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Gadolinium nanoparticles as a dual switch for genetic targeting of receptors for cancer and Alzheimer's disease

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The regulation of cellular activities in a controlled manner is one of the most challenging issues for drug targeting. Nanoparticles have the potential of becoming useful tools for controlling cell signalling pathways in a space and time selective fashion. Here, we developed magnetic nanoparticles that turn on apoptosis cell signalling by using a magnetic field in a remote and noninvasive manner. The magnetic switch consists of Gadolinium magnetic nanoparticles, conjugated with a targeting moeity curcumin, which is particular for the human epidermal growth factor receptor (HER2) by triggering downregulation of AP1, cyclin D1, Cyclin E, upregulation of p21, p27, p53 resulting in cell proliferation repression. On the other hand, the conjugate is able to cross the blood brain barrier and reach the Beta amyloid plaques in case of Alzheimer's. The magnetic switch, is switched on when a magnetic field is applied to aggregate magnetic nanoparticle bound curcumin, promotes apoptosis signalling pathways. It is demonstrated that the magnetic switch is operable at the macro scale as well. That is, apoptosis signalling can be turned on in cancer cells like MCF 7 and in a zebrafish *in vivo* model by using a magnetic switch. This magnetic dual switch may be broadly applicable to any type of clinically useful surface membrane receptors that exhibit cellular functions. The design of an extrinsic apoptosis agonist that can avoid p53 mutation-induced drug resistance is important and the magnetic switch can serve as a selective inducer. Magnetic field may be important in endocytosis of most of the membrane bound nanoparticle conjugates which is otherwise only around 30-40%. Previous studies have shown that magnetic nanoparticles are rapidly cleared from the organs and exhibit little systemic toxicity as compared to corresponding salts/chelates used in MRI. The magnetic nps target the mitochondria, which result in the release of cytochrome C from the mitochondria and the activation of caspase-3 and caspase-9 after they entered the cells. This raises the possibility that they could be used to cure melanoma and some other common types of cancers prevalent globally.

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