

## HISTONE PHOSPHORYLATION ASSOCIATION WITH METASTATIC LUNG CANCER

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**Abstract:** Cancer is the second leading cause of death in the United States as of 2017 and lung cancer is the leading cause of cancer death. Each year, more people die of lung cancer than of colon, breast, and prostate cancer combined. Lung cancer is an autonomous replication of cells that line the bronchi and lung tissue called the alveoli. There are two types of lung cancer: non-small (NSCLC) and small cell lung cancer (SCLC). NSCLC is the most prevalent with a metastatic (stage IV) 5-year survival rate of ~ 1%. Cancer metastasizes in three ways: invade nearby tissue, travel through the lymphatic system, or cardiovascular system. Those diagnosed with lung cancer experience symptoms such as shortness of breath, coughing, bloody phlegm, chest pain, fatigue and weakness. Cancer is caused by a mutation in the cell's DNA that can be a result of normal aging, environmental, or biological factors. DNA can be damaged from double stranded breaks (DSBs). Cisplatin is used to treat several cancers and induces DSBs. DSB leads to the H2AX foci formation, resulting in the phosphorylation of H2AX by PI3K. Once phosphorylated,  $\gamma$ -H2AX is a biomarker in the DNA damage response (DDR). The use of plant extracts is becoming a trend for those interested in natural treatment options. They have been reported as less toxic with decreased side-effects compared to traditional treatment options. The objective of the experiment was to identify the effects of Cisplatin and Xanthohumol on the cancerous nature of a cell line. More specifically, we hope to determine which treatment option whether in combination or individual, would effective result in the phosphorylation of H2AX. Overall, we are searching to find a more natural and less toxic way to treat cancer. We hypothesize that H2AX will be phosphorylated by extract plant Xanthohumol. To test this hypothesis, we performed immunohistochemistry on a H1299 metastatic cell line, applied various concentrations of Xanthohumol and Cisplatin and analyzed the outcome by fluorescence microscopy. Fluorescent microscopy analysis indicated that the combination of 25 $\mu$ M of Cisplatin and 25  $\mu$ M of Xanthohumol was the most effective in the process of phosphorylating H2AX. More foci are present for the treatments that consisted of both the Xanthohumol and Cisplatin. The foci indicate sites of histone phosphorylation, a biomarkers for DNA repair.

**Keywords:** Cisplatin, Xanthohumol, Metastatic, DSBs, gamma H2AX, Foci

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