

P77 Nanoparticles Encapsulated with Tolecine® for Anti-Cancer Therapy

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PURPOSE/OBJECTIVE:

Resveratrol is a promising drug for treating cancer, because it inhibits the cellular events associated with all three stages of carcinogenesis (initiation, promotion, and progression). However, the enthusiasm of resveratrol has been dampened due to its instability and low aqueous solubility. In order to solve the stability issue, our research team had developed a resveratrol analog entitled Tolecine. Tolecine, unlike resveratrol, does not undergo conformational changes and become inactivated. However, since Tolecine has limited solubility in aqueous solutions, we have explored the use of tea delivery systems for Tolecine.

METHODS AND RESULTS:

We have formed two distinct delivery devices by encapsulation Tolecine into nanoparticles using L-Tyrosine polyphosphate (LTP), a novel polymer, and by formation into micelles with linear polyethylenimine. LTP is biodegradable polymers that have been designed specifically for biomedical applications. LTP is biocompatible and has a fast degradation rate in the order of days. Linear polyethylenimine is a cationic polymer that is common employed as a carrier for DNA in gene therapy applications. Both devices have been uniquely designed for intracellular delivery of Tolecine and have activity against an ovarian cancer cell line. In addition, LTP nanoparticles have been adapted for cellular targeting.

CONCLUSION:

Therefore, nanoparticles encapsulating Tolecine shows promise for cancer therapy.

P78 Redistribution of Fibrillarlin Following Treatment of Human Bladder Carcinoma Cells with Apatone®

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PURPOSE/OBJECTIVE:

Apatone® (Vitamin C (VC), Vitamin K3 (VK3) in a ratio of 100:1) kills tumor cells by autophagy. In this study, vitamin-induced changes in nucleolar structure were evaluated as markers of autophagy.

METHODS:

Human bladder carcinoma (T24) cells were overlain with vitamins at high doses (4,064 µM VC, 40.64 µM VK3 or 4,064 µM VC / 40.64 µM VK3), low doses (1,016 µM VC, 10.16 µM VK3 or 1,016 µM VC / 10.16 µM VK3) or with culture medium. Vitamins were removed at one hour intervals from one to four hours and the cells were washed with PBS and prepared for electron microscopy, immunogold labeling of rRNA and rDNA or immunofluorescent labeling of nucleolar proteins.

RESULTS:

Unlike VC and VK3 alone, Apatone produced marked ultrastructural alterations in nucleolar structure including: redistribution of nucleolar components, formation of ring shaped nucleoli, condensation and increase of the proportion of perinucleolar chromatin and the enlargement of nucleolar fibrillar centers. Immunogold labeling of the rRNA revealed an identical pattern in treated and sham-treated cells (labeling of the granular portion of the nucleolus), while immunogold labeling of the rDNA revealed a shift of the DNA from the fibrillar centers to the condensed perinucleolar chromatin in the treated cells. While the patterns of nucleolar distribution of RH-III/Go, B23 and p120 were not affected by treatment, the fibrillarlin staining pattern shifted from one that coincided with the fibrillar centers and adjacent regions to a more homogeneous staining of the entire nucleolus and was more pronounced with the Apatone. However, the percentage of cells displaying these changes was consistent with the percentage of autophagic cells detected by flow cytometry. The fact that autophagy entails the sequential reactivation of DNase I and DNase II and that DNase I treatment induced nucleolar changes identical to those observed following Apatone treatment suggest that the nucleolar changes are indicative of autophagy.

CONCLUSION:

Changes in fibrillarlin localization in the nucleolus is a marker of autophagy.