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Antimicrobial peptides as carriers of drugs

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The insect-derived antimicrobial peptide pyrrochoricin and its derivatives have recently been described by Laszlo Otvos and colleagues of the Wistar Institute in Pennsylvania (http://www.wistar.upenn.edu/) as being one of the best vehicles for drug delivery found so far [1]. Drug-delivery carriers need to have specific features and two of the prime requisites are low toxicity and the ability to penetrate cells. Proline-rich cationic molecules are usually selected in the search for drug carriers for their ability to penetrate cell membranes.

The balance of toxicity and cell penetration

Unfortunately, however, these cationic molecules often show high levels of toxicity. Pyrrochoricin and its designed analog (Pip-pyrr-MeArg) are proline-rich cationic molecules with the added advantage of showing no toxicity in *in vivo* and *in vitro* experiments.

Otvos *et al.* show that the molecules can easily penetrate bacterial cells and also human cells, and that the designed analog is able to penetrate several types of human cells including fibroblasts. The system could be used to deliver drugs to intracellular pathogens and as an efficient carrier for other drugs. Studies are in progress to determine the limitations of the system, in particular, the size limit for the cargo and whether the cargo needs to possess a specific charge.

Potential for immunotherapy

The antimicrobial peptide and its analog are also capable of penetrating human monocyte-derived dendritic cells (DC), a quality that makes it a good candidate for being a carrier of epitope-based vaccines. In their experiments, Otvos and colleagues show that the peptides can penetrate DCs easily without showing toxicity, can stimulate the immune system and can activate DCs. This offers a potential for this system to be used in vaccine development and anticancer therapy.

DC vaccination, albeit still at an early stage, is a promising strategy to induce immunity to cancer and the use of DCs loaded with a specific peptide antigen is becoming increasingly popular in cancer immunotherapy. The efficacy of such vaccines has been correlated with DC activation and, because of the ability to stimulate DCs pyrrochoricin and its derivatives could become powerful tools to construct carriers of peptide antigens.

Otvos is optimistic that this system could become the system of choice for the design of drug-delivery in eukaryotes and possibly the system of choice for dendritic cell-based immunotherapy.

Reference

1 Otvos, L. *et al.* (2004) An insect antibacterial peptide-based drug delivery system. *Mol. Pharmac.* DOI: 10.1021/mp049974e (E-Pub ahead of print; http://pubs.acs.org/journals/mpohbp)

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