Evaluate characteristic of PTD that aim to optimize intracellular drug therapy.

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Recently, many disease-related proteins are identified by disease proteomics study. Therefore, the establishment of the treatment strategy that control these function is attracted. Because these therapeutic targets are generally located inside the cell, it is necessary to establish novel technology of drug delivery that facilitate the delivery of macromolecular drug such as therapeutic proteins or nucleic acid-based drugs across the cellular membrane. Protein transduction domains (PTD) are candidates for novel drug carriers because of their unique ability to facilitate protein transport into the cytosol. Although understanding the mechanisms or the pathway of transduction are important for PTD-based therapeutics, these information remain poorly resolved. Here, we have compared the intracellular properties of four well-known PTD: Tat-PTD, Rev-PTD, VP22-PTD and antennapedia (Antp)-PTD. At first, we attempted to estimate the transduction efficiency of PTD by using FAM-labeled PTD. As a result, transduction efficiency of PTD were different depending on cell types. Next, we check the localization in cytosol using confocal laser scanning microscopy. The localization of PTD were almost in the endosome and there were a little difference between four PTD. To achieve more efficiency intracellular delivery, we used influenza HA2 peptide, increase permeability of endosome membrane, and organelle targeting signal (use nuclear localization signal ; NLS). Combined HA2 peptide and NLS, fluorescence protein were escaped from endosome and went to the nucleus efficiently. Our results are useful to the development of PTD-based drug delivery system.