

Novel Cell Penetrating Peptide Mimics

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While scientists have been studying synthetic polymers for almost 100 years, compared to proteins and DNA, these molecules remain relatively unsophisticated. We are interested in elucidating the rules required to program synthetic polymers with the necessary chemical information to express function that rivals, or even outperforms, natural proteins. In particular, we focus on cell penetrating peptides (CPPs), which readily transverse cell membranes. Inspired by HIV-TAT, a naturally occurring, guanidinium-rich CPP, novel ring-opening metathesis polymerization (ROMP)-based polymers were designed as mimics. Previous studies indicated that guanidine (cationic) and hydrophobic groups are essential for protein transduction. Our group has also illustrated that aromatic functionalities are important for improved uptake. After incorporating various aromatic functionalities into our monomers, we utilized HPLC to assess their relative hydrophobicities. Dye leakage experiments concluded that the incorporation of phenyl substituents resulted in improved activity compared to polymers containing cyclohexyl substituents. It is believed that the quadrupole moments and flat, rigid structures of these aromatic groups result in improved interactions with cell membranes and better activities. Further studies will be conducted to see how changing the electron densities of the aromatic substituents effect activity.

