



SIRT1 siRNA loaded cationic liposomes showed enhanced cell death of Prostate Cancer Cells with different p53 expression patterns

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Abstract

Sirtuin 1 (SIRT1) is a histone deacetylase (HDAC) from Sirtuin family. High expression of SIRT1 induces activation of DNA repairing factors eventually leading either tumor suppression or tumor development in cellular context dependent manner. Most of the chemotherapeutics induce apoptosis by creating DNA damage in tumor cells. However, SIRT1-activated repair of the chemotherapeutic-induced DNA damage results in decreased apoptosis and finally chemotherapy resistance. Therefore, inhibition of SIRT1 is a promising strategy both in anticancer therapy and preventing chemotherapy resistance.

In this study, SIRT1 siRNA carrying liposomal formulations have been formulated by using N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTMA) as cationic lipid by freeze drying method. Their effect on SIRT1 silencing has been determined as 2.5-4 folds both on mRNA and protein levels on prostate cancer cells (LNCaP, Du145, and PC3) with different p53 expression pattern. Efficiency of the formulations to enhance the activity of doxorubicin, which is a chemotherapeutic performing its activity by creating DNA damage has been studied and found to increase the activity of doxorubicin on cell death although they have no effect on cell viability when they applied onto cells alone. Besides, enhanced DNA damage recognition after SIRT1 silencing by the formulations has been determined as the underlying cause of increased cell death. Further, no negative effect of the formulations on cell viability of normal prostate cells has been evaluated as a promising result for selectivity on cancer cells.

As a conclusion, a series of siRNA carrying liposomal formulations for SIRT1 inhibition is able to enhance the chemotherapy efficiency in combinatorial use with DNA-damaging chemotherapeutics on prostate cancer cell lines.

Biography

Bilge Debelec Butuner has completed her PhD in 2012 from Ege University, Turkey and postdoctoral studies from Ege University, Faculty of Pharmacy. She has been working in the same department as Assistant Professor since 2016 with the focus on cancer therapeutics, drug delivery, cancer immunology and immunotherapy.