NOVA BIOPHYSICA
SEPTEMBER 4-6, 2019
LISBON, PORTUGAL
RABBIT

Multifunctional Gold Nanoparticles for Chemoradiotherapy of Glioblastoma

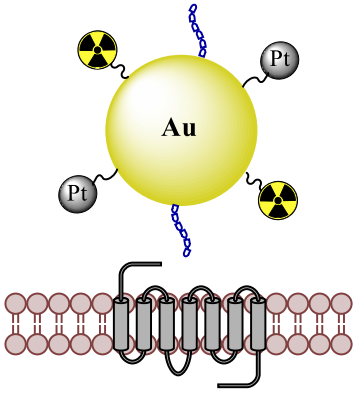
Carolina I. C. Mendes[1], Francisco Silva[1], Alice D'Onofrio[1], Cristina Oliveira[1], Fernanda Marques[1], Maria Paula C. Campello[1], Lurdes Gano[1], Mauro Ravera[2], Ana Belchior[1], Paula Raposinho[1], António Paulo[1]

[1]*Centro de Ciências e Tecnologias Nucleares, Instituto Superior Técnico, Universidade de Lisboa; Estrada Nacional 10 (km 139,7), 2695-066 Bobadela LRS, Portugal*

[2]*Dipartimento di Scienze e Innovazione Tecnologica, Università del Piemonte Orientale "Amedeo Avogadro", Alessandria, Italy*

cmendes@ctn.tecnico.ulisboa.pt

Glioblastoma multiforme (GBM) is the most common brain tumor of glial cell origin and one of the most aggressive, invasive and undifferentiated. Patient prognosis is generally very poor and current care remains mostly palliative. For these reasons, there is a pressing need for groundbreaking therapeutic strategies targeting GBM. Nanotechnology can play a key role in the design of new strategies for cancer diagnosis and treatment. In this scope, we explore gold nanoparticles (AuNPs) as multifunctional platforms for image-guided chemoradiotherapy of glioblastoma. AuNPs arise as interesting platforms for medical applications due to their good biological half-life, biocompatibility and easy functionalization. The proposed theranostic approach relies on the simultaneous delivery of Pt(IV) prodrugs and medically relevant radionuclides (e.g. ^{67}Ga, ^{125}I, ^{177}Lu) via multifunctionalized AuNPs. We will address the synthesis, characterization and biological evaluation of these nanoparticles, carrying a DOTA-based chelator[1] for radiometal coordination and a bioactive peptide (Substance P (SP) derivative) that recognizes the NK1 receptor overexpressed in GBM cells. Furthermore, some of the SP-containing AuNPs were also labeled with ^{125}I benefiting from the presence of a Tyr residue in the peptide sequence. The studies included the evaluation of cellular uptakes and (radio)cytotoxic activity for the designed multifunctional nanoparticles in different glioblastoma cell lines, aiming to assess their suitability for targeted chemoradiotherapy of glioblastoma.



Schematic representation of the multifunctional AuNPs, carrying a medically relevant radionuclide (^{67}Ga, ^{177}Lu), a Pt(IV) drug and a Substance P derivative to target the NK1 receptor overexpressed in GBM cells.

1. Silva F, Zambre A, Campello MPC, et al. Interrogating the Role of Receptor-Mediated Mechanisms: Biological Fate of Peptide-Functionalized Radiolabeled Gold Nanoparticles in Tumor Mice. *Bioconjug Chem*. 2016;27(4):1153-1164. doi:10.1021/acs.bioconjchem.6b00102

Acknowledgements: This work is supported by Fundação para a Ciência e Tecnologia (projects PTDC/MED-QUI/29649/2017 and UID/Multi/04349/2013).