PNRR Missione 4, Componente 2, Investimento 1.4 "Potenziamento strutture di ricerca e creazione di "campioni nazionali di R&S" su alcune Key Enabling Technologies"
Iniziativa finanziata dall'Unione europea –- NextGenerationEU.
National Center for Gene Therapy and Drugs based on RNA Technology
Sviluppo di terapia genica e farmaci con tecnologia a RNA
Codice progetto MUR: **CN00000041** – CUP UNINA: **E63C22000940007**

SPOKE 8 (Platform for DNA-RNA delivery)

Peptide-based nanostructures as delivery tools for active pharmaceutical ingredients

Gene therapy has been recently proposed as a promising alternative to conventional chemotherapeutic treatments in fighting cancer. In literature there are evidence that small interfering RNA (siRNA) or microRNA (miRNA) can efficiently modulate and silence the expression of specific genes implicated in tumour initiation, growth, and metastasis formation. However, some drawbacks, such as the *in vivo* degradation of nucleic acids and their inability to overcome biological barriers, still obstacle their clinical employment. In this context, positively charged nanoparticles (lipidic and polymeric ones) have been proposed as suitable delivery carriers.

Due to their high biocompatibility and high synthetic accessibility (low cost, well-assessed synthetic process, suitability of groups for functionalization), peptide sequences have been investigated to generate nanostructured aggregates. The aim of the project is the development of novel target selective peptide platforms such as hydrogels (HGs) and nanogels (NGs) for the co-delivery of siRNA or miRNA and conventional anticancer drugs.

Nanoplatforms will be prepared using self-assembling cationic peptide sequences as hydrogelators. The choice of cationic sequences is aimed to favour non-covalent encapsulation of nucleic acids mediated by electrostatic interactions. Submicronization of macroscopic HGs, in presence of suitable stabilizing agents, can allow obtaining injectable nanometric particles, namely nanogels. The outer surface of NGs will be decorated by post-functionalization approach with bioactive molecules (antibody fragments, small organic molecules, homing peptides) able to selectively recognize receptors overexpressed in cancer organs. The resulting nanogels filled with nucleic acids will be fully characterized from the structural point of view (size, colloidal stability, morphology and peptide secondary structure). The stability of nanoplatforms in biological fluids and the drug release will be studied over time. The *in vitro* and *in vivo* toxicity and tumour growth inhibition of nanovectors will be also assessed on appropriate models.