

Extracellular Vesicle Signaling in Systemic Disorders: Novel Directions for Precision Cellular Treatment

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DESCRIPTION

Extracellular vesicles have emerged as an important focus of biomedical research because they participate in communication among nearly every cell type within the human body [1]. These membrane-bound particles are released into biological fluids by living cells and transport proteins, lipids, messenger ribonucleic acid, micro ribonucleic acid, metabolites, and other signaling molecules to neighboring or distant target cells. Through this continuous exchange of molecular information, extracellular vesicles influence tissue maintenance, cellular differentiation, vascular function, wound repair, and host defense. Their broad biological activity has generated considerable interest in chronic systemic disorders, where alterations in cellular communication contribute to prolonged tissue injury and organ dysfunction. Understanding the biology of extracellular vesicles is creating opportunities for highly selective therapeutic approaches designed to modify pathological signaling while preserving normal physiological functions.

Cells continuously produce extracellular vesicles throughout their life cycle [2]. The two principal categories include exosomes, which originate from intracellular endosomal compartments, and microvesicles, which form directly through outward budding of the plasma membrane. Although these populations differ in their formation mechanisms and size, both carry biologically active cargo reflecting the physiological state of their parent cells. Healthy tissues release vesicles containing molecules that support tissue homeostasis, whereas stressed or activated cells frequently produce vesicles enriched with inflammatory mediators, adhesion molecules, enzymes, and regulatory nucleic acids capable of influencing surrounding cellular populations.

The molecular composition of extracellular vesicles varies according to the originating cell type. Lymphocytes, dendritic cells, macrophages, endothelial cells, epithelial cells, fibroblasts, platelets, and stem cells each generate vesicles containing distinct combinations of proteins and nucleic acids. This diversity allows highly specialized communication between tissues under changing physiological conditions [3]. Vesicle cargo may alter

gene expression, protein synthesis, cellular metabolism, migration, proliferation, or programmed cell death after uptake by recipient cells.

One of the most important characteristics of extracellular vesicles is their ability to protect fragile biological molecules during transport. Messenger ribonucleic acid and micro ribonucleic acid are highly susceptible to enzymatic degradation within body fluids [4]. Encapsulation inside lipid membranes allows these molecules to remain stable while circulating through blood, lymphatic vessels, saliva, urine, cerebrospinal fluid, and other biological compartments. Once delivered to recipient cells, these nucleic acids regulate protein production by influencing transcriptional and post-transcriptional pathways.

Extracellular vesicles contribute significantly to communication between antigen-presenting cells and lymphocytes. Dendritic cell-derived vesicles may contain major histocompatibility complex molecules carrying processed antigenic peptides together with co-stimulatory proteins capable of influencing T-cell activation [5]. Vesicles released by B lymphocytes transport antibody-related molecules and signaling proteins that influence neighboring immune populations. Macrophage-derived vesicles similarly regulate cellular recruitment, tissue remodeling, and communication with fibroblasts and endothelial cells during tissue repair.

Endothelial cells continuously release extracellular vesicles into the circulation where they participate in regulation of vascular integrity. Under physiological conditions these vesicles support normal endothelial function and communication with circulating leukocytes [6]. During chronic disease, however, endothelial vesicles frequently contain adhesion molecules and cytokines that encourage recruitment of inflammatory cells into affected tissues. These observations suggest that endothelial vesicles may contribute to progression of vascular injury and represent useful biomarkers for monitoring disease activity.

Fibroblasts also participate actively in extracellular vesicle signaling. These structural cells release vesicles carrying extracellular matrix proteins, growth factors, and regulatory nucleic acids that influence neighboring fibroblasts and

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Received: 24-Feb-2026, Manuscript No. IDIT-26-43955; **Editor assigned:** 26-Feb-2026, PreQC No. IDIT-26-43955(PQ); **Reviewed:** 12-Mar-2026, QC No. IDIT-26-43955; **Revised:** 19-Mar-2026, Manuscript No. IDIT-26-43955 (R); **Published:** 26-Mar-2026, DOI: 10.35248/2593-8509.26.11.251

Citation: Reinhardt S (2026). Extracellular Vesicle Signaling in Systemic Disorders: Novel Directions for Precision Cellular Treatment. *Immunol Disord Immunother.* 11:251.

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epithelial cells [7]. During wound healing this communication supports restoration of normal tissue architecture. Persistent alterations in vesicle production may instead contribute to excessive extracellular matrix deposition and progressive fibrosis within organs including the lungs, liver, kidneys, and skin.

Stem cell-derived extracellular vesicles have received particular scientific attention because many beneficial biological effects previously attributed to stem cells appear to result from molecules transported inside their vesicles [8]. Mesenchymal stromal cell-derived vesicles contain growth factors, regulatory micro ribonucleic acids, anti-inflammatory cytokines, and proteins involved in tissue regeneration. Experimental investigations indicate that administration of purified vesicles may reproduce several beneficial effects associated with stem cell therapy while avoiding some practical challenges related to transplantation of living cells.

Extracellular vesicles are also attracting considerable interest as therapeutic delivery systems. Their natural biocompatibility, low immunogenicity, and capacity to transport diverse biological molecules make them attractive alternatives to synthetic drug carriers [9]. Investigators are developing methods for loading vesicles with anti-inflammatory agents, messenger ribonucleic acid, small interfering ribonucleic acid, proteins, peptides, and gene-editing components before administration. Surface modification techniques additionally allow vesicles to preferentially accumulate within selected tissues, improving therapeutic specificity.

Engineering of extracellular vesicles has become increasingly sophisticated. Parent cells may be genetically modified to produce vesicles enriched with selected therapeutic molecules [10]. Alternatively, purified vesicles may undergo laboratory manipulation through electroporation, chemical loading, or membrane fusion techniques to incorporate desired cargo. These approaches seek to maximize therapeutic benefit while minimizing systemic exposure and unwanted adverse effects.

CONCLUSION

Ongoing investigations into extracellular vesicle signaling continue expanding understanding of cellular communication,

molecular transport, tissue repair, vascular regulation, and biological homeostasis. These discoveries are expected to support development of increasingly selective diagnostic methods and therapeutic strategies capable of modifying disease-associated signaling while preserving essential physiological functions. Continued collaboration between laboratory researchers, clinicians, engineers, and pharmaceutical scientists will remain fundamental for translating extracellular vesicle biology into practical clinical applications that improve long-term outcomes for individuals living with chronic systemic disorders.

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