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SPOKE 8: Platform for DNA-RNA delivery

Polymeric nanoplatforms for precision targeting of siRNA to solid tumors

Recently, much attention has been paid to the potential application of RNA interference (RNAi) for cancer treatment[1]. The administration of siRNAs targeted to specific oncogenes and Multi Drug Resistance (MDR) related genes involved in cancer progression, could represent a keystone to develop personalized medicines and optimize patient chances of responding. Nevertheless, the major challenge to translate siRNA therapy into the clinic is related to their high susceptibility to *in vivo* degradation, and scarce cell uptake. Nanodelivery of siRNA is a fascinating option since it's based on the ability of a nanoplatform to protect siRNA, drive interactions with tumor cells at the molecular/cellular scale and target specific elements of the tumor[2]. Amid nanoplatforms for siRNA delivery, polymeric nanoparticles (NPs) show several advantages such as biocompatibility, biodegradability and the opportunity to tailor their composition and properties[2-4].

On these premises, the aim of the PhD project is the development of novel biodegradable polymeric NPs engineered for the delivery of siRNA to solid tumors. Specific objectives are 1) the development of polymeric NPs able to deliver siRNA, and eventually a second drug, at controlled rate to have a synergic anticancer effect 2); the development of strategies to functionalize NP surface with moieties targeted to cancer cells in order to have a more selective effect; 3) the knowledge on the physical-chemical features of targeted NPs; 4) microfluidic production of NPs on a gram scale. As base material, we will employ polyesters such as poly(lactic-co-glycolic acid) (PLGA) that will be selected since it is a clinically used biocompatible copolymer with the possibility of tailoring its composition and degradation profile[5]. Cationic materials able to transfect siRNA (e.g. Polyethyleneimine, protamine) will be added to the formulation or conjugated to PLGA. As siRNA, different therapeutic siRNA, eventually in combination with conventional anticancer drugs, will be loaded inside NPs. After fabrication and extensive characterization, the toxicity and trafficking of siRNA-loaded NPs will be tested in different cancer cell lines and in in vivo model of solid tumors.

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