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Commentary

Circulating Extracellular Vesicles as Mediators of Immune Cell Communication in Chronic Inflammatory Airway Disease

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DESCRIPTION

Chronic inflammatory airway disorders such as persistent asthma and chronic obstructive airway pathology are increasingly associated with complex intercellular communication networks extending beyond the respiratory tract. Among the circulating factors involved, extracellular vesicles derived from epithelial cells, endothelial cells, and immune populations have gained attention due to their capacity to carry proteins, lipids, and nucleic acids that influence distant cellular responses. These vesicles are released into the bloodstream and local tissue microenvironments, where they interact with leukocytes and structural cells, modifying immune activity and tissue behavior over prolonged periods of disease activity. In individuals with chronic airway inflammation, the quantity and molecular composition of circulating vesicles differ significantly from those observed in healthy subjects, suggesting an association between vesicle cargo and inflammatory status.

Airway epithelial cells exposed to environmental irritants such as particulate matter, allergens, and microbial components show altered vesicle production. These epithelial-derived vesicles frequently contain micro Ribonucleic Acids (RNAs) and inflammatory mediators that influence macrophage polarization and T lymphocyte differentiation. In experimental observations, vesicles from inflamed airway epithelium promote a shift in macrophages toward a phenotype associated with increased secretion of inflammatory mediators, while simultaneously reducing their capacity for efficient clearance of cellular debris. This imbalance contributes to sustained inflammatory signaling within airway tissues and systemic circulation.

Endothelial cells lining the pulmonary vasculature also contribute to vesicle populations under inflammatory conditions. These vesicles often display adhesion molecules and signaling proteins that facilitate leukocyte interaction with vascular walls. The interaction between endothelial vesicles and circulating neutrophils enhances neutrophil activation and prolongs their survival in circulation. As a result, neutrophils retain their ability to release reactive oxygen species and proteolytic enzymes for extended periods, which may indirectly influence airway tissue integrity. Although neutrophils are typically short-lived cells, vesicle-mediated signaling modifies their lifespan and activity in ways that contribute to persistent inflammatory activity.

Immune cell-derived vesicles represent another important component of circulating extracellular vesicle populations. Activated T lymphocytes release vesicles containing signaling molecules that influence antigen-presenting cells and other lymphocyte subsets. These vesicles may carry receptors and regulatory microRNAs that alter gene expression in recipient cells. B lymphocyte-derived vesicles also participate in immune modulation by transferring immunoglobulin fragments and regulatory proteins to target cells. These interactions collectively shape immune responses in chronic airway disease and extend their influence beyond the local pulmonary environment.

The molecular cargo of extracellular vesicles varies depending on disease stage and inflammatory intensity. In early stages of airway inflammation, vesicles often contain regulatory signals that attempt to maintain tissue equilibrium. However, as inflammation becomes persistent, vesicle composition shifts toward molecules that reinforce immune activation and metabolic alteration in recipient cells. MicroRNA profiles within vesicles have been shown to regulate pathways involved in cytokine production, cell survival, and metabolic adaptation. These changes influence both innate and adaptive immune responses, resulting in prolonged activation of immune signaling networks.

Systemic effects of airway-derived vesicles have been observed in distant organs such as the liver, skeletal muscle, and bone marrow. Hepatic cells exposed to inflammatory vesicles demonstrate changes in lipid metabolism and acute-phase protein production. Skeletal muscle cells respond with altered insulin signaling and reduced glucose uptake capacity, indicating that airway inflammation may extend its metabolic consequences beyond the respiratory system. Bone marrow exposure to vesicle-associated signals influences hematopoietic activity, leading to modified leukocyte production and release into circulation.

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Environmental and genetic factors contribute to variability in vesicle production and composition. Exposure to tobacco smoke, industrial pollutants, and recurrent infections enhances vesicle release from airway epithelial and immune cells. Genetic predisposition may influence the regulatory pathways controlling vesicle biogenesis and secretion, thereby affecting individual susceptibility to chronic airway inflammation. These combined influences result in heterogeneous vesicle profiles among affected individuals.

Therapeutic interventions targeting extracellular vesicle production or uptake are being explored in experimental models. Approaches aimed at reducing vesicle release from inflamed epithelial cells or blocking vesicle uptake by immune cells have shown potential in reducing inflammatory signaling intensity. Additionally, modifications in vesicle content through pharmacological intervention may alter their biological activity, shifting their influence toward less inflammatory outcomes. However, the complexity of vesicle-mediated communication requires further detailed examination before clinical application can be fully realized.

CONCLUSION

Extracellular vesicles serve as important mediators of communication between epithelial cells, immune cells, and distant tissues in chronic inflammatory airway conditions. Their ability to transport diverse molecular cargo enables them to influence immune responses, metabolic pathways, and tissue function across multiple organ systems. Alterations in vesicle quantity and composition contribute to sustained inflammatory activity and systemic effects associated with airway disease. Continued investigation into vesicle biology may provide deeper understanding of intercellular communication networks involved in chronic inflammation and support development of targeted interventions aimed at regulating these signaling processes.

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