

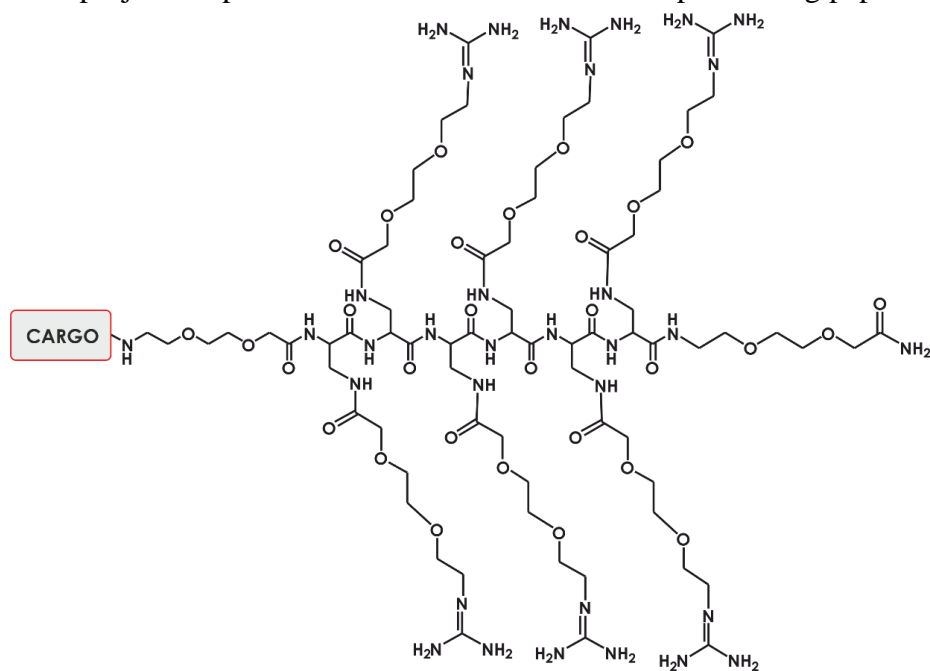
## New class of nucleus penetrating peptides. Design, synthesis and mechanism of action.

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Arginine rich peptides, belong to class of cell penetrating peptides that are able to transport the wide variety of attached chemical entities (cargos) through the cell membrane. Diversity of transported molecules is impressive and includes: DNAs, siRNAs, peptides, proteins and small drugs. Polyarginines comprise over five residues of L-arginine efficiently penetrate the cell membrane, and in some instances are part of more complex molecule which is able to deliver cargos to nucleus through nuclear localisation signal (NLS).

The general aim of this proposal is to reveal the mechanism of action novel cell penetrating peptidomimetic which structure is presented on figure 1. Such molecule contains several instances of L-2,3-diaminopropionic acid (DAP) connected through the peptide bond and modified on its side chain amino groups by substitution of functionalised PEG moiety (8-amidino-3,6-dioxaoctanoic acid further abbreviated as (GO2)). For group of compound we proposed the abbreviation DAPEG that is merged DAP and PEG. Obtained peptidomimetic which is labelled by 5/6-carboxyfluorescein moiety efficiently penetrates cell membrane and is transported directly to nucleus of primary and transformed cell without significant toxicity. Such compounds are also resistant to protease action inside the cells. Since there are no reports describing such short nuclear penetrating peptidomimetics or peptides we would like to investigate properties and structural requirements of such molecules able to deliver cargo into nucleus. We will deeply analyse the cell effect of such compounds on healthy and cancer cell line. Also the influence of cargo types deliver to the nucleus on cell properties will be tested. In order to do so we plan to design a set of analogues of leading compound that will be used as chemical tools for this project.

In effect of this project we plan to obtain new class of nucleus penetrating peptidomimetics.



**FIGURE 1.** The structure of DAPEG peptidomimetic where in cargo position 5/6-carboxyfluorescein moiety was present.