Amphipathic proline-rich cell penetrating peptides for mitochondria targeting

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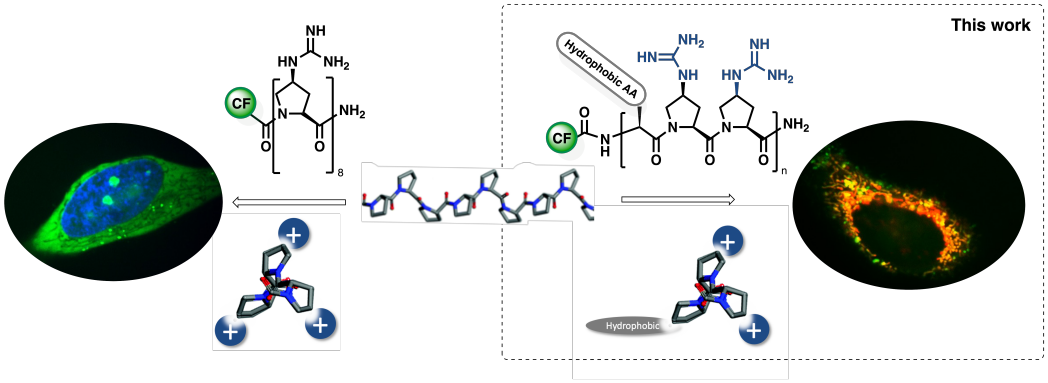
Cell penetrating peptides (CPPs) cross the lipophilic barrier of the cellular membrane and serve as delivery vectors to translocate cargo into cells.[1] They can also be useful for target-specific delivery, for example, of bioactive molecules to a specific cellular organelle. Here, targeting mitochondria constitutes an important goal since mitochondria dysfunction is associated with many diseases, including neurodegenerative and auto-immune diseases, diabetes, and cancer.[2] Selective delivery of bioactive compounds to mitochondria is challenging due to the dense and hydrophobic double membrane.[3]

Our group developed a cytoplasm and nucleus penetrating oligoproline (Z_8) CPP, which exhibits higher cellular uptake in comparison to more flexible peptides (e.g. octaarginine).[4] Here, we showcase that oligoproline peptides with hydrophobic amino acids installed at every third position allow mitochondria targeting. Selectivity is achieved by the PPII helix conformation with two cationic faces and one hydrophobic face enabling the crossing of the mitochondria membranes. The localization of the amphipathic peptides inside cells was evaluated by confocal microscopy, and the cellular uptake efficiency by fluorescence-activated cell sorting (FACS).



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