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# The Development of Biological Molecular Sensing Techniques to detect Micro particles: Focus on Clinical Medicine Benefits

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## Abstract

Microparticles (MPs) are defined a heterogeneous population of vesicles (diameter 100-1000 nm) that are released by cellular vesiculation and fission of the membrane of cells and play a pivotal role in various diseases including cardiovascular diseases, cancer, sepsis, eclampsia, autoimmune and metabolic states. Currently there is no standardization regarding analytical methods of MP detection. Conventional methods have crucial limitations regarding complicated assay and suffers from relatively low sensitivity and accuracy because of resolution problems occurring for the majority of commercially available flow cytometers. Alternatively, recently recognized as a method for quantification and sizing of biological nanoparticles surface plasmon resonance-based imaging microscopy (SPRi microscopy) might be significantly useful to resolve the majority problems affected MPs recognition. Probably Raman micro-spectroscopy, micro nuclear magnetic resonance technique, small-angle X-ray scattering, and anomalous small-angle X-ray scattering might compete with SPRi microscopy and flow cytometery. Sort comment is discussed contemporary approaches regarding novel techniques of microparticle determination, measurements and assay.

**Keywords:** Microparticles; Analytical assay; Flow cytometry; Western blot analysis; Electron microscopy; Surface plasmon resonance-based imaging microscopy; Nuclear magnetic resonance techniques

Developments of technologies that attenuate recognize, determination, and measurements of microparticles (MPs) obtained from various cells appear to be indispensable tool to clinical medicine [1]. Recent investigations have been shown that MPs as derivate of cellular membrane are discussed powerful paracrine regulators of target cell functions affected growth of tissue, reparation, vasculogenesis, inflammation, apoptosis, infection, and malignancy [2-4]. There is large body of evidences regarding association between immune pattern of MPs originated from different cells (endothelial cells, mononuclear, dendritic cells, platelets) and nature evolution of various diseases including cardiovascular diseases, cancer, sepsis, eclampsia, autoimmune and metabolic states, etc. [5-8].

MPs are defined a heterogeneous population of vesicles (diameter 100-1000 nm) that are released by cellular vesiculation and fission of the membrane of cells [9]. This mechanism affects genome and may mediate by some triggers [10]. In is well known that MPs appear to be found into circulation in response to many situational changes (physiological conditions, stress) micro environmental stimulation, coagulation / thrombosis, endotoxinemia, endothelial shear stress, activated cells or those undergoing apoptosis, ischemic injury, hypoxia, and malignancy [11-13].

The current stand of knowledge regarding morphology, transcriptomics, and proteomics of circulating MPs is still not fully [14,15]. The difficulty of separating MPs realized from other types of cells limits or efforts to extend actual cognitions in features affected biogenesis, secretion, and subsequent biological role of MPs. Therefore, there are no standardized protocols regarding methods of isolation and analysis of MPs [16].

The conventional approach for measuring the MPs is based on commonly used flow cytometry and nanoparticle tracking analysis (NTA), Western blot analysis and electron microscopy, although the definition of MPs using these techniques is still an area of great debate. Unfortunately, all methods have crucial limitations regarding complicated assay and suffers from relatively low sensitivity and accuracy because of resolution problems occurring for the majority of commercially available flow cytometers [17,18]. The next serious barrier created surmountable problems for NTA is sizing of small MPs (50 nm and less). However, the utilization of flow cytometers specifically designed for analysis of small-size MPs is probably to provide considerable methodological advantages and should be the preferable options [17]. In addition, problems with concentration limits of NTA measurements restrict the use of this method for clinical samples [18]. Western blot analysis and electron microscopy allow to optionally recognizing MPs depending on determination of different markers, represents a useful tool for examining particles. However, Western blot analysis and electron microscopy require subsequent technical efforts and are much expensive.

Alternatively, recently recognized as a method for quantification and sizing of biological nanoparticles surface plasmon resonance based imaging microscopy (SPRi microscopy) might be significantly useful to resolve the majority problems affected MPs recognition. SPRi is discussed a highly sensitive label-free biochemical surface sensor measurement technique that has only recently been applied to the field of cell-biology. This method is based on phenomenon known as surface plasmon resonance that associates with a high resolute diffraction generated at a thin metal surface [19]. The high contrast in SPR signal between cell edges and substratum facilitates identification of cell edges and segmentation of cell areas [20]. Importantly that several cells, cellular components (i.e., focal adhesions, nucleus, and cellular secretions), viruses, bacteria, micro- and nanoparticles have not just became visible, but they are able to be calculable [19,20].

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As expected, a quantitative interpretation of SPRi imaging might improve resolution of MP determination and allow investigators unprecedented to overcome flow cytometry limitations regarding low detectable small-size MPs [21]. Moreover, simultaneous application of a high-sensitive fluorescent microscopy and SPRi microscopy should enhance the sensitivity and selectivity of a created biosensor platform [22,23]. This might have a high value for identification of small-size MPs originated from different cells that were recently determined as debris [24]. Probably small-size MPs derived from apoptotic cells play a pivotal role in tissue injure, inversely MPs secreted activated cells, i.e., mononuclear, endothelial cells, dendritic cells, may have a positive effect on tissue repair and homeostasis [25].

A highly sensitive fluorescent (HSF) microscopy also permits to detect individual sub-micro and nano-MPs. As compared with SPRi microscopy, this technique could provide higher detection sensitivity due to a large fluorescence excitation and a high effective quantum yield of fluorescence. Therefore, there are at least four methods that are not commercially available: Raman micro-spectroscopy, micro nuclear magnetic resonance technique, small-angle X-ray scattering, and anomalous small-angle X-ray scattering [26]. All these methods are currently being explored to assay MPs, while an incorporation of these techniques into routine analytical practice is probably addressed in the future.

In conclusion, a standardization of the methods of nano- and micro- particles determination is extremely required. Commonly used procedures, such as flow cytometry with NTA, Western blot analysis and electron microscopy, might not have universal utility for MP determination; especially for small-size MPs. Novel techniques regarding identification of MPs based on real-time and label-free optical biosensors and principles of SPR phenomena appear to be much attractive and could sufficiently overcome limitation of option methods of MP determination.

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