

P021 Cell-penetrating peptide–polymer conjugates with strongly increased bioactivity inside the cell

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Rationally designed synthetic peptides provide a rich resource of bioactive inhibitors of molecular interactions. However, poor membrane permeability and low stability against proteases still limit the applicability. The aim of this work was to increase the peptide stability and simultaneously enable an efficient cellular uptake by conjugation of cell-penetrating peptides to a soluble polymeric backbone. A fluorescein-labelled proapoptotic peptide and an unlabelled cell-penetrating peptide were synthesized as independent building blocks and chemoselectively conjugated to the inert polymer HPMA (N-(2-hydroxypropyl)-methacrylamide) by native chemical ligation. The stoichiometry of conjugated peptides was quantified by fluorescence correlation spectroscopy. The bioactivity of the proapoptotic peptide was analysed by an apoptosis assay and compared to the related peptide-CPP-conjugate not bound to HPMA. The cellular uptake of HPMA-conjugated and unbound peptides was compared by flow-cytometry. The HPMA-conjugated peptides showed a strong increase in bioactivity compared to the free CPP-peptide conjugates.