Analysis of Volatile Organic Compounds Specific to The Treatment of Small Cell Lung Cancer by Cisplatin and Etoposide

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Background

Lung cancer is the leading cause of cancer-related deaths globally, claiming 1.59 million lives annually. Numerous efforts have been made to reduce mortality, however, 33% of small cell lung cancer patients still experience a relapse within the first two years [1]. This challenge is driven by limitations in diagnostics, which are unable to accurately evaluate the tumor treatment response over time. Due to altered biochemical pathways, it is hypothesized that different cancer cells have unique VOC expression [2]. This study, therefore, utilizes recent research by examining VOCs specific to small cell lung cancer under the administration of chemotherapeutics such as cisplatin and etoposide in the headspace of in vitro cell cultures. The VOCs were initially collected from the headspace of the Biodome (a custom glass culture dish interconnected to a gas flow system) using a specialized sorbent carbon material. The samples were then run through a comprehensive two-dimensional gas chromatography coupled with time of flight mass spectrometry and the VOC relative abundances were analyzed. The results revealed unique VOC patterns validated by metabolic pathways. These VOC patterns can then be utilized by oncologists to examine the tumor shrinkage and treatment response over time in a noninvasive way

Experimental Methods

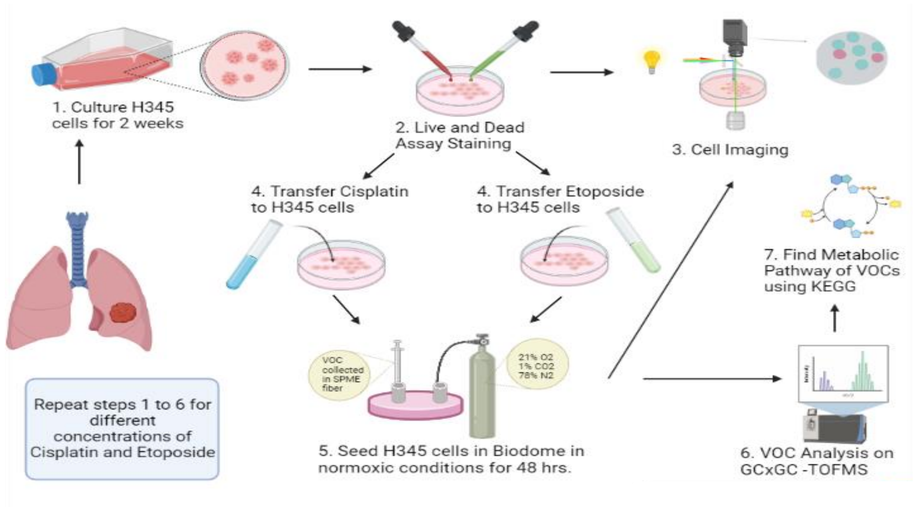

Figure 1. A schematic of a step by step experimental procedure used to measure VOCs specific to H345 cells under the administration of cisplatin and etoposide over a period of 48 hrs. The procedure also involves the live and dead assay staining of the H345 cells to validate their apoptosis from the chemotherapeutics.

Research Goals

The goal of the research project is to identify VOCs specific to the apoptosis of small cell lung cancer under the administration of Cisplatin and Etoposide

Results

Live and Dead Assay Staining of H345 Cells

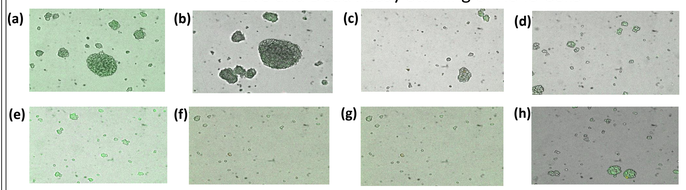

Figure 2. Staining of the H345 cells before the administration of Cisplatin in images (a), (b), (c) and (d) . Staining of the H345 cells after the administration of Cisplatin in images (e), (f), (g) and (h) .

Green staining represents live H345 cells while red staining shows dead H345 cells

Mass Spectra of VOCs Specific to Cisplatin and Etoposide induced H345 Cells

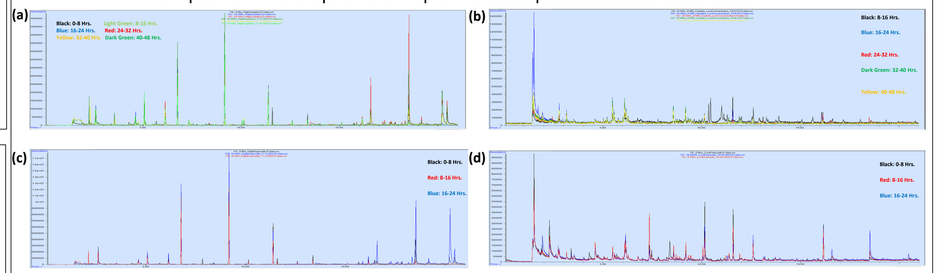

Figure 3. Mass Chromatograms of VOCs specific to the administration of a) 10.uM Cisplatin b) 1.66 uM Cisplatin c) 10 uM Etoposide d) 1 uM Etoposide

Line and Bar plots of abundant VOCs in Cisplatin and Etoposide Induced H345 cells

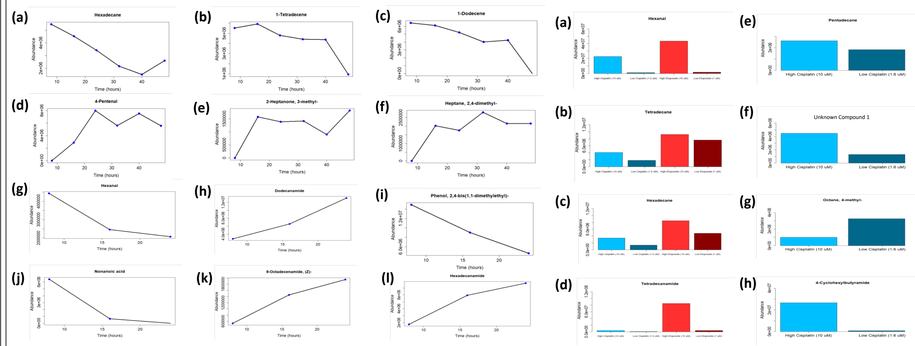

Figure 4. Line plots illustrates chemical abundance over a time period of 24-48 hrs. of (a) Hexadecane (b) 1-Tetradecene (c) 1 – Dodecene in 10 uM Cisplatin induced H345 cells, (d) 4 - Pentenal (e) 2-Heptanone, 3-methyl- (f) Heptane, 2,4-dimethyl in 1.66 uM Cisplatin induced H345 cells, (g) Hexanal (h) Dodecanamide (i) Phenol, 2,4-bis(1,1-dimethyethyl)- in 10 uM Etoposide induced H345 cells, (j) Nonanoic Acid (k)9-Octadecanamide, (Z)- (l) Hexadecanamide in 1 uM Etoposide .

Figure 5. Bar plots illustrate the chemical abundance of (a) Hexanal (b) Tetradecane (c) Hexadecane (d) Tetradecanamide over a period of 24 hrs., (e) Pentadecane (f) Unknown Compound 1 (g) Octane, 4-methyl- (h) 4-Cyclohexylbutylramide over a period of 48 hrs. in different concentrations of Cisplatin and Etoposide.

Obstacles

One of the hypoxic sample runs had to be repeated due to a technical error in the insertion of the SPME fiber into the mass spectrometer which led to the loss of the VOC collection data. It was difficult preparing the Cisplatin stock solution due to very low water solubility .

Conclusion

Through the data analysis of the metabolites measured across the 24 to 48 hrs. time period, unique VOC patterns have been identified for both Cisplatin and Etoposide induced H345 cells. There was a decreased expression of VOCs such as Hexadecane, 1-Tetradecene and Hexanal, Nonanoic acid in Cisplatin and Etoposide induced H345 cells respectively. On the other hand, VOCs such as 4 - Pentanal and 2-Heptanone,3-methyl- increased over time in Cisplatin induced H345 cells compared to Dodecanamide and Hexadecanamide in Etoposide induced cells. Compounds such as Tetradecanamide and unknown compound 1 were found more abundant in H345 cells induced with higher concentrations of Cisplatin and Etoposide over time. These VOCs can be used to evaluate tumor treatment response over time as their increased or decreased abundance over time would indicate tumor shrinkage. Future work will include the validation of the VOCs using RNAi.

Acknowledgments

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References

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[2] Jia, Zhunan, et al. "Detection of Lung Cancer: Concomitant Volatile Organic Compounds and Metabolomic Profiling of Six Cancer Cell Lines of Different Histological Origins." ACS Omega, American Chemical Society, 31 May 2018, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6044508/.

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