STRATEGIES AND CHALLENGES TO IMPROVE THE TARGETING ABILITY OF ANTICANCER NANOMEDICINES

Silvia Arpicco
Department of Drug Science and Technology, University of Torino, Italy

The side effects of drugs used in the therapy of some diseases, like cancer, would be reduced by selectively delivering them into those cells or tissues where their action is required.
Ideally, a drug designed for clinical use should have a high therapeutic index, which is the ratio between the drug efficacy (therapeutic effect) and its toxicity (side effects). A drug with a low therapeutic index but high activity should be delivered in a higher concentration to the target cells (thereby increasing efficacy) avoiding non-target cells (thereby reducing toxicity). This delivery approach, called drug targeting, provides a mean to increase the therapeutic index of the drugs and achieving more effective therapy, with possible economic benefit.
Many different systems have been explored to selectively target antineoplastic agents to cancer cells or tissues. One of the most general approaches is the linkage to a carrier molecule (such as protein, polysaccharide, natural or synthetic macromolecule, lectin or antibody, small molecules) by a covalent bond to an active moiety, such as an antitumoral drug or a cytotoxic protein (1).
A useful alternative approach to target antineoplastic drugs to tumor cells is the use of vesicular or particulate systems, such as liposomes and nanoparticles, to improve the drug concentration at the target by altering both tissue distribution and the drug pharmacokinetics. To further enhance the cytotoxic effect, selective delivery of drugs to target cells can be achieved by conjugating vesicles to various targeting ligands; in this way, the conjugated nanovescicles are potentially able to bind to a specific receptor on target cell membranes, triggering their own internalization by the mechanism of endocytosis.
Different targeting agents and drug delivery systems designed for the smart delivery of antitumoral drugs will be illustrated and discussed (2-4).

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