Scholars LITERATURE

Journal of Clinical Oncology and Therapeutics

Literature Review

DOI: https://doi.org/10.47275/2690-5663-121
Volume 3 Issue 2

Exosomes in Cancer Therapy-Literature Review

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Abstract

Nanovesicles known as exosomes have intrigued the scientific and clinical communities' curiosity. As a messenger that can directly communicate with different and distinct target cells via blood circulation with their membrane associated particles or transport their contents into cells as a direct stimulus, tumour exosomes play an important role in targeted therapy. They are expressed at high levels during tumorigenesis. They serve as a biomarker for the development of cancer. Because exosomes are biocompatible and biodegradable, they can be used in cancer therapy because they are low toxic and immunogenic.

Keywords: Exosomes; Target Therapy; Tumor; Biomarkers

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Citation: Seema K (2021) Exosomes in Cancer Therapy-Literature Review. J Clin Oncol Ther, Volume 3:2. 121. DOI: https://doi.org/10.47275/2690-5663-121

Received: June 07, 2021; **Accepted:** June 21, 2021; **Published:** June 26, 2021

Introduction

Endosomal nanovesicles (70-150 nm in diameter) released by cells are known as exosomes. Cellular intercellular communication has recently attracted much attention from the scientific and clinical communities because of its participation in practically all physiological and pathological processes there are exosomes in every cell and they share the same lipid bilayer, transmembrane proteins, and panel of encapsulated soluble proteins and RNAs with their parent cell. The secretion pathway of exosomes is being unravelled [1]. For example, the release of exosomes and microvesicles from adipocytes is dramatically decreased with inhibition of histone H3 lysine9 methyltransferase G9a and histone H3 lysine4 demethylase LSD1 [2]. H3K9me2 and H4Kme3 may be necessary for the release of exosomes in mammalian cells, as demonstrated by this study. A recent study found that histone methyltransferase G9a and its G9a-like protein partner maintain DNA methylation at imprinted loci in embryonic stem cells, indicating that aberrant DNA methylation distribution might also drive the release of exosomes, as recently reported. Using surface receptors, recipient cells are able to identify and grab exosomes, and the exosomes themselves can alter the physiological state of the recipient cells they encounter. A closer look into the possibilities of these exosomes may be done:

1. As a biomarker in many diseases, to help diagnose ailments before they worsen, and/or
2. As a target to be blocked or destroyed to improve cancer patients' health.

Tumour Exosomes as Targeted Therapy

It is possible for exosomes, which have membrane-associated particles, to interact with various and unique target cells via blood circulation, or to carry their contents into the cells as a direct stimulation [3]. Exosomes have been shown to have a role in carcinogenesis by data from animal models and clinical samples from cancer patients [4]. Multiple myeloma, colorectal cancer, and gastric cancer cells get miRNAs and soluble factors from exosomes generated from mesenchymal stromal cells (MSC) or fibroblasts, which promotes cancer growth and medication resistance [5]. A cluster of miRNAs called miR-1792 is transferred to brain tumours by exosomes from astrocytes [6]. Exosomes are also produced by malignant cells to boost endothelial cell proliferation and improve angiogenesis, which aids tumour growth [7]. Immunosuppression can also be induced in the tumour microenvironment by cell-derived exosomes. Tumor survival and proliferation are facilitated by this tumour exosome-educated microenvironment. The pre-metastatic niche for tumour metastasis can be formed by cancer cell-derived exosomes fusing with the cells at their projected destination [6]. Cancer cell exosomes, on the other hand, have the ability to transform normal epithelial cells into tumours in mice [8]. For example, exosomes from acute myeloid leukaemia cells can carry miR-155 into normal hematopoietic stem and progenitor cells (HSPCs) and decrease c-Myb expression, which hinders normal blood cell production and facilitates leukemic cell proliferation. All of these findings demonstrate the significance of exosomes as a means of cell-to-cell communication throughout the advancement of cancer. Drugs and functional RNA have been effectively delivered to cancer patients using exosomes, which take use of their inherent transportation potential. Recent years have also seen an increase in the number of researchers working to enhance exosome-mediated nano delivery's ability to deliver drugs more precisely, selectively, and specifically.

Advantages of Exosomes for Cancer Therapy

Toxic and immunogenic exosomes differ from manufactured nanoparticles because they are more biocompatible and biodegradable. Exosomes, on the other hand, are smaller and more homogeneous than other cell-derived EVs, which limits their use for drug loading and distribution. Most cell types can produce exosomes, making them

a simple reagent to work with and because of their tiny size and high stability in biological fluids, exosomes may bypass lung clearance and cross the blood-brain barrier with ease [9-11]. Exosomes are 10 times more likely than liposomes of comparable size to adhere and be internalised by tumour cells, showing a higher level of cancer-targeting specificity for exosomes. This is due to the fact that nanometric exosomes tend to concentrate more often in tumour cells with irregularly formed blood arteries than they do in normal tissues, allowing them to reach and transport drugs more effectively to the majority of cancerous tissues. Additional tumor-targeting proteins and peptides can be added to exosomes, allowing for targeted medication and therapeutic nucleic acid delivery. Exosomes are an excellent possibility for cancer-targeting treatment because of these features.

Exosome Modifications for Specific Targeting

Because only a limited number of compounds may be utilised for cell targeting, synthetic nanoparticle-mediated delivery has a poor level of selectivity. However, the receptors on the surface of natural cell-produced exosomes allow them to distinguish distinct cell types. If you have Tspan8 in your exosomes, for example, they preferentially attach to CD11b and CD54 positive cells [12]. Exosomes with receptors may also be engineered from donor cells, allowing researchers to better identify cells. The majority of exosome changes are derived from surface display technology, which uses exosome membranes to show candidate proteins or peptides. Exosome membrane proteins such as lysosome-associated membrane glycoprotein 2b (Lamp2b) and tetraspanins CD63 and CD9 can be fused with candidate proteins or peptides to place them on the exosome's surface [13]. Scientists have altered dendritic cells (DCs) to express an iRGD peptide specific to integrin v and a Lamp2b fusion protein, enabling the modified DCs to secrete exosomes that contain the iRDG peptide. In a mouse model of breast cancer, these modified exosomes significantly improved drug delivery and anti-tumor effects on integrin-positive breast cancer cells [14]. These findings suggest that exosomes that have been modified for use in the treatment of neurocancerous tumours might be a valuable resource. Additional benefits of exosome glycosylation include resistance to proteasomal breakdown in circulation, which makes them more stable and even more effective in delivering drugs to specific locations.

A magnet-based technique was recently employed in research to boost tumour targeting specificity even more. An external magnet was placed on the tumour in vivo, allowing Jin Q, et al. (2021) [10] to deliver magnetic exosomes to the target tumour cells, thereby suppressing tumour development. They did this by connecting superparamagnetic-conjugated transferrin to transferrin receptor-positive blood exosome surfaces. Despite the fact that magnetic exosomes cannot directly target CSCs, the huge enrichment of exosomes loaded with effective CSC-targeting medications surrounding solid tumours might greatly increase therapeutic efficiency and reduce their side-effects by confining pharmaceuticals on tumour site. Presenting particular anti-tumor antibodies on the exosome surface can boost anti-tumor specificity even more. A designed anti-epidermal growth factor receptor (EGFR) nanobody and exosome anchor signal peptide glycosylphosphatidylinositol (GPI) fusion protein were transfected into donor cells to produce nanobody-presenting exosomes in one research. They were able to specifically target EGFR-positive tumour cells with these exosomes [15].

For cancer therapy, preventing hepatic clearance of drug-loaded exosomes is essential. Exosome clearance in the liver was drastically decreased and tumour growth was increased when the scavenger receptor class A family (SR-A), a monocyte/macrophage uptake receptor, was suppressed [16]. In order to improve their selectivity and stability, researchers also employed an exosome-liposome hybridization strategy [17].

Conclusion

The combination of various exosomal adaptation approaches provides an excellent cancer therapy and CSC treatment potential, and the success of these ways will further enhance the outcome of exosome-mediated CSC targeting.

Conflict of Interest

No potential conflict of interest.

Funding

This work did not receive any specific grant from funding agencies.

Acknowledgment

GITAM (Deemed to be University) management for their support.

References

1. Von Schulze A, Deng F (2020) A review on exosome-based cancer therapy. J Cancer Metastasis Treat 6: 42. https://doi.org/10.20517/2394-4722.2020.79
2. Liu XY, Li H (2017) Reduced histone H3 lysine 9 methylation contributes to the pathogenesis of latent autoimmune diabetes in adults via regulation of SUV39H2 and KDM4C. J Diabetes Res 2017: 8365762. https://doi.org/10.1155/2017/8365762
3. Zhang Y, Liu Y, Liu H, Tang WH (2019) Exosomes: Biogenesis, biologic function and clinical potential. Cell Biosci 9: 19. https://doi.org/10.1186/s13578-019-0282-2
4. Whiteside TL (2016) Tumor-derived exosomes and their role in cancer progression. Adv Clin Chem 74: 103-141. https://doi.org/10.1016/bs.acc.2015.12.005
5. Roccaro AM, Sacco A, Maiso P, Azab AK, Tai YT, et al. (2013) BM mesenchymal stromal cell-derived exosomes facilitate multiple myeloma progression. J Clin Invest 123: 1542-1555. https://doi.org/10.1172/JCI66517
6. Hoshino A, Costa Silva B, Shen TL, Rodrigues G, Hashimoto A, et al. (2015) Tumour exosome integrins determine organotropic metastasis. Nature 527: 329-335. https://doi.org/10.1038/nature15756
7. Wang Z, Chen JQ, Liu JL, Tian L (2016) Exosomes in tumor microenvironment: Novel transporters and biomarkers. J Transl Med 14: 297. https://doi.org/10.1186/s12967-016-1056-9
8. Melo SA, Sugimoto H, O'Connell JT, Kato N, Villanueva A, et al. (2014) Cancer exosomes perform cell-independent microRNA biogenesis and promote tumorigenesis. Cancer Cell 26: 707-721. https://doi.org/10.1016/j.ccell.2014.09.005
9. Xia X, Wang Y, Huang Y, Zhang H, Lu H, et al. (2019) Exosomal miRNAs in central nervous system diseases: biomarkers, pathological mediators, protective factors and therapeutic agents. Prog Neurobiol 183: 101694. https://doi.org/10.1016/j.pneurobio.2019.101694
10. Jin Q, Wu P, Zhou X, Qian H, Xu W (2021) Extracellular vesicles: novel roles in neurological disorders. Stem Cells Int 2021: 6640836. https://doi.org/10.1155/2021/6640836
11. Kawikova I, Askenase PW (2015) Diagnostic and therapeutic potentials of exosomes in CNS diseases. Brain Res 1617: 63-71. https://doi.org/10.1016/j.brainres.2014.09.070
12. Rana P, Anson B, Engle S, Will Y (2012) Characterization of human-induced pluripotent stem cell-derived cardiomyocytes: Bioenergetics and utilization in safety screening. Toxicol Sci 130: 117-131. https://doi.org/10.1093/toxsci/kfs233
13. Stickney Z, Losacco J, McDevitt S, Zhang Z , Lu B (2016) Development of exosome surface display technology in living human cells. Biochem Biophys Res Commun 472: 53-59. https://doi.org/10.1016/j.bbrc.2016.02.058
14. Tian L, Alizadeh AA, Gentles AJ, Tibshirani R (2014) A simple method for estimating interactions between a treatment and a large number of covariates. J Am Stat Assoc 109: 1517-1532. https://doi.org/10.1080/01621459.2014.951443

15. Kooijmans SAA, Fliervoet LAL, Van Der Meel R, Fens MHAM, Heijnen HFG, et al. (2016) PEGylated and targeted extracellular vesicles display enhanced cell specificity and circulation time. J Control Release 224: 77-85. https://doi.org/10.1016/j.jconrel.2016.01.009

16. Watson DC, Bayik D, Srivatsan A, Bergamaschi C, Valentin A, et al. (2016) Efficient production and enhanced tumor delivery of engineered extracellular vesicles. Biomaterials 105: 195-205. https://doi.org/10.1016/j.biomaterials.2016.07.003

17. Sato YT, Umezaki K, Sawada S, Mukai SA, Sasaki Y, et al. (2016) Engineering hybrid exosomes by membrane fusion with liposomes. Sci Rep 6: 21933. https://doi.org/10.1038/srep21933