Computational Modeling of Tumor Growth in Mouse Cells

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PURPOSE

This experiment aims to:

1. Analyze the global effects of promoters and inhibitors of adipogenesis and cell differentiation on cellular metabolites and identify treatment-specific biomarkers.

2. Study how computational modeling and analysis of mass spectrometry data can be used in this process of identification of biomarkers

INTRODUCTION

1. Motivation / Previous Work

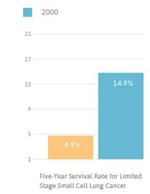


Figure 1. Despite research analyzing cancer cells, scientists have not yet discovered an effective therapy that operates at the the cellular level. As a result, doctors **resort to using chemotherapy to treat this deadly disease**, **which only provides short-term possible remission,** and it does not contribute to an actual cure for cancer (Claudino, 2007).

2. Goal / Gap

This project aims to study cancer at the **cellular level,** analyzing the process of adipogenesis (the differentiation of cancer cells into fat cells) in order to **identify treatment-specific biomarkers** that can be targeted in future cancer cell therapies (Krumsiek, 2016). Unlike chemotherapy or radiotherapy, which destroy both healthy cells and cancer cells, future cancer treatments targeting the biomarkers identified in this study will be more streamlined so the **treatment can destroy mostly cancer cells**.

3. Approach / Technique

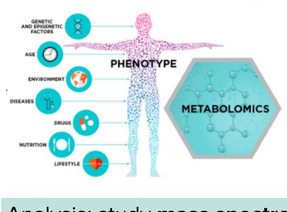


Figure 2. Technique: **metabolomics** - the study of the substances involved in cellular processes and reactions using tools such as mass spectrometry

Inquiry approach: **descriptive research** based on true experimental research

Computational modeling/Statistical Analysis: study **mass spectrometry data** using quantitative methods to identify treatment specific biomarkers (Allmaras, 2013)

RESEARCH METHODOLOGIES

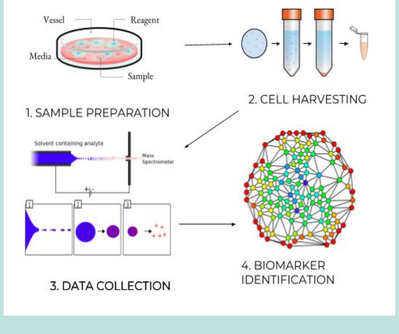


Figure 3.
There are four main segments for this project -

(1) Experiment

2) Manual Data Analysis

(3) Computational Modeling and Data Analysis

(4) Identification of Treatment Specific Biomarkers.

DATA AND RESULTS

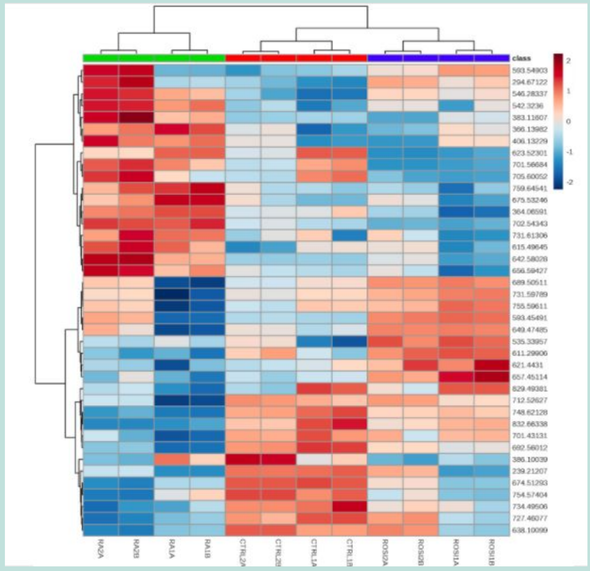


Figure 4. This heatmap compares the prevalence of different features that vary between the control, Retinoic Acid, and ROSI, the difference chemicals that were added to each sample. The **clusters of red versus** blue show how chemical inhibiting adipogenesis in the cells acted in an almost opposite manner to those that promoted adipogenesis. This suggests there is a strong correlation between the added chemicals and the lipogenic pathway.

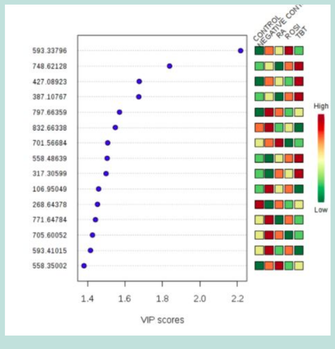
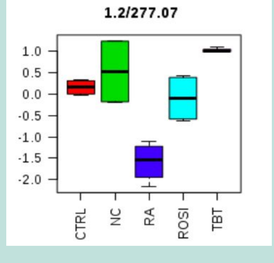


Figure 5 (left). PLS-DA Important Features Graph highlighting features that exhibit the targeted behavior of RA and TBT/ROSI **behaving in the opposite manner**.

- Point at (1.9, 748.62128) shows low RA level vs. high TBT/ROSI levels

Figure 6 (right). This chart highlights one of the significant features which show a strong contrast between the behavior of RA versus TBT and ROSI. Such behavior suggests the **future therapies can target the features** illustrating the strong contrast will most likely affect fat production.



DISCUSSION, IMPLICATIONS, AND NEXT STEPS

Discussion

Based on the results, the process of adipogenesis was likely affected by the inhibitors and promoters. The data from the mass spectrometer was analyzed and it was found that **each of the analytes had their own distinct metabolites**, showing that the chemicals did indeed have an effect on lipogenesis in the cells. Probable metabolites were identified and cross referenced by using databases like METLIN and HMDB. One compound that was found in this process was **ceramide** (C41H18NO3), a waxy lipid molecule involved in lipogenesis. This compound was analyzed further with the Kegg Pathway Database and it was found that **this compound is involved in the process of apoptosis, or cell death**. This suggests that the chemicals added to the cells may have affected their apoptosis rate.

Implication

There are many applications of this research in future experiments. One possible experiment is to test adipogenesis is to study the process of adipogenesis under hypoxic conditions. **Hypoxia**, or oxygen deficiency, often occurs in cancer tumors as they cut off the body's blood vessels. These **hypoxic conditions are a precursor to the process of adipogenesis** and therefore, it would interesting to further study their relationship for future cancer therapies (Claudino, 2007). Another pathway that could also be studied in future research is the **HIF-α pathway**, another way in which cancer cells gain energy. **Understanding the connection between the two pathways is crucial in understanding how they can be targeted in future cancer therapies.**

Next Steps

In order to check if this compound actually is significant, the student researcher is now looking into how to create a **computer program modeling the results** to perform this manual work of choosing compounds that show significant variance between the different tests to then by analyzed further (Brodland). This computer program will be tested in order to see if it matches up with the analysis presented in this paper. Such a program would **not only verify the data, but it would also make further data analysis more efficient**.

ACKNOWLEDGEMENTS / REFERENCES

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