Nanoparticle-mediated delivery of drugs and nucleic acid therapeutics for cancer treatment: physicochemical and technological studies

Nucleic acid therapeutics, such as antisense oligonucleotides, siRNA, miRNA, aptamers, are attractive in cancer treatment due to their ability to change the expression of target endogenous genes and modulate the immune responses. Due to their intrinsic susceptibility to enzymatic degradation, the delivery of nucleic acid therapeutics faces multiple challenges. Hence, it is crucial to develop nanosized drug delivery systems that can carry, protect, and specifically deliver and release nucleic acid therapeutics to target tissues and cells. On the other hand, nucleic acids, such as G-quadruplex found in oncogene promoters, will also be used for their tumour targeting ability. Therefore, in this project, nanoparticles for the delivery of drugs and nucleic acids will be designed and decorated superficially with suitable active targeting molecules. The project scheme is reported hereunder:

Aims

The project, starting from complementary expertise of proponents, can be schematized as follow:

- ✖ Studies on solubility and distribution phenomena: solute-solvent interactions, influence of solvents on the solubility of drugs.
- ✖ Complexation and protein binding: organic molecular complexes, inclusion compounds, protein binding (equilibrium dialysis, Circular Dichroism, UV spectroscopy, isothermal titration calorimetry ITC)
- ✖ Design, production, and physicochemical/technological/biological characterization of nanoparticles for the delivery and targeting of the selected molecules: type, size, shape, zeta potential. Different nanoparticle formulations will be produced, and the most promising ones will be selected based on their ability to encapsulate and target the nucleic acid therapeutics.
- ✖ Delivery of nucleic acid therapeutics: determination of the release kinetics of the nucleic acid therapeutics (e.g. aptamers),
- ✖ Furthermore, the biological performance of the optimized nanoparticle formulations will be investigated on representative

Feasibility

The feasibility of the project can be attested by the collaboration already in place and by the combination of previous studies of the two proponents to develop new strategies for the delivery of DNA aptamers and drugs that target unusual DNA structures.