

GS02-6 Development of drug delivery techniques based on exosomes modified with arginine-rich peptides

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Exosomes are approximately 30-200 nm vesicles secreted by various types of cells and included in body fluids such as blood, urine and so on. Exosomes encapsulate miRNAs and enzymes and play important roles in cell-to-cell communications [1]. In addition, exosomes are highly expected as next generation drug delivery tools owing to their pharmaceutical advantages, such as i) no cytotoxicity, ii) controlled immunogenicity, iii) modification and encapsulation of artificial molecules. However, cellular uptake efficacy is insufficient to be utilized as drug delivery tools. Our research group recently found that cellular uptake efficacy of exosomes is enhanced by activation of macropinocytotic pathways [2]. In this study, we developed arginine-rich peptide [3]-modified exosomes, which can actively induce macropinocytosis, leading to increased cellular uptake efficacy of exosomes [4]. Furthermore, we demonstrated the effects of the number of arginine residues in the peptide sequence on cellular exosome uptake and cytosolic release of encapsulated biofunctional molecules in the exosomes.

[1] Katsuda, T. *et al. Proteomics* **14**, 412-425 (2014), [2] Nakase, I. *et al. Sci. Rep.* **5**, 10300 (2015), [3] Nakase, I. *et al. Acc. Chem. Res.* **45**, 1132-1139 (2012), [4] Nakase, I., Noguchi, K. *et al. Sci. Rep.* **6**, 34937 (2016), [5] Nakase, I., Noguchi, K. *et al. Sci Rep.* **7**, 1991 (2017)