Targeting solid tumors with multifunctional polymeric nanoparticles

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In the past thirty years, nanotechnology has been proposed as a valuable tool to target chemotherapeutics to solid tumors with the goal to improve response to conventional pharmacological therapies, to alleviate toxicity as well as to overcome multidrug resistance.

Polymeric nanoparticles (NPs) are in the limelight in cancer nanotechnology due to the advantages of prompt manipulation of the overall features (size, surface hydrophilicity/charge, release rate, biodegradability) through appropriate tailoring of the chemistry of building blocks. In this context, NPs with core-shell architectures have demonstrated a great potential in delivering chemotherapeutics to solid tumors. Suitably designed core-shell NPs can thus vary their properties in response to the biological environment can indeed long-circulate in the blood, penetrate tumor barrier and ECM, undergo shedding and accumulate inside target cells. Furthermore, core-shell NPs can incorporate multiple drugs with different physical-chemical properties and deliver them at different release rate, which can be crucial to attain desired synergic/additive effects.

Amphiphilic block copolymers of poly(ethylene glycol) (PEG) can form easily core-shell NPs providing a wide arsenal for drug delivery applications. In the context of cancer therapies, PEG-modified poly(ε-caprolactone) (PEG-PCL) copolymers with different hydrophilic/lipophilic balance and architecture have gained attention in preclinical studies and in clinical settings with the promise to ameliorate chemotherapy and to decrease treatment toxicity. As far as PEG-PCL NPs for intravenous injection are concerned, PEGylated surface can help to escape mononuclear phagocyte system, to attain long-circulation and to promote extravasation in inflamed tissues with a typical dysfunctional capillary bed such as in tumors (Bertrand and Leroux, 2012). PEG segments can be further functionalized with specific ligands to attain multifunctional NPs.

In this contribution, our experience in building PEG-PCL NPs for the delivery of chemotherapeutics will be illustrated. After a short overview on the basic principles to design NPs for cancer therapy, including some biological design guidelines, representative examples of NPs developed in our laboratory for cocktail therapy will be described, highlighting how a translational developmental plan can provide advanced proof-of-principles of therapeutic concepts.