EFFECTS OF RESVERATROL ON PACLITAXEL-SENSITIVE AND –RESISTANT TRIPLE NEGATIVE BREAST CANCER CELLS

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Treatment of drug-resistant cancer cells remains a difficult problem in cancer therapy because most resistant cells can pump out drugs or upregulate other survival pathways to bypass a targeted therapy. The poly-phenol natural compound, resveratrol, has been shown to inhibit cell growth of multiple cancer types, but it is not cytotoxic to normal cells. However, the effects of resveratrol in triple negative breast cancer cells as well as cancers that are resistant to the common cancer drug, paclitaxel, are not well under-stood. In this study, the effects of resveratrol were investigated in the triple negative breast cancer cell line MDA-MB-231 as well as a novel paclitaxel-resistant MDA-MB-231 derived line generated in our laboratory. Both cell lines exhibited a reduction in cell proliferation after resveratrol treatment, with the paclitaxel-resistant cells to a greater extent. In addition, resveratrol decreased the ability of both cell lines to form colonies when plated at low density indicating reduced cell survival capacity. Resveratrol treatment also increased the amount of DNA fragmentation associated with cell death in both cell lines, again with the paclitaxel resistant cells being more sensitive. By protein expression analyses, we observed that in both the parental and resistant cell lines, resveratrol may be acting by through NAD-dependent deacetylase sirtuin (SIRT1) activity by decreasing the expression of the in-hibitor-of-apoptosis protein, survivin, as well as increasing the activator-of-cell death, caspase 7. These data suggest that resveratrol can inhibit prolif-eration and induce cell death in triple negative breast cancer cells, including paclitaxel-resistant cells. In addition, these results provide rationale for the use of resveratrol as an important starting point for the development of a novel anti-cancer agent for drug resistant, aggressive cancers as well as in combination with other anti-cancer drugs without significant toxicity to nor-mal cells.