Unusual HPRT Expression in Prostate Cancer Cells and its Impact on Potential Treatment

Michelle H. Townsend¹, Abi M. Felsted¹, Michael D. Anderson¹, Richard A. Robison¹, Kim L. O’Neill¹

¹Department of Microbiology and Molecular Biology, Brigham Young University, Provo UT 84602

Introduction: The purpose of this study is to evaluate the expression and possible upregulation of the salvage pathway enzyme hypoxanthine guanine phosphoribosyltransferase (HPRT) in prostate cancer cells to determine if it could serve as a biomarker for prostate cancer diagnosis and potential treatment. In men, prostate cancer is the second most lethal cancer, and 27,540 men died from the disease in 2015. We chose to evaluate the salvage pathway enzymes due to a historically known relationship between Thymidine Kinase 1 (TK1), a salvage pathway enzyme, and prostate cancer. TK1 is a reliable biomarker for prostate cancer detection and development, which led us to the investigation the other pathway enzymes to determine whether similar relationships were present in lung cancer.

Materials and Methods: Two prostate cancer cell lines were utilized for this analysis (PC3 and DU145) along with cancer tissue and healthy tissue from 35 different prostate carcinoma patients. The surface localization of HPRT was determined utilizing flow cytometry, confocal microscopy, and scanning electron microscopy, while upregulation within tissue was assessed using immunohistochemistry.

Results: Throughout our investigation, we found a significant association between HPRT and the plasma membrane of DU145 cells but no presence was observed on PC3 cells. Using fluorescently conjugated antibodies, flow cytometry analysis showed minimal to zero changes in cell fluorescence when PC3 cells were exposed to HPRT antibody. There was a significant increase in fluorescence when DU145 cells were treated with HPRT antibody as the average population fluorescence enlarged by over 30%. This expression is statistically significant from the fluorescence increase observed in isotypic IgG controls (p value = 0.0004). Meanwhile, HPRT binding in PC3 cells was insignificant (p value = 0.1419). To determine the distribution of HPRT across the membrane and ensure the observed expression was not due to cytoplasmic HPRT, gold conjugated antibodies were used for cell staining. The distribution of the gold on the cell surface showed random HPRT binding across the membrane with no clear pattern of expression. This analysis aided in confirming HPRT presence as the gold weight % of the sample increased significantly when DU145 cells were exposed to HPRT antibody (p-value < 0.0001). In addition to being presented on the surface of non-small cell lung cancer cells, the general upregulation of the protein was evaluated in human cancer tissue to determine whether the enzyme had differential expression in clinically relevant samples. Using IHC, an upregulation of HPRT within cancer tissue was seen when compared to healthy tissue. Because of the differential expression between these cell lines, this expression may be limited to only a few types of prostate cancer.

Conclusions: These results strongly indicate a unique relationship between prostate cancer cells and HPRT and suggest HPRT as a possible biomarker for the detection and potential treatment of some prostate cancers.