Abstract of Presentation

Noninvasive delivery systems for therapeutic peptides and proteins

We have been developing noninvasive delivery systems for therapeutic peptides and proteins through the years. One of our recent findings is that the intestinal and nasal absorption of therapeutic peptides and proteins including insulin can be significantly improved by co-administration of cell-penetrating peptides (CPPs) in the animal studies [1-3]. The CPPs are known to be efficiently taken up by numerous cells and can bring other molecules ranging from small compounds to large proteins and particles into the intracellular compartment. In the past few decades, many types of CPPs have been identified, such as TAT peptide and penetratin. At present, CPPs are regarded as one of the most attractive tools for intracellular delivery of therapeutic proteins and nucleic acids because of their ability of macropinocytosis. We have employed the CPP's ability to accomplish the permeation of peptides and proteins from intestinal lumen and nasal mucosa to circulation. Finally we have found that peptides and proteins absorption from the biological membrane could be enhanced significantly in the presence of CPPs, and the effect of CPPs on the drug absorption has been identified using positron emission tomography (PET) [4]. In addition, our study verified the hypothesis that the electrostatic interaction between drug and CPP is related to the enhancing effect of the CPP on the intestinal absorption of therapeutic peptides and proteins [3]. Furthermore, we have tried to find CPPs that are highly effective for the delivery of macromolecules and do not induce toxic effects on the membrane, and we found that L-penetratin had the strongest ability to enhance macromolecules absorption from mucosal membrane.

In conclusion, CPPs are likely to become powerful tools for overcoming the low permeability of therapeutic peptides and proteins through the epithelial cell membrane, the major barrier to their noninvasive delivery. Further advantage of this promising strategy is that this successful intestinal and nasal absorption could be achieved by more convenient methodology, coadministration of CPP with drugs via intermolecular interaction among them.

References

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