Evaluation of Manganese (Mn) Binding Proteins in Lung Carcinoma Cells

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Introduction

Despite significant improvements in lung cancer therapies in recent years, lung cancer remains as the leading cause of cancer-related death due to its inclination to metastasize. Recent findings highlight the metastatic capacity of tumor cells as a result of overexpression of the Golgi integral membrane protein 4 (GOLIM4), which is frequently amplified in many human cancers, including lung squamous cell carcinoma (LUSC). GOLIM4 forms a complex with ATPase Secretory Pathway Ca²⁺ transporting 1 (ATP2C1) on the trans-Golgi and promotes pro-metastatic vesicle trafficking. Highly expressed GOLIM4 drives lung cancer growth and metastasis. Manganese (Mn) is an essential element that is present in tiny amounts in the human body. Mn treatment causes GOLIM4 degradation and inhibits the growth of chromosome 3q-amplified LUSC cells. To identify other factors that may mediate the antitumor functions of Mn, we performed a pull-down assay and identified several Mn binding proteins.

Hypothesis

We have shown that GOLIM4 is a Mn binding protein which is degraded upon Mn exposure. We found that Mn treatment effectively suppressed the growth of chromosome 3q-amplified lung cancer cells. We will examine the functions of these Mn binding proteins. We hypothesize that Mn functions by targeting several oncogenic proteins.

Methods

We identified several significant Mn binding proteins (BLMH, S100A8, SERPINB8, TIMP3) in a Mn pull-down assay. We used specific siRNAs to knock down these proteins and assess cell proliferation using the WST-1 method and cell migration using the Boyden chamber trans-well assay. In addition, we examined the levels of these proteins following Mn treatment by performing a Western blot to investigate if Mn caused degradation of these proteins.

Results

We found that these Mn binding proteins play critical roles in cell proliferation and migration. However, Mn treatment did not result in degradation of these proteins, suggesting that they may not be primary Mn targets in chromosome 3q-amplified lung cancer cells. Thus, we conclude that GOLIM4, but not other Mn binding proteins, are responsible for Mn-induced cancer cell growth inhibition. In the future, we will focus on the functions of GOLIM4 in lung cancer growth and metastasis.

Conclusion & Future Directions

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References

1) https://lcfamerica.org/