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Dual targeting nano-medicine with gefitinib-embedded cetuximab-capped mesoporous silica efficiently overcomes drug resistance of epidermal growth factor receptor (EGFR) mutant lung cancer

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Drug resistance to epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) is the main obstacle for efficient treatment of EGFR-mutant lung cancer patients, which requires novel strategies to overcome. We here design a novel nano-medicine which can specificly target EGFR-mutant cells, by using cetuximab (CET)-capped mesoporous silica nanoparticles as drug carriers. We find that this novel nano-medicine embedded with doxorubicin (DOX) has the capability to efficiently inhibit EGFR-mutant tumor cell growth while sparing normal human lung epithelial cells. In order to alleviate the drug resistance to EGFR-TKI, PC9-derived resistant cells (PC9-DR) were treated with the gefitinib (GEF)-loaded CET-capped mesoporous silica nanoparticles and the sensitivity of PC9-DR to GEF is significantly restored. More importantly, the mesoporous silica nano-medicine can successfully suppress the progression of PC9-DR xenograft tumors in nude mice. This suppression is mediated through the increased specificity which can recruit larger amount of nano-medicine as well as the higher level of glutathione (GSH) generated by PC9-DR which can induce effective drug release. Collectively, our study provide a novel approach to overcome EGFR-TKI resistance by using CET modified mesoporous SiO_2 nanoparticles (MP-SiO_2 NPs) with the great potential of effective drug delivery into EGFR-overexpressing or EGFR-mutant non-small cell lung cancer (NSCLC) cells.

Biography:

Zhanxia Zhang was born in 1982 in China. She received her Master Degree in Food Science from Jilin University in 2007. And she received her PhD Degree in Analytical Chemistry from Changchun Institute of Applied Chemistry, Chinese Academy of Sciences in Jan. 2011, her research focus on using nanoparticles to construct optical and electrochemical biosensor. From Apr. 2011 to Apr. 2014, she collaborated with Prof. Itamar Willner as a Post-Doctoral student at the Hebrew University of Jerusalem in Israel, her research interest shifted from biosensor to the field of controlled release of mesoporous silica nano-medicine. From Apr. 2014 until now, she collaborated with Prof. Hongbin Ji as an associate professor at the Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences in China, her research interests are mainly in the field of anti-cancer nano-medicine.

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