Inhibition of Programmed Death Ligand 1 (PD-L1) in Triple-Negative Breast Cancer Cells by Liposomal Hesperidin

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264,000 people are diagnosed with breast cancer annually in the US, with 10% to 20% of diagnoses attributed to triple-negative breast cancer (TNBC). TNBC is characterized by the lack of progesterone, estrogen, and human epidermal growth factor receptor 2 (HER2). Additionally, programmed death ligand 1 (PD-L1) is overexpressed in TNBC, aiding tumor growth by inducing immune escape. Hesperidin, a natural bioflavonoid, has recently been shown to inhibit the expression of PD-L1 in breast cancer cells. However, Hesperidin's anticancer activity is low due to its limited solubility. We hypothesized that delivering hesperidin through liposomes could overcome its low solubility and enhance treatment efficacy. The present study aims to verify this hypothesis and demonstrate that liposomal hesperidin (Lip-H) can suppress PD-L1 expression in TNBC cells. MDA-MB-231 (TNBC) and MCF-7 cells were incubated with Lip-H for 48 h. RNA was extracted from the harvested cells, and expression of the PD-L1 gene was measured by real-time quantitative polymerase chain reaction (RT-qPCR). Confocal microscopy revealed that the liposomes were internalized by cancer cells and localized in the cytoplasm and nuclei. PD-L1 gene expression in the untreated TNBC cells was 40x higher than the untreated MCF-7 cells, and Lip-H significantly inhibited PD-L1 expression in TNBC cells. Consequently, we verified the hypothesis and showed that the inclusion of hesperidin in liposomes strongly decreased the expression of PD-L1. This work supports the viability of this approach and shows the high therapeutic potential of liposomal hesperidin in the treatment of triple-negative breast cancer. This research was supported by R01CA251438 and R25ES020721 grants.