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Smart multifunctional erlotinib loaded SPION as therapy and biomarker for treatment response prediction of metastatic cancers

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Overexpression of the epidermal growth factor receptor (EGFR) is linked to the aggressiveness, invasiveness and metastasis of lung cancers. The use of small-molecule tyrosine kinase inhibitors such as erlotinibhas proved to be highly selective for the EGFR tyrosine kinase, resulting in cell cycle arrest, inhibition of proliferation and apoptosis of cancer cells.Despite the success erlotinib achieved in fighting lung cancers, the problem of grading and monitoring the tumor as well as predicting the treatment responsemay result in failure of the therapy and resistance of the tumor.

As an attempt to solve this problem, we designed a novel theranostic nanoparticle formulation (NPs) of superparamagnetic iron oxidecore coated with a thin dextran layer and linked to erlotinib (79 µg/mg Fe).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 cellsproducing high contrast in the magnetic resonance imaging (MRI) and beingnon-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 imaging, TEM and Prussian blue staining results. Furthermore, we tested the molecular mechanisms that may account for the potent activity of ourNPs and found that the NPs inhibited the phosphorylation of the overexpressed EGFRas well as the oncogenic signaling pathwaysdownstream of the EGFR such as the ERK and NF-κB pathways which was confirmed by Western blotting and confocal immunocytochemical imaging.Moreover, the NPs inhibited the expression of the angiogenesis stimulating protein VEGF, the invasion and migration enhancing protein MMP-9, the proliferation regulating proteinCyclin D1 and the apoptosis inhibiting protein XIAP.

Biography:

Ahmed Atef Ahmed Ali is a PhD candidate in Academia Sinica and National Defense Medical Center. He published 4 papers in highly reputed journals and submitted 4 more papers which are currently under review. He received his B.Sc. and M.Sc. degrees from Cairo University with “Distinction honor” total grade and received the “Shield of Excellence” award from the Egyptian Pharmacist Syndicate for advancing the pharmaceutical industry by his research. Owing to his academic excellence, he got exempted from payingthe tuition fees for the whole duration of study.He worked as a lecturer at Misr International University for 8 years where he received the “Outstanding and Commendable Performance” award for his achievements. He was elected as the representative of the Molecular Cell Biology program in the Graduate Student Association of Academia Sinica in Taiwan for two years.