Research Interest:

- **Cancer Biology**

The goal of our research effort is to understand the biology of cancer cells. From an understanding of the defects in a cancer cell, rational strategies for treatment can be developed. The progression from a normal cell that is responsive to its environment, to a tumor cell that proliferates uncontrollably, requires several genetic alterations to overcome built in protections against unwanted cell proliferation and cancer. Perhaps the most important protection against cancer is a program for cell suicide called apoptosis. Apoptosis is a default response to excess DNA damage or inappropriate cell division signals. To overcome the cells ability to commit suicide, cancer cells must acquire mutations that result in the activation of what are known as “survival signals” that suppress default apoptotic programs. Survival signals in cancer cells are ideal targets for therapeutic intervention because – in principle – suppression of survival results in apoptosis. Our lab has been working on survival signals generated by phospholipase D (PLD), an enzyme whose metabolic product phosphatidic acid suppresses apoptosis induced by both DNA damage and partial cell division signals. Importantly, elevated PLD has been observed in several human cancers including breast, gastric, colon, lung, pancreatic and renal cancer. Our recent work has indicated that inhibiting the signals generated by PLD in breast cancer cells leads to apoptosis, suggesting that PLD could be a good therapeutic target in cancers where PLD signals are keeping the cancer cells alive. PLD and phosphatidic acid contribute to the activation of an enzyme known as mTOR (the mammalian target of rapamycin), which has also been implicated in cancer cell survival signaling. Importantly, mTOR can be targeted with rapamycin and rapamycin induces apoptosis in human cancer cells that are surviving because of their PLD activity. The lab is currently trying to evaluate the potential for targeting PLD and mTOR in cancer cells with elevated PLD activity.