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[^{18}F] GE11-PDA-Pt@USPIOs Nanoformulations to Dual-Regulate Tumor Microenvironment for PET/MRI/PAI-Guided Chemo/Radiotherapy of Cancer

Chengcheng Yang, Xuan Mi, Chunfu Zhang

School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai 200230, China.

Corresponding author. E-mail: cfzhang@sjtu.edu.cn

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Abstract

Chemo-radiation combination therapy has synergetic therapeutic effect on tumors. However, tumor microenvironment, e.g. hypoxia and elevating H_2S level, limit the treatment efficacy. In this study, we developed a cisplatin-loaded, poly dopamine-coated and GE11 peptide-conjugated and radioisotope fluorine-18 labeled multi-functional tumor theranostic system ([^{18}F]GE11-PDA-Pt@USPIOs) based on poly acrylic acid coated superparamagnetic iron oxide nanoparticles (PAA@USPIOs) for PET/MRI/PAI guided chemo-radiation therapy of tumor. Thick PAA coating on USPIOs allowed for high efficient cisplatin loading through complexing carboxylic groups with cisplatin prodrug. A thin layer of poly dopamine (PDA) coating following drug loading provided a means for further surface functionalization, imparted the particles photo-thermal property, but did not impede drug and iron ion release. GE11 peptide was conjugated and fluorine-18 was labeled sequentially by "click chemistry". [^{18}F] GE11-PDA-Pt@USPIOs had high specificity for EGFR positive tumor cells and exhibited chemo-radio synergetic therapeutic effects under the hypoxia condition in vitro. Once delivered intravenously, PET, MRI and photoacoustic imaging (PAI) revealed the probes were able to accumulate in tumors high efficiently. More importantly, free irons released from USPIOs responsive to the tumor acid microenvironment catalyzed the decomposition of endogenous H_2O_2 and consumed H2S in the tumor tissue, leading to relief of the hypoxic condition in the tumor and making tumor sensitive to radiation therapy. As a result, the chemo-radiation therapy significantly inhibited tumor growth. Our study indicates that [^{18}F] GE11-PDA-Pt@USPIOs is highly effective for theranostic of EGFR positive tumors.

Keywords: Superparamagnetic iron oxide nanomaterials; Cisplatin; Polydopamine; EGFR; 18F; PET/MRI/PAI; Chemo-radiation therapy