Abstract and key words

Mouse polyomavirus-derived virus-like particles composed from major capsid protein VP1 (MPyV VP1-VLPs) are interesting structures for use as a delivery system of various cargos into cells. VP1 protein self-assembles into icosahedral particles of 45 nm in diameter that are hollow highly regular nanoparticles.

In this work, model small molecule cargo, Cyclodextrin-Based Bimodal Fluorescence/MRI Contrast Agent, was encapsidated into MPyV VP1-VLPs. The cargo was stably associated with VLPs and was delivered into mammalian cells using these VLPs.

To prevent VLPs entrapment in endolysosomal compartments and increase the potential of VLPs applications, MPyV VP1 protein was modified by insertion of histidine-tag (6 histidine long sequence surrounded by glycine and serine) sequences into VP1 surface loop DE, because histidine modification of synthetic systems had enhancing effect on endosome escape and cargo delivery. With the use of in Bac-to-Bac® baculovirus expression system His-VP1 protein was expressed in insect cells and a variety of VP1-assemblies was obtained: long tubules and small 20nm VLPs formed from VP1 with 4 histidine-tags in DE loop, and novel VP1 nanostructure, which we named nano-jumpers, formed from VP1 with 2 histidine-tags. Nonetheless the endosome escape properties of His-VLPs and nanostructures were analysed and it was proved that histidine modification enhanced endosome escape of these structures.

Moreover, the effects of histidine-rich peptide ($KH_{27}K$) and known endosome disrupting agent polyethylenimine (PEI) were tested. $KH_{27}K$ had similar effect on endosome disruption as PEI, which was detected using endocyted fluorescent antibody. The effect of $KH_{27}K$ and PEI on MPyV infectivity was also investigated. It was shown for the first time that endosome membrane disruption enhances MPyV infectivity.

Key words:

mouse polyomavirus, VLPs, endosome escape, cargo, delivery, histidine