Image-Guided Nanodelivery of Pt(IV) Prodrugs to PC3 Prostate Cancer Cells Overexpressing the Gastrin-Releasing Peptide Receptor

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Gold nanoparticles (AuNPs) have been considered interesting tools for drug delivery and theranostic applications in cancer treatment. Moreover, Pt(IV) prodrugs are emerging as alternatives to Pt(II) complexes, like cisplatin for chemotherapy, due to the reduction of Pt(IV) to Pt(II) inside the cells, with the binding of reduction products to DNA and other cellular targets. Searching to design an image-guided nanodelivery approach of Pt(IV) prodrugs to GRPR(+) tumors, we have synthesized AuNPs carrying a DOTA derivative, a GRPR-targeting bombesin analog and a Pt(IV) prodrug attached to the AuNPs. In the GRPR(+) prostate PC3 cells, the most promising AuNP-BBN-Pt displayed the lowest IC_{50} value comparable to that of cisplatin. In non-tumoral RWPE-1 prostate cells, expressing vestigial GRPR, AuNP-BBN-Pt was without effect, while cisplatin displayed a cytotoxic effect indicating better selectivity for AuNP-BBN-Pt. Using ^{67}Ga-AuNP-BBN-Pt radiolabeled nanoparticles, the uptake and internalization was high. In vivo studies were performed in PC3 tumor-bearing mice after intratumoral administration of ^{67}Ga-AuNP-BBN-Pt. Results showed a prolonged retention of the nanoparticles compared to that of cisplatin, with good in vivo stability. Finally, microSPECT imaging studies confirmed the uptake and retention of the ^{67}Ga-AuNP-BBN-Pt in the tumors. Overall, these results show the potential of these targeted AuNPs loaded with Pt(IV) prodrugs for prostate cancer theranostics.

Biography

Fernanda Marques is a Scientific Researcher at Centro de Ciências e Tecnologias Nucleares, Radiopharmaceutical Science Group, Instituto Superior Técnico, Universidade de Lisboa, Portugal. She is a Chemical Engineer from Instituto Superior Técnico, and received her doctoral degree in Biochemistry from the University of Lisbon (Portugal). She has co-authored > 120 peer-reviewed original articles published in international journals and participated in 13 research projects. She works in the area of Health Sciences with expertise in irradiation techniques (X- and gamma rays, neutrons) radionuclides production in nuclear reactors and cancer therapy. She has also expertise in radiochemistry in the synthesis of radiolabeled compounds for cancer therapy. She has also been dedicated to the biological evaluation of (radio)metal based compounds for cancer theranostics.

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