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Synthesis of Hybrid Nanoparticles Containing siRNA and Quercetin for Targeting Triple-Negative Breast Cancer

Orhan Burak Eksi[1,2], Omer Aydin[1,2,3,4]
[1]Nanotechnology Research and Application Center (ERNAM), Erciyes University, 38039, Kayseri, Turkey
[2]NanoThera Lab, Drug Application and Research Center (ERFARMA), Erciyes University, 38039, Kayseri, Turkey,
[3]Biomedical Engineering, Erciyes University, 38039, Kayseri, Turkey,
[4]Clinical Engineering Research and Implementation Center (ERKAM), Erciyes University, 38030, Kayseri, Turkey,

Extended Abstract

Triple-negative breast cancer (TNBC) presents a formidable challenge in oncology due to its aggressive nature and the absence of targeted therapies.[1] In this study, we aimed to devise an innovative strategy for TNBC treatment by combining chemotherapy with siRNA-based gene therapy.

Eukaryotic Elongation Factor 2 Kinase (eEF2K) functions as a protein that regulates protein synthesis to enable the survival of cancer cells through energy conservation. eEF2K prevents cells from engaging in unnecessary protein synthesis, thereby assisting cancer cells in surviving for extended periods.[2],[3],[4] Due to this property, we purposed to silence eEF2K protein by using eEF2K siRNA.

Also, quercetin is a flavonoid found in fruits, vegetables, and plants, and it has been suggested to have positive effects in combating cancer. Research indicates that quercetin stimulates programmed cell death (apoptosis) in cancer cells, inhibits cancer cell growth and spread through caspase activation and various signaling pathways.[5],[6] Additionally, quercetin can reduce cellular stress, which may hinder the growth of cancer cells.[7] Consequently, quercetin is believed to possess anti-cancer properties and has the potential to contribute to cancer management through different mechanisms.[5],[6],[7]

In this study, we harnessed the chemotherapeutic properties of quercetin (Qu), a flavonoid, to synthesize silver nanoparticles (AgNPs) as a nanocarrier. Surface modification of AgNP+Qu complex was covered by positively charged polymer and facilitated the electrostatic interaction with eEF2K siRNA. To mitigate potential toxicities associated with positively charged nanoparticles, we employed the negatively charged polymer. Finally, a hybrid nanoparticle was developed.

Extensive characterization of the hybrid nanoparticle confirmed their size to be 133 nm and a zeta potential of approximately -36 mV. The combination of siRNA-based gene therapy and chemotherapy demonstrated remarkable efficacy in reducing the viability of TNBC cells in vitro.

In conclusion, our study establishes the feasibility of employing AgNPs as a nanocarrier for the delivery of eEF2K siRNA and quercetin, offering a promising avenue for the development of targeted therapies for TNBC, a malignancy with limited treatment options. Further investigations are warranted to assess the safety and efficacy of this approach in in vivo models.

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