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Smart targeted erlotinib-SPION nanoparticles for MRI applications

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Despite the success erlotinib achieved in fighting lung cancers, the problems of grading and monitoring the tumor as well as predicting the treatment response may result in failure of the therapy and resistance of the tumor, which requires the use of a suitable diagnostic tool that can monitor the treatment and predicting the treatment response. As an attempt to address such problems, we designed a novel theranostic nanoparticle formulation (NPs) of superparamagnetic iron oxide core, coated with a thin dextran layer (as determined by transmission electron microscope (TEM) imaging and dynamic light scattering) and linked to erlotinib. Such NPs are smart, targeting cancer cells that overexpress the EGFR, releasing the active drug intracellularly rather than in the blood stream, accumulating inside the cancer cells producing high contrast in the magnetic resonance imaging (MRI) and being non-toxic to the EGFR-negative cells. Cellular uptake of the NPs was higher than the product used commonly in clinical practice as MRI contrast agent, this was evident from the MRI, TEM and Prussian blue imaging results. Furthermore, we tested the molecular mechanisms that may account for the potent activity of our NPs and found that the NPs inhibited the phosphorylation of the overexpressed EGFR as well as the oncogenic signaling pathways downstream of the EGFR such as the ERK and NF-κB pathways which was confirmed by Western blotting and confocal immunocytochemical imaging. Moreover, the T2-weighted MRI images of the BALB/c nude mice showed significant decrease in the normalized signal within the tumor post-treatment with the NPs compared to the non-targeted control iron oxide nanoparticles.

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