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Year in School: Sophomore
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Funding Sources: Burch Agricultural Internship Endowment, MU Office of the Provost, EXPRESS Program funded by the National Institutes of Health

Characterization of cell proliferation and death factors in MMTV-neu tumors

Apoptosis, or programmed cell death, is a biochemical process that is mediated by a multitude of cellular proteins to have the proper balance of cell growth and cell death. Altered apoptosis can give rise to cancer; tumors arise due to the ability of cancer cells to bypass the normal apoptotic pathways. Bcl-xL, an anti-apoptotic protein, and Bax, a pro-apoptotic protein, are expressed in a wide array of tissues at many developmental stages. Several breast cancer cell lines and primary breast tumors overexpress Bcl-xL. We hypothesize that Bcl-xL can accelerate tumor formation in the mouse mammary gland, while Bax can limit this progression. Since tumor formation is dependent upon the interactions of a variety of cell types within the mammary gland, mouse models are necessary to determine the functions of Bcl-xL and Bax in mice that are susceptible to tumor formation. Female transgenic MMTV-neu mouse form mammary gland tumors by 4 months of age. We have isolated mammary gland tumors generated from this line and are characterizing gene expression by RT-PCR and protein expression by immunohistochemistry for cell proliferation (akt) and cell death (bax, bcl-x, bad) proteins. We are also determining whether overexpression of bax in WAP-bax; MMTV-neu bi-transgenic mice can reduce the progression of mammary gland tumors.