Reconstituted High-Density Lipoproteins for the Treatment of Pediatric Cancer

Ahluwalia, Ruhani (School: Harmony School of Innovation - Fort Worth)

Ewing’s sarcoma (EWS) is a highly aggressive type of cancer that primarily occurs in children and young adults. Doxorubicin (DOX) is a commonly used anti-cancer drug for the treatment of EWS. Unfortunately, the cumulative dose-dependent cardiotoxicity of DOX can often lead to cardiac damage in children many years after treatment. To address this problem, targeted therapy in the form of high-density lipoprotein (rHDL) nanoparticles (NPs) was explored. DOX inside rHDL NPs is selectively delivered to SR-B1-positive cancer cells by avoiding the heart cells as they lack SR-B1 receptors. Western blot analysis showed higher expression of SR-B1 in EWS cells relative to normal cardiomyocytes (H9c2). Three different DOX formulations were tested (free DOX, rHDL-DOX, and Doxoves). The effectiveness of rHDL-DOX relative to free DOX and Doxoves in killing TC-32 but not H9c2 cells was evaluated. Based on cell viability assays, free DOX was more toxic to TC-32 cells than Doxoves and rHDL-DOX. Whereas, rHDL-DOX and Doxoves formulations were less toxic toward H9c2 cells than free DOX. Moreover, free DOX and Doxoves caused a substantial decrease in glutathione peroxidase 1, an antioxidant enzyme in heart cells, compared to rHDL-DOX. In addition, there was less mitochondrial damage of cardiomyocytes with rHDL-DOX relative to the treatments with free DOX and Doxoves. Preliminary evidence from these studies show the potential efficacy of the rHDL NPs as drug delivery vehicles that should enhance as well as maintain the selective killing of tumor cells, while significantly reducing the side effects of chemotherapy in pediatric cancer patients.

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