Personalized Nanomedicine Tailored to Lung Cancer Metabolomic Analysis

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Introduction

Introduction:

- Encapsulating chemotherapeutics in nanoparticles (NPs) may minimize chemotherapy side effects, provide sustained-release, and decrease dosing. Cancer metabolomics enables a specialized view of each patient's cancer and may provide information to tailor personalized nanomedicine.

Objective:

- The long-term goal of this project is to modulate NP formulations to improve the release of active agents as a potential treatment modality. Software-based analysis of patients' metabolic profiles was performed from NSCLC biopsies as a first step towards synthesizing the metabolomic data for NP-design purposes.

Methods:

- NPs encapsulating Rhodamine B were synthesized using either a nanoprecipitation or electrospraying technique with acetone or acetonitrile as solvents. NPs were evaluated based on yield, loading, and release profile. NSCLC patient metabolic data were analyzed using R Studio.

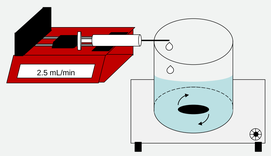
Results:

- Electrospraying method results were superior to nanoprecipitation results on the basis of yield, encapsulation efficiency, and extended release.
- Polyvinyl alcohol (PVA) was used as a stabilizer to improve nanoprecipitation synthesis.
- Heat maps were created for a set of 22 patients, highlighting specific metabolites to consider for patient-specific NP design.

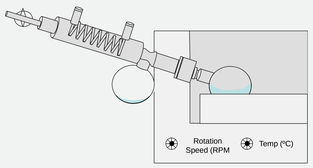
Conclusion:

- We envision that metabolomics data will be useful to personalize nanomedicine by developing a decision tree to determine NP parameter values that may maximize patient response.

Nanoprecipitation Methods



8 mg/mL PLGA Dissolved in Organic Solvent with 1% Rhodamine B and added at 2.5mL/min to Aqueous Phase



Rotovap 45ºC, 500 mmHg, 80 RPM

Figure 1: Schematic of Nanoparticle Precipitation Fabrication Procedure.

NSCLC Metabolic Data Analysis

NSCLC Tissue Processing:

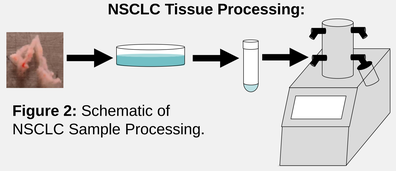


Figure 2: Schematic of NSCLC Sample Processing.

1) Obtain metabolic data from mass spectroscopy of patient biopsy samples.

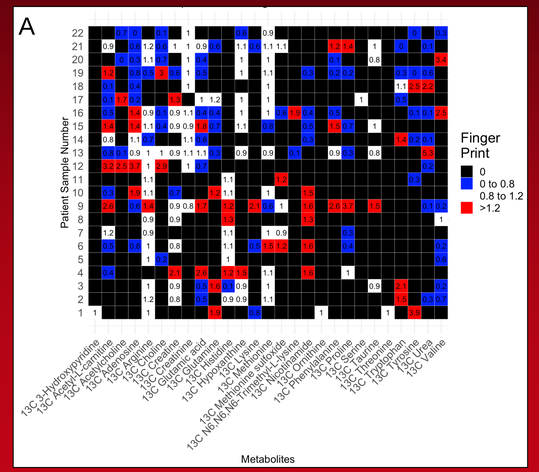
2) Statistical analysis of metabolic data using R Studio.

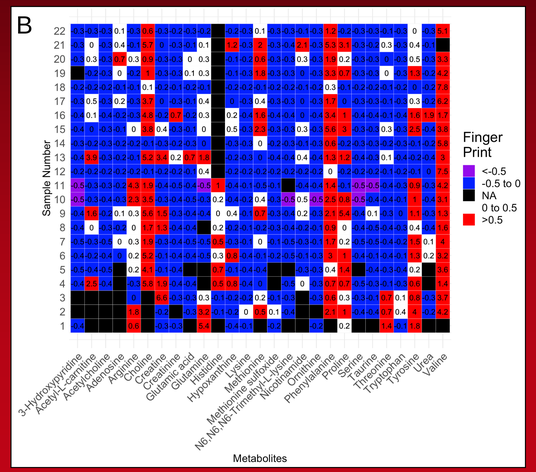
3) Use metabolic data to determine key metabolites.

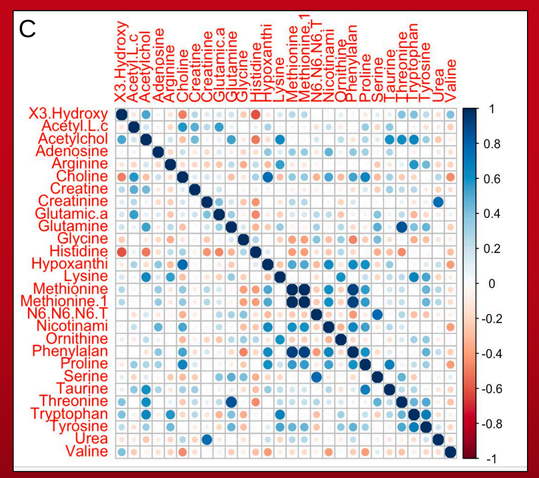
4) Determine effect of these metabolic conditions on NP transport and efficacy.

5) Tailor NP design to these metabolic conditions to customize nanotherapy.

NSCLC Biopsy Metabolic Expression Analysis







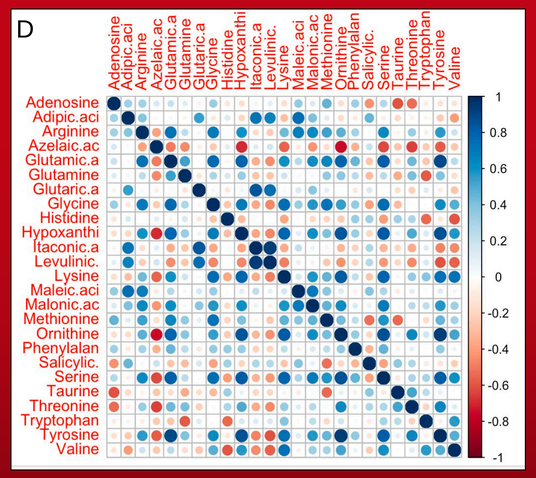


Figure 3: (A) Unscaled Heat Map with Ratio of Sample C13 Labeling Divided by the Average Ratio of 13C/Unlabeled for Each Metabolite; **(B)** Unlabeled (No C13 Glucose) Heat Map Centered and Scaled; **(C)** Positive Spin Metabolites Correlation Matrix; **(D)** Negative Spin Metabolites Correlation Matrix.

Scanning Electron Microscopy Images of Nanoparticles

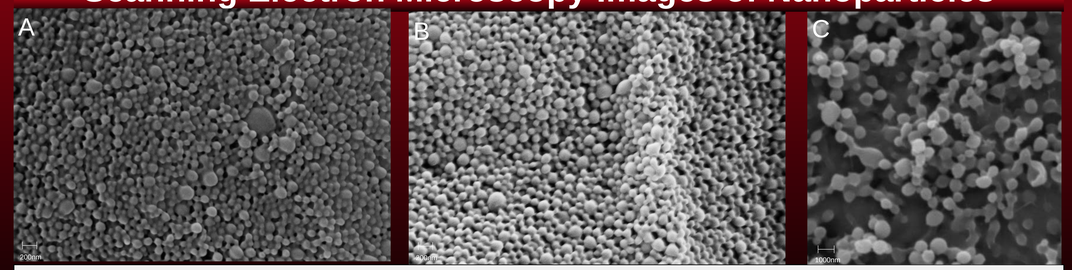
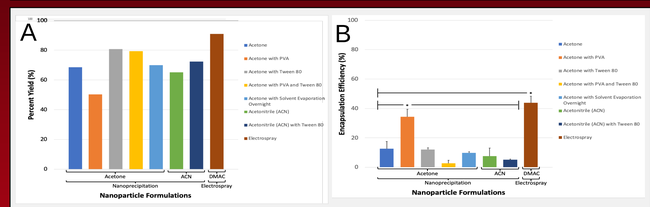


Figure 4: (A) Acetone Nanoprecipitation SEM; **(B)** Acetone with PVA Nanoprecipitation SEM; **(C)** Electrospray SEM.

Nanoprecipitation Methods



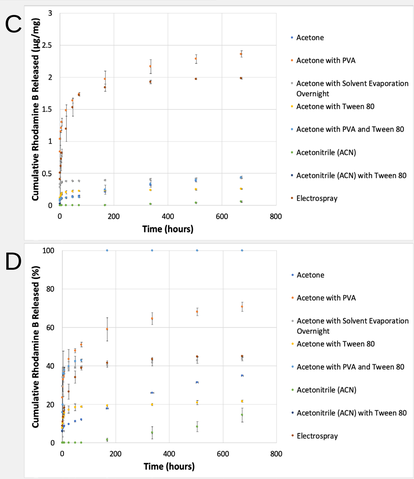


Figure 5: (A) Percent Yield of Nanoparticle Formulations; **(B)** Encapsulation Efficiency of Nanoparticle Formulations where * Indicates Significance at α = 0.001; **(C)** Extended Release (µg/mg) of Nanoparticle Formulations; **(D)** Extended Release (%) of Nanoparticle Formulations.

Conclusions

- The electrosprayed NPs demonstrated higher yield (91%) and loading (43%) compared to nanoprecipitated NPs.
- Nanoprecipitation with polyvinyl alcohol (PVA) as a stabilizer in acetone had higher sustained-release (78%) over 4 wk compared to the electrospray method (47%).
- Among the nanoprecipitation formulations, acetone with Tween 80 had the highest yield (81%), while acetone with PVA had the highest loading (30%).
- The metabolomics data may be useful in the era of personalized medicine in developing a decision tree for determining nanomedicine parameters optimized to patient tumor-specific metabolic parameters..

Acknowledgements

- Research was supported by the University of Louisville Cancer Education Program NIH/NCI R25-CA134283.
- This work was partially supported by the National Institutes of Health – National Cancer Institute (grant number R15CA203605 - H. Frieboes).
- The NSCLC metabolomic data in this study was previously obtained in collaboration with Dr. V van Berkel, Dr. D Miller, Dr. J Yan, Dr. X Zhang, and the CREAM facility at UofL.