

The Role of Fatty Acid Metabolism in Cancer Development

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Introduction

Cancer is a disease caused by an uncontrolled division of abnormal cells in a part of the body. They use the cellular building blocks (nucleic acid, protein, and lipids) that normal cells use, and form lumps (tumors) that keep growing, and eventually make up billions of copies of cancerous cells. Globally, the number one leader in causing cancer is 'Unbalanced diet' like high-glycemic carbohydrates and too many calories leading to obesity, followed by smoking and alcohol use, then chronic infections like HIV, human T-cell leukemia and lymphoma (2008, Benjamin Cummings). There are four different types of Cancers classifications, Carcinomas – cancer rising in the epithelial tissue of the skin or of the lining of the internal organs. Sarcomas – tumor that occurs in the bones and soft tissues. Lymphomas – A cancer of the lymphatic system. Leukemia –A cancer of blood-forming tissues, prevents the body from being able to fight infections. According to the Cancer Action Network, Cancer cases in 2014 totaled over 87.8 billion dollars, of that 87.8 billion dollars, nearly 4 billion was in out-of-pocket costs.

Most cancer tumors share the same physiological attributes but have a distinctly different genetic makeup. Proto-oncogenes, a group of genes that encode for proteins that stimulate cell division, inhibit cell differentiation and halt death when mutated lead to oncogenes. Oncogenes in turn work to increase cell division, decrease cell differentiation and inhibit cell death. Cancer cells are known to develop and utilize multiple other pathways to maintain their homeostasis and support their constant cell divisions.

In most cancer cells, there are some protein accumulations that are noted, like is the case in clear cell renal carcinoma cells, there was a high expression of HMGB1 noted as well as a huge accumulation of lipids and free fatty acids deposits in the cells. Although the significance of the lipid deposition in the cells is still undefined, a positive relationship exists between the development of the cancer cells and the accumulation of the lipids. Different pathways have been linked to this phenomena and current research being conducted will help establish which specific pathways are responsible and the impact the accumulation of the fatty acids has on the survival of these cells. This findings led to the experiment at hand, as we work to investigate which are some of the other fatty acid sensitive proteins that could be potentially used as biomarkers.

Research and Design Methods

Cell culture and cell lines

Three different cell lines will be used, one non-cancerous cell line (293T) and five cancerous cell lines. Of the five, two are kidney cancer cell lines (SW156 & 786O), one lung cancer cell line (HCC827c) and one breast cancer cell line (MDA231). They were all cultured in DMEM (5% glucose), a complete growth medium and incubated at 37 degrees and the cells were split every couple of days.

Protein Analysis

Protein analysis by immunoblot was performed on cancer cells that are known to have increased lipids and compared to normal (non-cancer) cells following exposure to unsaturated and saturated fatty acids. Cells that were responsive to unsaturated fatty acids were then tested for metastatic capability by using transwell invasion assays.

Immunoblots

Immunoblots were run to compare the expression of HMGB1 across the different cancer cell lines and compared.

Results

Basal expression of HMGB1 in Cancer cell lines

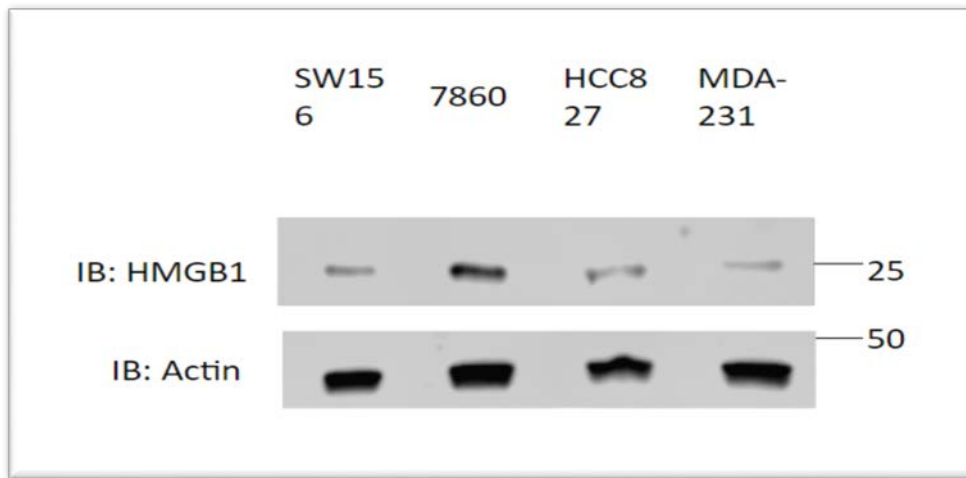


Figure 1: Immunoblot showing the expression of HMGB1 and Actin across four different cancer cell lines

Cells delipidated 24 hrs 4-hr treatment with Oleate-BSA

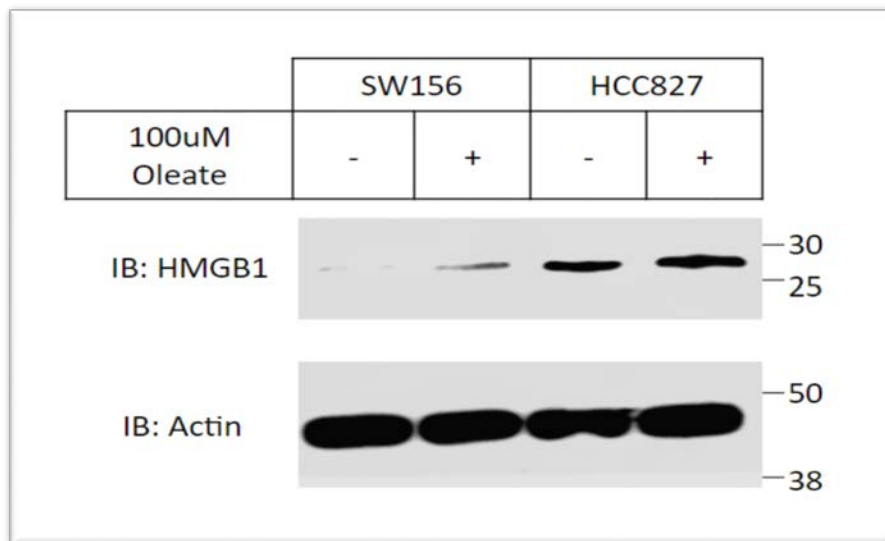


Figure 2: 5ug of protein/well

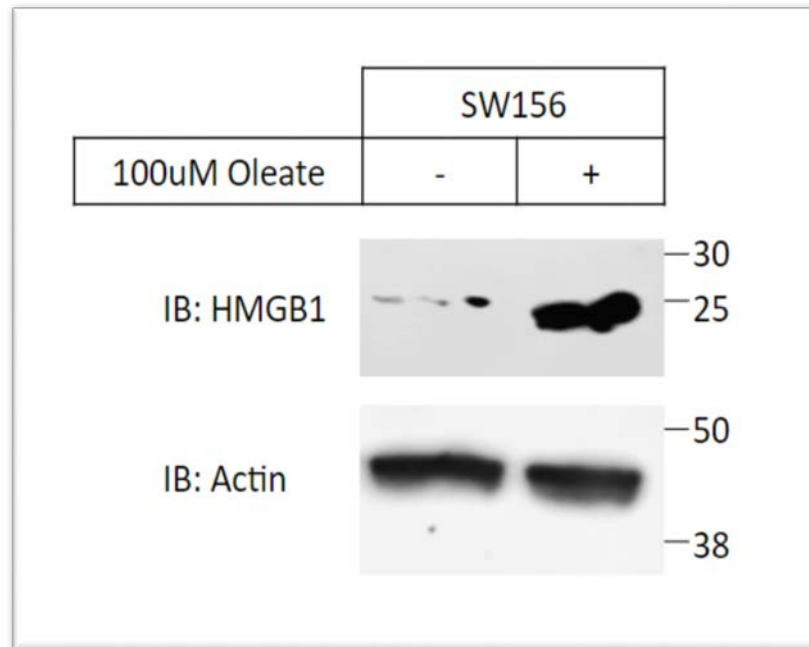


Figure 3: Cells delipidated 24 hrs 4-hr treatment with Oleate-BSA, for SW156 & HCC827 cells in a 5ug and 20ug of protein/well

Works Cited

Keung J.Y and Kim W.Y. Stearoyl Co-A Desaturase 1 as a ccRCC Therapeutic Target Death by stress. *Clinical Research* 19, 3111 – 31113 (2016)

Kim H. et al. Unsaturated Fatty Acids Stimulate Tumor Growth through stabilization of B-Catenin: *Cell Reports* 13, 495-503 (2015)

Spector, Arthur, A. The Importance of Free Fatty Acid in Tumor Nutrition. *Cancer Research* 27, 1967

Zhang, J. et al. EGFR modulates monounsaturated fatty acid synthesis through phosphorylation of SCD1 in Lung cancer. *Molecular Cancer* 16, (2017)

Acknowledgements

Funded by the McNair program at the University of Wisconsin Superior and the University of Minnesota Medical School Duluth.