Fursultiamine Prevents Lung Cancer Growth

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Background

Lung cancer is the leading cause of cancer death in men and the second leading cause of cancer death in women worldwide. Cigarette smoke-induced oxidative and inflammatory responses are the major risk factors for the development of lung cancer. Developing effective treatment methods had been the aim of many studies over the years. Several compounds have been tested for their efficacy in preventing lung cancer. However, very few compounds have gone through clinical studies

Hypothesis

We hypothesize that with its potent anti-oxidative and anti-inflammatory actions, fursultiamine (BF1), a disulfide lipid-soluble derivative of vitamin B1 (thiamine), could prevent lung cancer growth and spread. The ability of fursultiamine to diffuse through cellular membranes could potentially make it a more effective lung cancer treatment than thiamine, which has already been effective for lung cancer treatment.

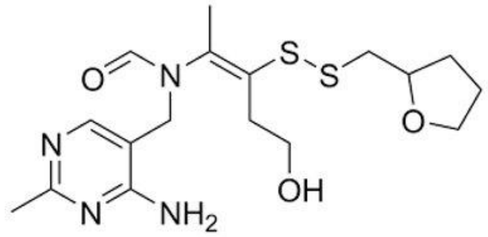


Figure 1. Chemical structure of fursultiamine.

Methods

Non-small cell lung cancer cells (A549 cells) will be used in vitro and in vivo. A549 cells will be treated with EGF without or with varying concentrations of fursultiamine for 24 hours. Cell viability will be determined by MTT assay, apoptosis by Annexin-V staining, and live and cell death assay. Specific antibody arrays will be used to examine the expression of various anti-apoptotic, pro-apoptotic, and pro-inflammatory factors. The expression of various cytokines and chemokines will be examined by Multiplex analysis. The generation of reactive oxygen species and activation of redox-sensitive transcription factors will be examined by specific assay kits. Subsequently, we will inject A549 cells in the athymic nude mice subcutaneously, and the mice will be treated without or with a diet containing fursultiamine. Tumor growth will be recorded regularly for 30 days. We will extract the tumors from nude mice xenografts, cut the sections, and will be analyzed immunohistochemically for the expression of various carcinogenic and inflammatory markers.

A lipid soluble derivative of thiamine could be more effective in lung cancer treatment than thiamine

Current Results

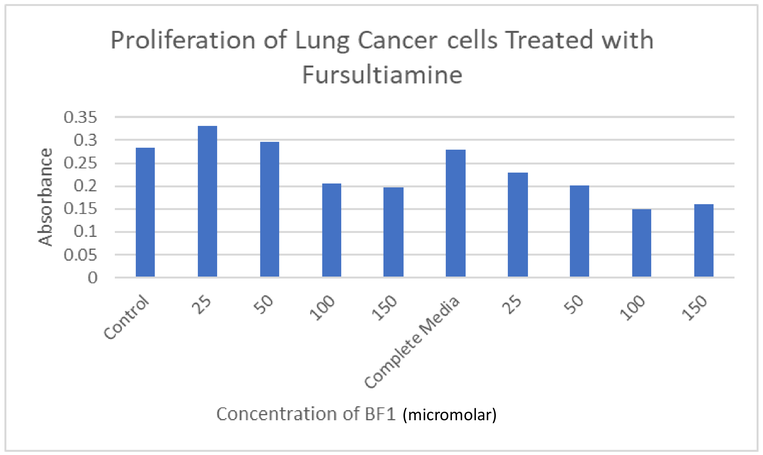


Figure 2. MTT assay of A549 lung cancer cells treated with fursultiamine. The first five bars represent the absorbance of cells treated with both 0.1% serum and the corresponding concentration of BF1. The next five bars represent the absorbance of cells treated with both Complete Media and the corresponding concentration of BF1. Absorbance is positively correlated to living cells.

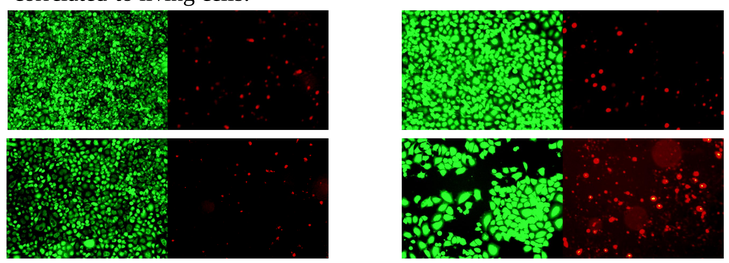
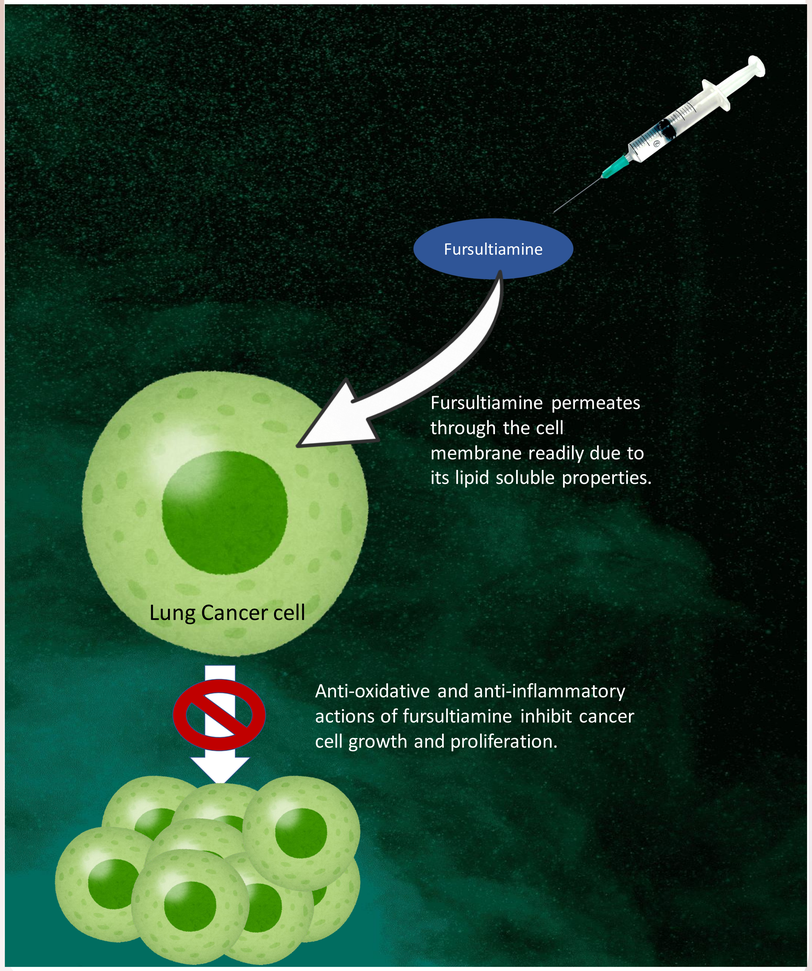


Figure 3. Live Green vs. Red Dead flourescence of A549 control cells (top left), A549 cells treated with 150 micromolar fursultiamine (bottom left), A549 cells treated with Complete Media(CM) (top right), and A549 cells treated with CM and 150 micromolar fursultiamine (bottom right).
Live Green and Red Dead capture images of living vs dead cells.

Schematic



Conclusion and Future Plans

Our preliminary data suggests that fursultiamine is indeed effective in attenuating the proliferation and growth of lung cancer cells. This is evident in both our MTT assay and Live Green imaging of A549 cells, which show notable death in cells compared to controls. We plan to continue our MTT assays to ascertain the optimal concentration of fursultiamine treatment. Afterwards, we will proceed with the experiments outlined in the methods section to further confirm the effectiveness of fursultiamine treatment.