Lipoprotein-based Therapeutic Approach to Combat Breast Cancer

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

Lack of effective treatment and substantial side effects of current chemotherapy have resulted in poor prognosis for triple-negative breast cancer (TNBC) patients. To avoid these side effects and to increase the quality-of-life of TNBC patients, targeted therapy in the form of high-density lipoprotein (rHDL) nanoparticles has been explored in this project. The drug (lapatinib) is released from these nanoparticles only when they are attached to a gatekeeper molecule (SR-B1) exclusively present on cancer cells with the exception of hepatocytes. The objective of the project was to determine whether lapatinib delivered by rHDL nanoparticles (rHDL-Lapatinib) via SR-B1 could inhibit cancer cell growth and proliferation. In this study, Western blot analysis showed high SR-B1 expression, which varied from 15- to 354-fold in three different breast cancer cell lines compared to normal cardiac cells. Based on the cell viability assays and IC50 values, the rHDL-Lapatinib nanoparticles were 1.22-, 2.4-, and 8.8-fold more effective than free lapatinib in killing MDA-MB-231, MDA-MB-468, and MCF-7 breast cancer cells, respectively. Moreover, the scratch-wound assays indicated that the rHDL-Lapatinib nanoparticles inhibited migration of cancer cells in-vitro. This result was in accordance with expression levels of Matrix Metalloproteinase 9 (MMP-9), which is a major contributor to cancer metastasis. MMP-9 levels were found to be 4- to 8-fold higher in breast cancer cells relative to normal cells. Preliminary evidence from these studies shows the potential of rHDL as a targeted drug delivery platform to deliver current chemotherapy drugs with substantially lower side effect, thereby enhancing quality-of-life for TNBC patients.