

The Potential Use of Exosomes as a Diagnostic and Prognostic Tool

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Commentary

Cells release distinct types of extracellular vesicles (EV). EVs are lipid bilayer enclosed membrane vesicles ranging from 40 nm to 5,000 nm in diameter. Depending on the pathways responsible for their biogenesis, EVs can be classified as apoptotic bodies, microvesicles and exosomes [1,2]. Apoptotic bodies are generated from the fragmentation of the cell membrane of apoptotic cells [1], while microvesicles are originated at the plasma membrane by outward blebbing and have a size ranging from 100 to 1000 nm [2]. On the other hand, exosomes are released after fusion of multivesicular bodies (MVBs) with the plasma membrane. MVBs are formed during the maturation of endosomes after the invagination of the endosomal membrane towards the lumen and consecutive scission, giving rise to intraluminal vesicles (ILVs). ILVs are named exosomes after being released to the extracellular space and have a size ranging from 50 to 100 nm [3]. EVs contain proteins, lipids and RNAs and are suggested to play different roles, from cell-to-cell communication to removal of misfolded proteins and tissue development].

Independently of their biological function, there is an increasing interest in using exosomes in clinic as biomarkers of several pathological conditions due to several reasons. Because of their intracellular origin, exosomes work as reporters of the biochemical changes occurring in many diseases, such as cancer, neurological or immunological conditions. Many groups managed to isolate a cell-specific population of exosomes from the blood of patients [4-11] what would allow physicians to monitor in real time the status of a patient or the efficacy of a medication by simply taking a blood sample and analyzing the content of exosomes from a specific cell-type. In addition, blood draws are carried out daily in clinical practice and they have low cost in comparison to other diagnostic methods. Blood draws are also less invasive than other diagnostic approaches (e.g. biopsies).

Different methods have been developed to isolate a specific population of exosomes from blood in order to analyze their content. The antibody-based methods use a capture antibody against an exosomal marker, either coupled to streptavidin or magnetic beads [8,11], coated on the wells of an ELISA plate [5] or used in flow cytometry separation [7]. For example, circulating glypican 1-bearing exosomes have been isolated by

flow cytometry and were shown to be diagnostic for early and late pancreatic cancer [7]. Another example is the use of ELISA plates coated with an anti-CD63 antibody to capture circulating exosomes from the plasma of patients with breast cancer. When combined with a detection antibody against Del-1 protein it showed useful for diagnosis of breast cancer [5]. Also, neural exosomes from human plasma isolated with superparamagnetic microbeads coated with anti-L1CAM antibody showed higher levels of synuclein in patients with Parkinson's disease [8].

On the other hand, some studies combine the precipitation of vesicles from a biological fluid by means of a chemical agent (e.g. Exoquick) with an antibody-based approach [5,6]. Using this method, it was possible to discriminate between controls and AD patients by determining the levels of A β 42 and certain phospho-specific tau species (p181 and p396) in blood-derived neural exosomes (exosomes can go across the blood brain barrier).

Differential centrifugation has also been used to isolate TGF β and MAGE 3/6-positive exosomes from the plasma of patients with ovarian carcinoma [9]. Finally, new and more sophisticated methods are being developed, and could be incorporated in the daily clinical practice as screening procedures for certain diseases in the near future. For example, Shao et al., showed that blood can be analyzed by a microfluidic chip-based detection method to monitor patients with glioblastoma, combining a CD63 antibody-based capture approach with a miniaturized nuclear magnetic resonance system [10].

In summary, blood-derived exosomes may become a useful diagnostic and prognostic tool for physicians. They can be obtained by low-invasive means and may become part of the daily clinical practice to diagnose or monitor patients in the near future.

References

1. Atkin-Smith GK, Tixeira R, Paone S, Mathivanan S, Collins C, et al. (2015) A novel mechanism of generating extracellular vesicles during apoptosis via a beads-on-a-string membrane structure. *Nat Commun* 6: 7439.
2. Raposo G, Stoorvogel W (2013) Extracellular vesicles: exosomes, microvesicles, and friends. *J Cell Biol* 200: 373-383.

3. Stoorvogel W, Kleijmeer MJ, Geuze HJ, Raposo G (2002) The biogenesis and functions of exosomes. *Traffic* 3: 321-330.
4. Winston CN, Goetzl EJ, Akers JC, Carter BS, Rockenstein EM, et al. (2016) Prediction of conversion from mild cognitive impairment to dementia with neuronally derived blood exosome protein profile. *Alzheimers Dement (Amst)* 3: 63-72.
5. Moon PG, Lee JE, Cho YE, Lee SJ, Jung JH, et al. (2016) Identification of developmental endothelial locus-1 on circulating extracellular vesicles as a novel biomarker for early breast cancer detection. *Clin Cancer Res* 22: 1757-1766.
6. Fiandaca MS, Kapogiannis D, Mapstone M, Boxer A, Eitan E, et al. (2015) Identification of preclinical Alzheimer's disease by a profile of pathogenic proteins in neurally derived blood exosomes: A case-control study. *Alzheimers Dement* 11: 600-607.
7. Melo SA, Luecke LB, Kahlert C, Fernandez AF, Gammon ST, et al. (2015) Glypican-1 identifies cancer exosomes and detects early pancreatic cancer. *Nature* 523: 177-182.
8. Shi M, Liu C, Cook TJ, Bullock KM, Zhao Y, et al. (2014) Plasma exosomal α -synuclein is likely CNS-derived and increased in Parkinson's disease. *Acta Neuropathol* 128: 639-650.
9. Szajnik M, Derbis M, Lach M, Patalas P, Michalak M, et al. Exosomes in Plasma of Patients with Ovarian Carcinoma: Potential Biomarkers of Tumor Progression and Response to Therapy. *Gynecol Obstet*.
10. Shao H, Chung J, Balaj L, Charest A, Bigner DD, et al. (2012) Protein typing of circulating microvesicles allows real-time monitoring of glioblastoma therapy. *Nat Med* 18: 1835-1840.
11. Rupp AK, Rupp C, Keller S, Brase JC, Eehalt R, et al. (2011) Loss of EpCAM expression in breast cancer derived serum exosomes: Role of proteolytic cleavage. *Gynecol Oncol* 122:437-446.