International Journal of Pharmaceutics 423 (2012) 1–2

Contents lists available at SciVerse ScienceDirect

International Journal of Pharmaceutics

journal homepage: www.elsevier.com/locate/ijpharm

Editorial

For the third time, International Journal of Therapeutics has agreed to publish a Special Issue based on results first presented at the annual meeting of the GTRV (Groupe Thématique de Recherche sur la Vectorisation) held in Toulouse in December 2010. The GTRV is a mainly French-speaking special interest group bringing together scientists from the public and private sectors interested in carrier systems or their targets. Carriers are defined as any system that could modify the distribution of a biologically interesting molecule at the tissue, cellular or sub cellular level *in vivo* or *ex vivo*. This covers not only drug delivery and diagnostics but also techniques used in experimental cell biology. During the meeting in Toulouse, emphasis was placed on the delivery of anticancer drugs, innovative systems for imaging, peptides and other ligands for targeting specific cells, and gene and phototherapy for cancer. These preoccupations are reflected in the articles that have been selected for this Special Issue.

New technological advances in drug delivery are constantly being developed. One of these is temporary electrically mediated permeabilisation of cell membranes to promote uptake of active molecules which would not normally cross cell membranes. This strategy, already used in the clinic for solid tumours, is reviewed by Teissie et al., who point out many other potential applications in cancer treatment. However, there is very often no correlation between *in vitro* and *in vivo* results, and Chopinet et al., address this question by the use of spheroids as a three-dimensional *ex vivo* model.

The use of an external magnetic field in conjunction with a magnetic drug carrier system is another method of increasing drug accumulation. Gautier et al. describe the formulation of poly(ethylene glycol) coated iron oxide particles loaded with doxorubicin destined for this approach. Progress is also being made with many other types of nanoparticulate systems. Al-Kattan et al. present the formulation and preliminary biological evaluation of nanoparticles formed from calcium phosphate apatites. The mineral-based nanoparticles were rendered biocompatible by coating with a phospholipid derivative. The importance of particle surface properties for interactions with cells was also highlighted by Merhi et al. in a study of the interactions of serum with cationic nanoparticles and their consequences for endocytosis by bronchial epithelial cells.

The well-known poly(lactide-*co*-glycolide) (PLGA) polymer was used to encapsulate a α-galactosylceramide analogue into micro- and nanoparticles by Macho Fernandez et al. These systems can be internalised by dendritic cells which then activate invariant natural killer cells. Lipid-based drug carrier systems continue to prove their usefulness. Huynh et al. have used lipid nanocapsules loaded with ferrociphenol to treat brain tumours in the rat. The study by Roger et al. with the same drug delivery system took the original approach of using mesenchymal stem cells, which take up the nanocapsules, to deliver the drug to glioma cells. Liposomes were chosen as the delivery vehicle for a natural flavonoïd fisetin, by Mignet et al., thus overcoming the problem of its limited water solubility.

Cell-penetrating peptides are very useful tools in drug delivery. Balzeau et al. have studied the Vimentin-Tubulin binding site peptide, which they observed to enter glioblastoma cells by endocytosis and to distribute into the cytoplasm and nucleus. When coupled to an apoptosis-inducing peptide, it inhibited cell proliferation.

A nanoparticle-based targeting approach was used by Huang et al. The ligand biotin was coupled to the surface of nanoparticles based on poly(malic acid) derivatives and targeting to biotin-expressing cells *in vitro* was demonstrated. Bourseau-Guilmain et al., have used monoclonal antibodies against a cancer stem cell marker, AC133, coupled to the surface of lipid nanocapsules. These constructs were able to bind to Caco-2 cells expressing the marker, as observed by confocal microscopy.

The use of nanoparticles for imaging has attracted a lot of interest recently. In particular, the concept of "theranostic" has emerged, in which the drug delivery system is able to identify the presence of target cells, deliver an active agent and monitor the outcome. For this purpose, nanoparticles that are identifiable and targeted to specific cell types are required. Maldiney et al. have approached this goal by developing particles with persistent fluorescence emission bearing low molecular weight ligands with an affinity for tumour cells. David et al. demonstrated that lipid nanocapsules containing a more conventional fluorescent probe were able to colocalise with bioluminescent melanoma cells. The same nanocapsules loaded with ganciclovir were able to reduce tumour growth.

Drug delivery systems can also be used to modify the immunogenicity of proteins and thus allow the development of effective vaccines. Ben Hali et al. showed that encapsulation in cationic glycolipidic particles increased the immunogenicity of the HIV Nef protein and induced a Th-2 type immune response. PLGA microspheres were used as a carrier for bee venom allergens by Trindade et al. By releasing the allergens in a gradual manner, they could reduce the number of injections necessary for desensitisation therapy.

The advantages of drug delivery technology for gene delivery are numerous. In particular, the search for efficient non-viral transfection systems continues. Rosazza et al. have attempted to understand more about the mechanisms of plasmid DNA transfer by electroporation. They demonstrate the role of cholesterol in the

0378-5173/$ – see front matter © 2011 Published by Elsevier B.V.
doi:10.1016/j.ijpharm.2011.12.021

translocation of DNA from the plasma membrane to the interior of the cell, suggesting the caveolin/raft mediated endocytosis was involved, as well as the clathrin pathway. Lipid-mediated transfection is also a major research axis. Perche et al. combined DNA and polycations within liposomes bearing histidine on the head-group of the phospholipids. This formulation has the advantage of being amenable to freeze-drying without significant loss of transfection ability.

The range of articles included in this Special Issue illustrates the wide range of drug delivery and imaging strategies which are being deployed at the moment and testifies to the fertile imagination of the research groups involved.

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Available online 23 December 2011