, X. Wang, H. Wang, K. Wang, Y. Lin and X. Wang (2018). "Exosomes Released from Tumor-Associated Macrophages Transfer miRNAs That Induce a Treg/Th17 Cell Imbalance in Epithelial Ovarian Cancer." Cancer Immunol Res **6**(12): 1578-1592.

Zhou, W., Y. Zhou, X. Chen, T. Ning, H. Chen, Q. Guo, Y. Zhang, P. Liu, Y. Zhang and C. Li (2021). "Pancreatic cancer-targeting exosomes for enhancing immunotherapy and reprogramming tumor microenvironment." Biomaterials **268**: 120546.

Zhou, Y., Y. Yuan, M. Liu, X. Hu, Y. Quan and X. Chen (2019). "Tumor-specific delivery of KRAS siRNA with iRGD-exosomes efficiently inhibits tumor growth." ExRNA **1**(1): 28.

Zhu, M., Y. Gao, K. Zhu, Y. Yuan, H. Bai and L. Meng (2024). "Exosomal miRNA as biomarker in cancer diagnosis and prognosis: A review." Medicine **103**(42): e40082.