BORIC ACID AND PHENYLBORONIC ACID INHIBITION OF PROSTATE AND BREAST CANCER CELL MIGRATION

by

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ABSTRACT

Forty years ago, President Nixon declared a War on Cancer, initiating a massive effort of unprecedented scope to find a cure for this devastating disease. The initiative generated an enormous amount of knowledge on mechanisms of the origins and progression of cancer, but scientists and physicians struggle to translate this knowledge into successful treatments in the clinic today. No current cancer treatments are universally curative, causing a great need for discovering new anticancer drugs and developing new approaches to the problem. Currently, the most widely used and successful treatments target the uncontrolled growth of cancer cells. However, cancer cell migration, not proliferation, accounts for 90% of cancer deaths but is still the least treatable and understood aspect of the disease. Therefore, the identification and characterization of novel compounds that selectively target the metastatic stage of cancer is a high priority in the field and could have the greatest impact on patient survival. This thesis aims to address the great need for improved models of cancer drug discovery and for identifying novel metastasis inhibitors. This project provides supportive evidence for the anticancer properties of, boric acid (BA). The anticancer properties of a derivative of BA, phenylboronic acid (PBA), were also studied to determine if BA can be modified to yield a derivative more potent at selectively reducing migration and proliferation of prostate and breast cancer cells *in vitro*. To meet these goals, this project is organized into the following three specific aims (SA1-3)**:** SA1 is to define the effect of BA and PBA on migration and adhesion on fibronectin in tumorigenic and non-tumorigenic cell lines from human prostate and breast tissues. SA2 is to define the effect of BA and PBA on cell viability and proliferation in our model. And SA3 is to define changes in regulatory proteins of the cell migration pathway in the presence of BA or PBA. Results indicate PBA is more potent than BA at inhibiting tumorigenic cell migration and viability in cancers of multiple organ origin without effecting adhesion, and both compounds are selective for cancer cells over normal cells. The approach to the identification and validation of BA and PBA as anticancer agents is also model for a new approach to cancer drug discovery.