

Abstract

The aim of this thesis is to reveal the potential of mouse polyomavirus (MPyV) based virus-like particles (VLPs) as possible nanocarriers for directed delivery of therapeutic or diagnostic compounds to specific cells or tissues. We have chosen mouse polyomavirus VLPs because they do not contain viral DNA and are considered safe for utilization in bio-applications.

In our research, we used a chemical approach for retargeting of MPyV based VLPs from their natural receptor to cancer cells. The chemical modification of the capsid surface exposed lysines by an aldehyde-containing reagent enabled conjugation of VLPs to selected molecules: transferrin and inhibitor of glutamate carboxypeptidase II (GCPII). Transferrin, as a transporter of iron to metabolically active cells, targeted VLPs to numerous types of cancer cells overexpressing the transferrin receptor. On the other hand, GCPII serves as a transmembrane marker specific for prostate cancer cells and conjugation of its inhibitor to VLPs resulted in successful recognition of these cells. Electron microscopy was used for visualization of modified VLPs and flow cytometry together with confocal microscopy for investigation of cell specific interactions and VLP uptake. Furthermore, we explored the influence of serum proteins on VLPs. The abundance of serum proteins in the blood stream is a major problem of *in vivo* targeting of various types of nanoparticles because these proteins interact with nanoparticle surface and form so called protein corona. The protein corona then masks the targeting ligands and prevents the specific targeting of nanoparticles. We used ELISA assays and flow cytometry to prove that the targeting of prepared VLPs is not affected by protein corona formation.

In conclusion, we demonstrated that polyomavirus based VLPs could be retargeted to either broadly distributed or type-specific cancer markers. This makes the VLPs an universal tool for addressing a wide range of tumors. The strong avidity and binding selectivity of VLP conjugates have a tremendous potential to increase the sensitivity and specificity of cancer therapies.

Key words: polyomavirus, virus-like particle, VLPs, nanoparticle, GCPII, transferrin