Cancer-Cell-Specific Mitochondria-Targeted Drug Delivery by Dual-Ligand-Functionalized Nanodiamonds Circumvent Drug Resistance

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Abstract

The application of nanodiamond is rapidly expanded from diagnosis to treatment due to its promising drug loading and non-photoquenching imaging properties. However, the delivery of sufficient drug amount to the targeted disease site is greatly importance in therapeutics. Hence, we developed a cancer-cell-specific sub-cellular organelle-targeted delivery based on photostable nanodiamond (ND), which is functionalized with folic acid and mitochondrial localizing sequence (MLS) peptides. This dual-ligand-functionalized ND platform does not only distinguish the cancer cells via the overexpression of folate receptors on cell membrane, it also localizes to mitochondria. Importantly, the doxorubicin (DOX) loaded dual-ligand-functionalized ND platform induces a significant cytotoxicity in drug resistance cancer cell (MCF-7/ADR) comparing to the free doxorubicin localized in lysosomes because the localization in mitochondria enhances the retention time of DOX inside the MCF-7/ADR, which has the significant circumvention of P-glycoprotein to pump out the drug inside the cell. This work successfully demonstrates nanodiamond-based nanocarriers for cancer-cell- specific mitochondria-targeted delivery and overcomes drug resistance in doxorubicin-resistant human breast adenocarcinoma cancer cells.

Reference

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