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EDITORIAL

Roles and Application of Extracellular Vesicles Occurring Endogenously and Naturally

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Extracellular vesicles (EVs) are lipid-bilayer membrane vesicles that are released by cells into the extracellular environment. Two main EVs subpopulations are exosomes, which are formed by the inward budding of the endosomal membrane, and ectosomes, which are formed by the outward budding and fission of the plasma membrane [1]. Exosomes are typically smaller than ectosomes, with a diameter of around 40–150 nm, while ectosomes can range from 100–1000 nm in a diameter. EVs carry a variety of molecules as cargo, including proteins, lipids, and nucleic acids such as DNA, mRNA and microRNA, and they play a crucial role in intercellular communication, allowing cells to exchange information and materials each other [2]. As such, they are involved in the regulation of various physiological and pathological processes such as immune system modulation, tissue regeneration, and cancer metastasis.

Since EVs may carry disease-specific protein or genetic markers of originated cells and tissues, they are expected as a potential tool for diagnosis and monitoring for diseases such as cancer, infections diseases, and neurological disorders [3]. Furthermore, EVs can be biomarkers of pharmacological/toxicological effects of drugs. When cells are exposed to drugs or toxins, they can release exosomes that contain specific biomolecules that are altered in response to the exposure. These changes in the biomolecular cargo of exosomes can reflect the pharmacological of toxicological effects of the exposure, making them useful biomarkers for monitoring drug- or toxin-induced effects. For example, studies have shown that exosomal microRNAs or exosomal proteins can serve as biomarkers for drug-induced liver injury [4] or drug-induced cardiotoxicity [5].

EVs obtained from food are emerging research area. Food derived EVs can affect human through various small and large molecules as cargo. Some studies have suggested that EVs from certain foods exhibit biological activity that could impact human health. For example, plant derived EVs exert a wide range of biological and pharmacological effects such as wound healing, anti-oxidant, anti-tumor, and anti-inflammatory effects [6]. It has also been demonstrated that microRNA in plant derived EVs regulate intestinal transporter expression, which may affect intestinal disposition of small molecular nutrients and clinically used drugs [7]. Bovine milk is rich source of small EVs. It is interesting that bovine milk small EVs and their small RNA cargo are bioavailable following oral administration in humans [8]. Research has shown that milk small EVs contain a range of bioactive molecules, which have been linked to various biological processes such as immune regulation, tissue repair and anti-inflammatory activity [9]. However, since the importance and potential applications of food derived EVs in human health are still not widely acknowledged, in depth investigation is required before food derived EVs are used as clinical biotherapeutics.

EVs are expected as a useful tool for delivery of large molecular drugs, since especially food derived EVs are generally believed safe and have a potential of specific interaction with human cells. Macromolecules such as proteins and nucleic acids are feasible to degradation in

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the intestinal lumen and hardly cross intestinal absorption barrier. However, their stability is improved by contained in EVs and EVs are taken up by cells. Accordingly, stability and permeability of intestinally administered macromolecules are improved in EVs. Further, they have a merit in production, because abundant source of them is available from food. Milk and plant-derived nanoparticles have been studied in past one decade and have shown to affect intestinal function. Furthermore, they might move to systemic circulation by passing through intestinal barrier in the form of nanoparticle, while such observation is still controversial. So, EVs derived from endogenously and from food are interesting fields both in basic science and application for drug delivery systems.

Finally, although there has been an exponential increase in the interest in exosomes for their potential applications in understanding the underlying mechanisms of various diseases or promising biomarkers for diagnosis, prognosis, and even therapeutic tools [10], the preparation of exosomes is still challenging due to their small size, heterogeneity, and similarity to other larger EVs. Different isolation methods have been developed including ultracentrifugation, density gradient centrifugation, and immunoaffinity capture, and they have own advantages and limitations. One of the major issues is the potential for contamination with non-exosomal components, such as proteins and lipoproteins, which affect downstream analyses and interpretation of results [11]. Another issue is the potential for loss or alteration of exosomal contents during isolation, which can affect their biological activity and potential clinical applications. Therefore, it is important to optimize the isolation method and minimize handling and processing time to preserve the integrity and function of exosomes [12, 13].

Overall, the roles and applications of EVs are diverse and still being explored. EVs are a promising area of research with numerous potential applications in various fields including medicine and biotechnology. This special issue describes current research on usefulness of EVs derived from internally and externally such as food and artificial ones.

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