Abstract template

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Click-activatable cell- penetrating peptides

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Cell-penetrating peptides (CPPs) have been shown to be able to cross cell membranes and are therefore reported as promising tools for the transport of molecules into the cell [1]. However, one important drawback of these peptides is their lack of cell-type specificity [2]. To overcome this, the activity of CPPs can be tuned, adding to their specificity. For this purpose, several strategies have been reported that use triggers for activation such as a change of pH [3], enzymatic reactions [4] or exposure to UV-light [5]. Previously we have reported an activation strategy based on synthetic short oligoarginines that were activated by extension of the oligoarginine stretch by disulphide bridge formation, resulting in active CPPs [6]. Our research focuses on increasing the bio-orthogonality of the activation of short oligoarginines, allowing for in situ activation of CPPs. Our strategy is to functionalize short oligoarginine stretches with clickable groups, which can function in joining two activated oligoarginine CPPs. The used peptides consist of a tetra-arginine with an N-terminal fluorescent label and a C-terminal tetrazine or azide functionality and of a tetra-arginine with an N-terminal alkyne, norbornene or BCN functionality. These peptides can join together to form active oligoarginine CPPs via SPAAC, CuAAC, or tetrazine-norbornene and tetrazine-BCN cycloadditions. The cellular uptake behaviour of the activated CPPs will be studied with confocal fluorescence microscopy and quantified using flow cytometry.

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