

CEIPEX MU TOPIC 8B

Položka / Field	Obsah / Content
NAME	prof. RNDr. Robert Vácha, PhD.
CEIPEX RESEARCH TOPIC LEVEL2	Structural Biology: Protein-protein and protein-membrane interaction
NAME OF THE RESEARCH GROUP	Interaction Protein-Protein and Protein-Membrane
TOPIC	Design Principles of Fusogenic Proteins for Lipid Vesicles
ABSTRACT	Cancer remains one of the leading causes of mortality worldwide, claiming nearly ten million lives each year. One promising treatment is cancer immunotherapy using mRNA encapsulated in lipid vesicles, which facilitate efficient drug transport into target cells. However, the delivery of mRNA into the cell remains a challenge due to limited endosomal escape. To overcome the endosomal escape barrier, this project aims to computationally design proteins that induce fusion between lipid vesicles and endosomes. Using mesoscopic simulations, we will identify the key structural features of proteins with a transmembrane domain that promote membrane fusion. These insights will inform the rational design of coiled-coil peptide sequences with said features and assess their capacity to induce membrane fusion using Martini coarse-grained simulations. This research will elucidate the molecular mechanism of protein-mediated membrane fusion, establishing a framework for the rational design of fusogenic proteins. The designed proteins will enable the development of lipid vesicles with increased endosomal escape efficiency, which has the potential to improve the intracellular delivery of mRNA. Collectively, these advances will contribute to the broader vision of developing clinically relevant platforms that expand the therapeutic potential of nucleic acid medicines and accelerate their translation into effective therapies.
WEBPAGE OF THE RESEARCH GROUP	https://vachalab.ceitec.cz/