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The golden doxorubicin: A tunable design of gold (III)-doxorubicin complex – PEGylated nanocarrier for oncological

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In the last five decades, metal complexes and organometallic compounds have been gaining importance in cancer therapy. Based on their structural and electronic similarity to cisplatin and cisplatin-related anti-tumor drugs, Au (III) species represent a promising class of potential anticancer agents. In this study, we report the synthesis, physico-chemical characterization and results of the biological behavior of doxorubicin-complex –gold COOH-terminated PEG-coated NPs (DOXO IN-PEG-AuNPs) before and after conjugation with antibody (anti-Kv11.1-pAb) to evaluate the influence of the nanocarrier and of the active targeting functionality on the anti-tumor efficacy of doxorubicin, with respect to its half-maximal effective concentration (EC₅₀) and to drug-triggered changes in the cell cycle. The anti-Kv11.1-pAb recognized specifically the Kv11.1 subunit of the hERG1 channel aberrantly expressed on the membrane of pancreatic cancer cells. The synthetic approach consist in four steps (Figure 1): Complexation between doxorubicin (DOXO) and tetrachloric acid (HAuCl₄) to form gold clusters; adsorption of COOH-terminated PEG molecules (PEG) onto DOXO-Au complex; reduction of metal ions in that vicinity, growth of gold particles and colloidal stabilization and bio-conjugation of anti-Kv11.1-pAb. Raman spectroscopies were performed for the vibrational characterization of each step of the synthesis of doxorubicin-nanocarrier, distinguishing them from the free drug, protonated or not on the phenolic part of its chromophores. The calculated characterization DOXO IN-PEG-AuNPs vibrational bands show qualitative agreement with the experimental observations. Although preliminary, data gathered from this study have a considerable potential in the application of gold complexes with high stability, for the treatment of PDAC, a disease with a dismal prognosis and one of the main current burdens of today healthcare bill of industrialized countries. Further studies are still envisaged, focused on assessing the *in vivo* assessment toxicity, pharmacokinetics and dynamics on relevant.

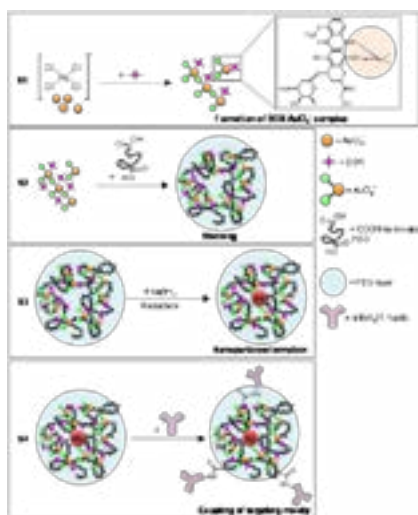


Figure 1: Schematic representation of the synthesis of DOX IN-PEG-AuNPs

Biography

Jolanda Spadavecchia is a Senior Researcher. Her research activities are focused on the realization of nanoparticles and biosensors. In particular, she is interested in the processes responsible for the bio-conjugation of protein, macromolecules or DNA oligonucleotides onto gold nanoparticles and substrates for the creation of optical biosensors. She is currently involved in the synthesis of polymeric nanoparticles and the development of nano-hybrid materials for nanomedicine. Actually, she has an active collaboration with Berlin and Louvre Museum in order to establish the mechanism responsible of the AuNP formation at the surface of ancient ivory objects from different archaeological and historical contexts.

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