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Biological evaluation of ^{64}Cu-radiolabeled gastrin-releasing peptide receptors antagonist conjugated to DOTHA$_2$a new bifunctional chelator bearing hydroxamic acid arms

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Gastrin releasing peptide receptor (GRPR) overexpression in prostate cancer provides an attractive target for cancer imaging and radiotherapy. The goal of this study is to validate a pegylated GRPR antagonist (PEG-RM26) conjugated to DOTHA$_2$, a new bifunctional chelate recently developed by our group for ^{64}Cu complexation and PET imaging. DOTHA$_2$-PEG-RM26 was synthesized on solid phase support. *In vitro* competition binding was assessed against ^{125}I-[Tyr^4]-BBN on PC3 cells. Cellular uptake and efflux studies were evaluated on human prostate cancer cell lines PC3 and LNCaP. Bio distribution was achieved on Balb/c female and male mice euthanized at 30 min post injection. Finally, bio distribution and micro PET images of maleathymic nude mice bearing PC3 and LNCaP tumors were obtained withor without pre-injection of unlabeled peptide. The inhibition constant of Cu-DOTHA$_2$-PEG-RM26 is 0.68±0.19 nM. The compound showed a fast cellular uptake with a maximum value at 15 min. The cellular efflux was maintained at around 25% of the retained activity over the 120 min for both cell lines. Male and female mice have similar bio distribution profile with bladder and kidneys being the organ with the highest tracer accumulation, indicating primary elimination via urinary system. Bio distribution and micro PET images showed accumulation in tumor and confirmed the renal excretion route. The *in vivo* blocking study demonstrates that the compound specifically targets GRPR in two prostate tumor models. In conclusion, bio distribution and imaging studies suggest that this ^{64}Cu/DOTHA$_2$ conjugate can be considered as a PET tracer of high interest for the diagnosis of GRPR-positive tumors.

Biography

Nematallah Mansour obtained MSc in Medical Physics from University of Surrey in 2003 (Guildford, UK). He has also done MSc in Radiopharmaceuticals & PET Radiochemisty from King's College London (London, UK) and he is currently pursuing his PhD at the Université de Sherbrooke (Sherbrooke, Canada).

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