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Short Communication

# The Emerging Role of Tumor-Derived Exosomes in Mediating Immune Evasion and Therapy Resistance in Solid Tumors

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## DESCRIPTION

Exosomes are nano-sized extracellular vesicles (30–150 nm) secreted by nearly all cell types, including cancer cells. Tumor-Derived Exosomes (TDEs) carry bioactive molecules such as proteins, lipids, mRNAs and non-coding RNAs that modulate intercellular communication. In solid tumors, TDEs have emerged as critical mediators of immune evasion and therapy resistance, thus playing a key role in tumor progression and treatment failure. TDEs contribute to immune escape by modulating various components of the immune system. Exosomes enriched with Programmed Death-Ligand 1 (PD-L1) can bind to PD-1 receptors on cytotoxic T lymphocytes, thereby inhibiting their function and promoting T cell exhaustion. Additionally, TDEs expressing Fas ligand (FasL) and galectin-9 induce T cell apoptosis, further weakening antitumor immunity. Transforming growth factor-beta (TGF-β) carried by TDEs promotes regulatory T cell (Treg) expansion and suppresses effector T cell function, skewing the immune response toward tolerance. Furthermore, TDEs facilitate the recruitment and expansion of immunosuppressive cells such as Myeloid-Derived Suppressor Cells (MDSCs) and Tumor-Associated Macrophages (TAMs). Exosomal heat shock proteins (e.g., HSP70) and microRNAs (e.g., miR-181a, miR-9) activate signaling pathways such as STAT3 and JAK/STAT in these cells, enhancing their suppressive capabilities. TDEs also express CD39 and CD73, which convert ATP to adenosine, a potent immunosuppressive metabolite that inhibits T cell activity and natural killer (NK) cell cytotoxicity.

In addition to immune evasion, TDEs promote resistance to anticancer therapies, including chemotherapy, targeted therapy and immunotherapy. Some TDEs can sequester therapeutic monoclonal antibodies such as HER2-positive exosomes binding to trastuzumab or CD20-positive exosomes neutralizing rituximab reducing drug efficacy. Moreover, TDEs transfer drug-efflux proteins like P-glycoprotein (P-gp), MRP2 and ATP-binding cassette transporters to neighboring cancer cells, spreading drug resistance. Exosomal microRNAs and long non-coding RNAs also play a role in resistance by modulating gene expression in recipient cells. For example, TDEs from cisplatin-resistant ovarian cancer cells have been shown to confer resistance to sensitive cells by transferring specific miRNAs that inhibit apoptosis pathways. In colorectal and breast cancers, TDEs activate signaling pathways such as Wnt/β-catenin, PI3K/AKT and MAPK, which support cell survival and proliferation in the presence of cytotoxic agents.

Exosomes are also involved in immune checkpoint blockade resistance. Elevated levels of circulating exosomal PD-L1 have been correlated with poor responses to anti-PD-1/PD-L1 therapy in multiple cancer types. These findings suggest that TDEs not only contribute to resistance mechanisms but may also serve as predictive biomarkers of treatment response. Importantly, the immunoediting theory which describes tumor progression in the stages of elimination, equilibrium and escape is increasingly being linked to exosome activity, particularly during the escape phase. By manipulating immune surveillance and fostering resistant tumor cell populations, TDEs function as central regulators of immune-tumor dynamics.

Given their significant roles, TDEs are being explored as therapeutic targets. Strategies include blocking exosome production (e.g., using GW4869 or neutral sphingomyelinase inhibitors), interfering with exosome uptake, or engineering exosomes to deliver therapeutic payloads. Despite the promise, challenges such as specificity, toxicity and delivery remain to be resolved before clinical application.

## CONCLUSION

Tumor-derived exosomes are increasingly recognized as multifaceted regulators of tumor progression, immune evasion and therapy resistance in solid tumors. By manipulating immune cell function and transferring resistance traits, TDEs help tumors adapt and survive under therapeutic pressure. Their emerging role as both biomarkers and therapeutic targets makes them a critical focus in current cancer research. Future investigations should aim to elucidate their molecular mechanisms more precisely and develop strategies to intercept their pathological functions. Targeting TDE-mediated pathways

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holds great promise in improving therapeutic outcomes and overcoming resistance in solid tumors.

## REFERENCES

1. Gustafson P. Soft tissue sarcoma: epidemiology and prognosis in 508 patients. Acta Orthop Scand Suppl. 1994;65:2-31.
2. Mettlin C, Priore R, Rao U, Gamble D, Lane W, Murphy GP. Results of the national soft-tissue sarcoma registry. J Surg Oncol. 1982;19(4):224-227.
3. Toro JR, Travis LB, Wu HJ, Zhu K, Fletcher CD, Devesa SS. Incidence patterns of soft tissue sarcomas, regardless of primary site, in the surveillance, epidemiology and end results program, 1978–2001: an analysis of 26,758 cases. Int J Cancer. 006;119(12): 2922-2930.
4. Alamanda VK, Delisca GO, Mathis SL, Archer KR, Ehrenfeld JM, Miller MW, et al. The financial burden of reexcising incompletely excised soft tissue sarcomas: a cost analysis. Ann Surg Oncol. 2013;20(9):2808-2814.
5. Cohen EK, Kressel HY, Perosio T, Burk Jr DL, Dalinka MK, Kanal E, et al. MR imaging of soft-tissue hemangiomas: correlation with pathologic findings. AJR Am J Roentgenol. 1988;150(5):1079-1081.
6. Griffith JF, Yip SW, Hung EH, Fong RC, Leung J, Ng AW, et al. Accuracy of ultrasound in the characterisation of deep soft tissue masses: a prospective study. Eur Radiol. 2020;30(11):5894-5903.
7. Gruber L, Loizides A, Luger AK, Glodny B, Moser P, Henninger B, et al. Soft-Tissue Tumor Contrast Enhancement Patterns: Diagnostic Value and Comparison Between Ultrasound and MRI. AJR Am J Roentgenol. 2017;208(2):393-401.
8. Cormier JN, Pollock RE. Soft tissue sarcomas. CA Cancer J Clin. 2004;54(2):94-109.
9. Frassica FJ, Khanna JA, McCarthy EF. The role of MR imaging in soft tissue tumor evaluation: perspective of the orthopedic oncologist and musculoskeletal pathologist. Magn Reson Imaging Clin N Am. 2000;8(4):915-927.
10. van Vliet M, Kliffen M, Krestin GP, Van Dijke CF. Soft tissue sarcomas at a glance: clinical, histological, and MR imaging features of malignant extremity soft tissue tumors. Eur Radiol. 2009;19(6): 1499-1511.