Development of supramolecular peptide nanosystems for the delivery of new bioinorganic drugs.

Keywords: Drug design, Bioinorganic drugs, Peptide supramolecular systems Delivery

In the context of the treatment of tumor pathologies and bacterial infections, phenomena of resistance to chemotherapy drugs and antibiotics represent a relevant drawback for human health. To overcome these effects, synthesis of new inorganic-based drugs and methodologies for their delivery are a goal of research in the field of health protection. In particular, metal-based drugs can interact with cellular targets of a protein nature by altering the metabolic pathways in order to induce cell death. To modulate their effects and have their action prolonged over time, metal complexes can be encapsulated in slow-release nanosystems for both applications through the skin or intravenous. In the case of tumor pathologies, if suitably functionalized with peptides, they can induce specific delivery target by reducing side effects and overcoming resistance phenomena.
The study will take place according to the following milestones.
1. Design of new drugs based on transition metal complexes. In addition to ruthenium, which has already demonstrated good anticancer properties, gold and silver complexes will be studied which, as is known, interact with Lewis soft ligands such as sulfur and selenium present in proteins identified as possible targets.
2. Chemical synthesis and physical-chemical characterization of the designed molecules
3. Study by spectroscopic methods of the interactions with the targets that will act as a screening to select the complexes
4. In vitro validation of the new bioactive molecules by identifying the altered metabolic pathways.
5. The selected complexes with pharmacological activity will be loaded in nanosystems for penetration through the cell membrane and delivery to tumor targets.
6. Determination of the physical-chemical characteristics of the supramolecular aggregates

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2 F. Guarra et al. A focus on the biological targets for coinage metal-NHCs as potential anticancer complexes *J Inorg Biochem* **2021**, 217, 111355 https://doi.org/10.1016/j.jinorgbio.2021.111355
3 Tesauro et al. Structure–Activity Relationships in NHC–Silver Complexes as Antimicrobial Agents *Molecules* **2023**, 28, 4435. https://doi.org/10.3390/molecules28114435

The economic resources for carrying out the research will be drawn from the project in collaboration with the Department of Pharmacy in agreement with the IC-CNR and CNRS (France): "The Bioinorganic Drugs joint laboratory: a multidisciplinary platform promoting new molecular target for drug discovery" and PRIN 2022