Cell-penetrating peptides as noninvasive transmembrane vectors for the development of novel multifunctional drug-delivery systems

Dongdong Zhang, Jiaxi Wang, Donggang Xu

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Cell-penetrating peptides as noninvasive transmembrane vectors for the development of novel multifunctional drug-delivery systems

Dongdong Zhang[a,b], Jiaxi Wang[a], Donggang Xu [a,b,*]

[a]Beijing Institute of Basic Medical Sciences, 27 Taiping Road, Beijing 100850, PR China

[b]Anhui Medical University, 81 Meishan Road, Hefei 230032, PR China

Abstract

Unique characteristics, such as nontoxicity and rapid cellular internalization, allow the cell-penetrating peptides (CPPs) to transport hydrophilic macromolecules into cells, thus, enabling them to execute biological functions. However, some CPPs have limitations due to nonspecificity and easy proteolysis. To overcome such defects, the CPP amino acid sequence can be modified, replaced, and reconstructed for optimization. CPPs can also be used in combination with other drug vectors, fused with their preponderances to create novel multifunctional drug-delivery systems that increase the stability during blood circulation, and also develop novel preparations capable of targeted delivery, along with sustainable and controllable release. Further improvements in CPP structure can facilitate the penetration of macromolecules into diverse biomembrane structures, such as the blood brain barrier, gastroenteric mucosa, and skin dermis. The ability of CPP to act as transmembrane vectors improves the clinical application of some biomolecules to treat central nervous system diseases, increase oral bioavailability, and develop percutaneous-delivery dosage form.

Keywords: Cell-penetrating peptides; Noninvasive transmembrane; Macromolecule transportation; Drug-delivery system

1. Introduction

Intercellular transposition of biomacromolecules is the basis of physiological and pathological processes. Cell-penetrating peptides (CPPs) act as cargo carriers and constitute a current hotspot in medical research. They are capable of entering the body in a noninvasive manner and accelerate the absorption of macromolecules via physiological mechanisms such as energy-dependent endocytosis and energy-independent direct penetration [1-4] (Fig. 1). Compared to some traditional techniques, such as microinjection and electroporation[5, 6], CPPs do not destroy the integrity of the cell membranes, and are considered highly efficient and safe, thus, providing new avenues for research and applications in life sciences.

Through biomaterial modification, CPPs can be refolded and assembled with synthetic nanostructures in order to ameliorate the disadvantages owing to nonselectivity, lower delivery efficiency, and decreased susceptibility to degradation[7-9]. CPPs can be also incorporated into versatile cargo-carrying platforms to create novel drug-delivery systems that ensures improved coated-drug uptake, as well as their targeted recognition and controlled release via stimulus-responsive mechanisms[10, 11]. The extensive use of CPPs in drug delivery will add considerable potency to protein- and nucleic-acid-based drugs[12-15], thereby increasing the

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* Corresponding author. Tel: +86 010 66931380. Fax: +86 010 68213039

E-mail address: xudg@bmi.ac.cn