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Polyomavirus based viral nanoparticles: a useful tool for targeting cancer cells affecting protein corona

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Statement of the problem: Nanoparticles are studied as potential nanocarriers for directed cell/tissue delivery of therapeutic or diagnostic compounds. However, their utilization could be limited by various factors. One of the up-to-date scientific topics is a formation of protein/biomolecule corona that influences the nanoparticle behavior in physiological conditions, especially the targeting capacity of nanoparticles.

Purpose: The purpose of this study is to prepare viral nanoparticles that could selectively interact with cancer cells without being restrained by the formation of protein corona. Viral nanoparticles (VNPs) based on mouse polyomavirus were used considering their safety for bio-applications.

Methodology & Theoretical Orientation: The chemical modification of the capsid surface exposed lysines by amidic coupling with alkyne-containing reagent enabled conjugation of VNPs to selected molecules (transferrin and inhibitor of PSMA) with azide residues. Electron microscopy was used for visualization of VNP modification and flow cytometry together with ELISA and confocal microscopy for investigation of cell specific interactions and nanoparticle uptake.

Findings: Chemical conjugation was proven a successful approach for retargeting of polyomavirus based VNPs from their natural receptor to cancer cells. Coupling of transferrin, a transporter of iron to metabolically active cells, targeted VNPs to numerous types of cancer cells overexpressing the transferrin receptor. Also, conjugation of small inhibitor of PSMA (a transmembrane marker specific for prostate cancer cells) resulted in recognition of prostate cancer by these VNPs. Furthermore, our modified VNPs were able to interact with specific receptor even in the presence of 10% or 55% sera, thus bypassing the issue of mistargeting of nanoparticles by associated serum proteins.

Conclusions & Significance: Functionalized polyomavirus derived VNPs could be retargeted to either broadly distributed or type-specific cancer markers. These VNPs with their strong avidity, binding selectivity and resistance to protein corona could increase the sensitivity and specificity of cancer therapies

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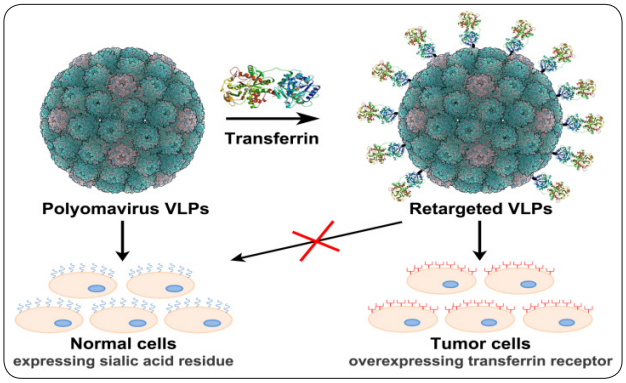

Figure 1: Schematic representation of experimental design. The transferrin molecules were coated on the VNP surface by chemical coupling leading to retargeting of these VNPs to tumor cells overexpressing transferrin receptor.

The same approach was used also for production of VNPs with conjugated PSMA inhibitor

Recent Publications:

1. Docter D et al. (2015) The nanoparticle biomolecule corona: lessons learned - challenge accepted? Chem Soc Rev. 44(17):6094-6121.
2. Piella J, Bastús N G and Puntes V (2017) Size-Dependent Protein–Nanoparticle Interactions in Citrate-Stabilized Gold Nanoparticles: the emergence of the protein corona. Bioconjug Chem. 28(1):88-97.
3. Salvati A et al. (2013) Transferrin-functionalized nanoparticles lose their targeting capabilities when a biomolecule corona adsorbs on the surface. Nat. Nanotechnol. 8(2):137-143.
4. Zackova Suchanova J et al. (2017) Retargeting polyomavirus-like particles to cancer cells by chemical modification of capsid surface. Bioconjug Chem. 28(2):307-313.
5. Neburkova J et al. (2018) Inhibitor-GCPII interaction: selective and robust system for targeting cancer cells with structurally diverse nanoparticles. Mol Pharm. Doi: 10.1021/acs.molpharmaceut.7b00889.

Biography

Jirina Zackova Suchanova received her Master's Degree in Cell Biology, Genetics and Virology from Charles University, Prague, Czech Republic in 2012. She continued her study at this university and currently is a PhD candidate in the Laboratory of Molecular Virology. Her research is focused on the utilization of polyomavirus-based nanoparticles as specific vehicles for delivery of therapeutic or diagnostic compounds to cancer cells. She studies various types of particle modifications, as well as the optimal conditions for disassembly and reassembly of these particles for further successful encapsidation of theranostic agents.

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