

MAGNETOELECTRIC CHITOSAN NANOPARTICLES LOADED WITH DAPT, A γ -SECRETASE INHIBITOR EFFECTIVELY INHIBITS NOTCH1 SIGNALLING PATHWAY IN BREAST CANCER STEM CELLS

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This study reports major improvements in the therapy of human breast cancer stem cells (BCSCs) with DAPT. Taking advantage of the unique properties of magnetoelectric chitosan nanoparticles (MECNs), these results suggest that GMO-MECNs effectively bind DAPT, by providing controlled intracellular drug delivery and specifically target human BCSCs. Recently developed MECNs are a novel class of nanoparticles that enable targeted drug delivery to cancer cells only. The unique properties of MECNs allow it to specifically target human BCSCs. Therefore, the primary aims are to bind drug (DAPT; a γ -secretase inhibitor which inhibits Notch1 signaling pathway) efficiently to MECNs (Fe_3O_4 at chitosan nanostructures). DAPT-loaded MECNs could be delivered into BCSCs via application of AC field and the drug could be released off MECNs on demand via application of an AC field without thermal damage, the physics is due to electric-field interactions (i) between MECNs and a drug and (ii) between drug-loaded MECNs and cells. The synthesis of core-shell MECNs is conventionally carried out in two successive steps: (i) the precipitation of the Fe_3O_4 NPs as a magnetic core. (ii) The creation of chitosan as a magnetic electric shell around each NP. MECNs can be localized to tumor sites, due to physical mechanism which acts independently of the enhanced permeability and retention effect that specificity exists because the nano electroporation threshold field for the malignant cells is significantly lower than the normal cells. The biodegradability of chitosan is by the kidney, while the biodistribution of the iron oxide particles is eventually phagocytosed or endocytosed by the reticuloendothelial system of the liver, spleen, lymph and bone marrow. Once compartmentalized within the lysosomes of RES cells, the iron oxide particles are broken down with the majority of the SPIO iron stored as ferritin and/or hemosiderin which are antiferromagnetic forms of iron.

Biography

Asmaa Makkey and Aya Darwish have completed their B.Sc. at the age of 22 years from Alexandria University, Faculty of Science Biochemistry Department and Mohamed Ismail has completed his Master's degree in Organic Chemistry at the age of 26 years from Alexandria University. They have worked together for more than two years as a research team; their team has won the first rank in the poster presentation competition in the 6th Student Research and Innovation Conference in Egypt. They have attended the Bio vision Conference in the Bibliotheca of Alexandria and participated in the ACS Nano Chemistry Conference, and now they are proceeding working on the chemical part of their project at the National Institute of Oceanography and Fisheries under the supervision of Prof. Dr. Ahmed El Nemr (Former Head of Marine Pollution Department and Director of National Institute of Oceanography and Fisheries), and they have successfully achieved good results.

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