The Use of MnSOD in Combined Modality Therapy to Sensitize Lung Cancer Cells to Ionizing Radiation and Chemotherapy

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Lung cancer is the deadliest cancer claiming 159,480 deaths in 2013 (American Cancer Society). Lung cancer may also become chemotherapy and radiotherapy resistant. Manganese Superoxide Dismutase (MnSOD), a naturally occurring enzyme, converts Superoxides into Hydrogen Peroxide (H_2O_2). If MnSOD levels are supplemented in cancer cells which are naturally deficient in catalase, then the excess production of H_2O_2 will weaken the cancer cell, causing the cell to be more responsive to chemotherapy and radiation, while potentially protecting healthy lung tissue due to higher levels of catalase. H1299 and HCC4006 resistant lung cancer metastases were used since metastasis and resistance are defining factors of patient prognosis. After supplementation with 24 μM MnSOD mimetic for one hour, the cells were exposed to Cisplatin and/or Ionizing Radiation. Next, the cells were seeded and colony formation was assessed. After determining clonogenic survival, Western Blotting was used to assay for PARP cleavage- indicating cell death through parthanatos. MnSOD and Cisplatin treatment was 1.72x (H1299) and 2.92x (HCC4006) more effective than Cisplatin treatment alone, shown by a 71% decrease in surviving fraction ($p<.001$). In addition, MnSOD, Ionizing Radiation, and Cisplatin treatment was 2.39x (H1299) and 2.22x (HCC4006) more effective than treatment without MnSOD, shown by a 42% decrease in surviving fraction ($p<.001$). Also, both cell lines exhibited PARP cleavage indicating parthanatos- potentially reducing inflammation and side effects for patients undergoing cancer treatment. The results showed that MnSOD was able to sensitize lung cancer cells to chemotherapy and Ionizing Radiation, and potentially protect healthy cells from cancer treatment.

Awards Won:

Second Award of $2,000