Michelle Thoma

Major: Biology
University: University of Missouri-Columbia
Faculty Mentor: Dr. Susan Deutscher
Mentor Department: Biochemistry
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Anti-galectin-3 peptides increase apoptosis in galectin-3 expressing human breast cancer cells

Michelle Thoma, Linda Landon and Susan Deutscher

A critical factor in the proliferation and the metastatic nature of carcinoma cells appears to be their resistance to natural programmed cell death (apoptosis). However, the molecular mechanisms that enable carcinoma cells to become resistant to cell death are unclear. Galectin-3 (Gal-3) is a protein that is found at elevated levels in a variety of primary and metastatic tumor cells that may play a key role in chemo-resistance and proliferation of carcinoma cells. Gal-3 has also been found to play a key role in the regulation of common apoptosis commitment pathways. Therefore, we hypothesize that peptides, which bind to and inhibit Gal-3 functions, could be used to reduce the anti-apoptotic activity of Gal-3 thus increasing the occurrence of cell death in carcinoma cells. Two cell lines were cultured, the human breast cancer cell line BT549 and a Gal-3-transfected derivative of BT549 (BT549/V). After undergoing apoptosis induction with 0.5 M staurosporine, apoptosis markers were detected fluorescently using flow cytometry. Our preliminary data suggests that, in the absence of anti-galectin-3 peptides, the parent BT549 cell line exhibits mitochondrial damage (decrease in mitochondrial membrane potential as detected by using MitoTracker Red fluorescence) by 6 hours of staurosporine treatment, whereas the BT549/V cell line shows little change in MitoTracker Red fluorescence even after 8 hours of apoptosis induction. A similar pattern is observed when changes in MitoTracker Red fluorescence are correlated with changes in phosphatidylserine translocation from the inner to outer surface of the plasma membrane. The current data suggest that cells transfected with Gal-3 have an increased rate of survival after apoptosis induction. In the next phase of this ongoing project, flow cytometric studies of changes in membrane permeability and DNA damage in parent and galectin-3 transfected BT549 cells will be conducted to further define the time-dependent apoptotic response of the BT549 parent versus BT549/V cells. Finally, we will observe and compare the effect of anti-Gal-3 peptides on induction of apoptosis in these two cell lines in order to determine if Gal-3 plays a key role in the anti-apoptotic nature of carcinoma cells and to test if anti-Gal-3 peptides are efficacious in inhibiting the anti-apoptotic functions of Gal-3.