



Signature of exosomes in cancer translational medicine

Rajib Dhar, MSc^a, Vinoth Kumarasamy, PhD^b, Vetrivelan Subramaniyan, PhD, FMSA^{a,*}

Dear Editor,

Cancer is the most complicated disease worldwide^[1]. Translational medicine research focuses on upgrading the health science based on findings of basic research. In this process, cutting-edge findings in basic research support the development of a solution for the diagnostic and therapeutic tools and as well as improvements in healthcare policy, ultimately benefiting human life^[2]. Cancer translational medicine majorly focuses on developing an effective, affordable theranostics solution for cancer. Exosomes are a subpopulation of Extracellular vesicles (EVs) and it originate from the endosomes^[3]. In general, exosome plays a vital role in cellular signaling. Current decade research decodes that exosomes (tumor-derived exosomes-TDXs) play a vital role in cancer development and progression. This phospholipid membrane-bound vascular structure transports multiple biologically active molecules in cellular systems such as DNA, RNA, proteins, metabolites, and phytochemicals (only in the case of plant source)^[3]. The most interesting fact about exosome cargos, a major player in cellular reprogramming. Researchers find that exosomes (TDXs) are messengers of cancer cells. It regulated uncontrolled tumor cell growth, Immunosuppression (downregulates the anti-cancer cytotoxic effect of dendritic cell, T cell, Natural killer cell and promotes M2 polarization of macrophage), angiogenesis (TDXs carry angiogenic factors like Vascular endothelial growth factor -VEGF), metastasis (in cancer TDXs mediated MMP2, and MMP9 higher expression promote cellular motility via remodeling of extra cellular matrix-ECM), epithelial-mesenchymal transition (EMT) and organ-specific metastasis (TDXs integrins provide the significant guidance of circulating tumor cells to migrate in specific organs. More specifically, α and β subunit expression pattern of integrin regulate it)^[3-5]. In cancer diagnostic exosomes introduce a new chapter. Exosome-based cancer liquid biopsy (source of exosomes like blood, plasma, serum, urine, saliva, tears, and sweat) is more efficient compared to the traditional tissue biopsy (due to its low

cost, minimum invasion, high sensitivity, and real-time drug response monitoring)^[6]. Cancer therapeutic research is a more challenging domain in cancer studies, due to its side effects, specificity, and affordability aspect. Therapeutic exosomes are found from different sources, such as animal origin (stem cells, immune cells), plant exosomes, synthetic exosomes, and modified exosomes^[3]. The exosome-based therapeutic approach is a cell-free approach^[3,5]. Advancement of this approach is that it is cell-free, non-toxic, biocompatible, non-immunogenic, with specific targeting efficiency, and has the ability to cross the blood-brain barrier (BBB)^[3,7]. Exosome-based drug delivery approach is more effective, efficient, and biocompatible compared to the traditional approach (liposome-based)^[3]. Exosome-based cancer translational medicine research opens a new horizon in cancer research. Day by day, this phenomenon becomes more interdisciplinary and combines with nanotechnology, omics science, AI, and machine learning (ML) for decoding several complications of it^[8,9]. Exosome research has some challenging point, like isolation, heterogeneity (exosomes origin, size and molecular diversity control it)^[8]. Omics profiling supports molecular-level investigation of exosomes (proteomic, genomic, lipidomic, and metabolomic). AI and ML support deep analysis of medical data and help predict the disease complications^[8,9]. The major challenges of exosomes research are that translation of exosome-based cancer theranostics approaches require approval of the concerned governing body, impurity of exosomes, we still need to explore multiple factors, and a lack of an standardize and scalable industrial production protocol^[10]. Currently several exosome-based clinical trials (<https://clinicaltrials.gov/search?cond=cancer&intr=exosomes>) are going on, out of which a large number focuses on cancer biomarkers, few are based on therapeutic development -Dendritic cell-derived exosomes and Stem cell-derived exosomes. Advancement of exosome research introduces some cutting-edge approaches for deep profiling and analysis of exosomes, such as single exosome profiling (this approach addresses isolation to molecular level understanding with reduced contamination within the EV subpopulations) and exosome barcoding (an advanced user-friendly approach for exosomes identification). The promising outcomes of exosome-based cancer translational research, exemplified by patents US 2017/0296626 A1 (pure exosome-based protein and nucleic acid delivery) and WO2016172598A1 (purification of exosomes and their inner RNA isolation), offer potential for a better understanding and prevention of cancer. Exosomes research has become a cutting-edge platform for an effective cancer translational medicine era. Hope it becomes a promising solution for a cancer-free future.

^aDivision of Pharmacology, Faculty of Medical and Life Sciences, Sunway University, Bandar Sunway, Selangor Darul Ehsan, Malaysia and ^bDepartment of Parasitology and Medical Entomology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

*Corresponding author. Address: Division of Pharmacology, Faculty of Medical and Life Sciences, Sunway University, Bandar Sunway, 47500 Selangor Darul Ehsan, Malaysia. E-mail: vetris@sunway.edu.my (V. Subramaniyan).

Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution-NoDerivatives License 4.0, which allows for redistribution, commercial and non-commercial, as long as it is passed along unchanged and in whole, with credit to the author.

International Journal of Surgery (2025) 111:4138–4139

Received 9 April 2025; Accepted 10 April 2025

Published online 22 April 2025

<http://dx.doi.org/10.1097/JS9.0000000000002413>

Ethical approval

Not applicable.

Consent

Not applicable.

Sources of funding

Not applicable.

Author contributions

R.D.: conceptualization, original draft preparation. V.K.: reviewing. V.S.: reviewing and editing.

Conflicts of interest disclosure

The authors are declaring no conflict of interests.

Guarantor

Prof. Vetriselvan Subramaniam, accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

Research registration unique identifying number (UIN)

Not applicable.

Provenance and peer review

This article is not commissioned/externally peer-reviewed.

Data availability statement

Not applicable.

Acknowledgments

Not applicable.

References

- [1] Siegel RL, Kratzner TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. *CA Cancer J Clin* 2025;75:10–45.
- [2] Jiang P, Sinha S, Aldape K, Hannenhalli S, Sahinalp C, Ruppel E. Big data in basic and translational cancer research. *Nat Rev Cancer* 2022;22:625–39.
- [3] Dai J, Su Y, Zhong S, *et al.* Exosomes: key players in cancer and potential therapeutic strategy. *Signal Transduct Target Ther* 2020;5:145.
- [4] Hoshino A, Costa-Silva B, Shen TL, *et al.* Tumour exosome integrins determine organotropic metastasis. *Nature* 2015;527:329–35.
- [5] Xu R, Rai A, Chen M, Suwakulsiri W, Greening DW, Simpson RJ. Extracellular vesicles in cancer – implications for future improvements in cancer care. *Nat Rev Clin Oncol* 2018;15:617–38.
- [6] Lone SN, Nisar S, Masoodi T, *et al.* Liquid biopsy: a step closer to transform diagnosis, prognosis and future of cancer treatments. *Mol Cancer* 2022;21:79.
- [7] Fu W, Lei C, Liu S, *et al.* CAR exosomes derived from effector CAR-T cells have potent antitumour effects and low toxicity. *Nat Commun* 2019;10:4355.
- [8] Morales RT, Ko J. Future of digital assays to resolve clinical heterogeneity of single extracellular vesicles. *ACS Nano* 2022;16:11619–45.
- [9] Shao H, Im H, Castro CM, Breakefield X, Weissleder R, Lee H. New technologies for analysis of extracellular vesicles. *Chem Rev* 2018;118:1917–50.
- [10] Wang CK, Tsai TH, Lee CH. Regulation of exosomes as biologic medicines: regulatory challenges faced in exosome development and manufacturing processes. *Clin Transl Sci* 2024;17:e13904.