**Metabolomic profiling of influenza: a 2009 pandemic H1N1 influenza in lean and obese mice (diet-induced obesity)**

Metabolomics Analysis: RTI RCMRC

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IACUC Number: 12-182.0-A (UNC Institutional Animal Care and Use Committee)

**Abstract:**

During the 2009 H1N1 influenza pandemic outbreak, obese individuals were reported to be at greater risk for morbidity and mortality from pandemic infection. However, the mechanisms contributing to greater influenza severity in infected obese individuals remain unclear. Given that one in ten individuals is obese, and worldwide influenza outbreaks are a consistent public health burden, garnering a better understanding of the pathways and mechanisms contributing to greater influenza severity in the obese is essential for limiting influenza infection mortality in this at-risk population. Closely paralleling pH1N1 infection outcome in humans, obese mice exhibit increased morbidity and mortality following pH1N1 infection. In mice, obesity impairs the function of natural killer cells, dendritic cells, macrophage, B cells and memory T cells. Further, several analyses of lung antiviral responses revealed that obese mice have greater lung damage, lung immune cell infiltration and impaired lung healing after infection. Nevertheless, it remains unclear how altered immune cell function contributes to greater lung damage and increased infection severity in obese mice. This study utilized metabolomics as a novel method to dissect the metabolic consequences of obesity on the immune response to pH1N1 infection, where we compared metabolic profiles of lung-specific and peripheral samples from uninfected and infected lean and obese mice during early and late phases of influenza immunity. In addition to using metabolomics for generating mechanistic hypotheses and guiding future research, we propose to use metabolomics as a potential diagnostic tool for human influenza virus infection in non-invasive biofluids. Taken together, this proposal will provide novel information regarding the enhanced pathogenesis of influenza infection in the obese and directly translational information that can be applied to modifying clinical approaches and methods of infection treatment in the obese.

56 weanling, male, C57BL/6J mice were randomly assigned to a high fat, low fat, or standard mouse chow diet. The 28 mice on the high fat diet (60% kcal fat) were expected to be obese at the end of 15 weeks and expected to weigh at least 50% more than the lean mice fed the low fat diet (10% kcal fat). After 15 weeks blood and lung tissue samples were obtained from 16 mice (8 lean and 8 obese) prior to infection with pH1N1. At four and eight days after influenza infection, blood and lung tissue samples were collected from infected/uninfected and high fat/low fat/chow diet mice with an n of 5-7 per group for each infection day.

This metabolomics study was conducted to provide data on the metabolic changes differentiating the response to pandemic influenza A (pH1N1) infection in lean and obese mice.

The data required for the metabolomics analysis can be found in the accompanying files:

Procedures: 1. BECK-LUNG\_DIET Metabolomics Procedure.docx

Study Design Table: 2. BECK-LUNG\_DIET Design Table And\_Subject\_ID.xlsx

Metadata: 3. BECK-LUNG\_DIET MetaData and Analytical Metadata.xlsm

Processed Data: 4a. Beck\_Lung\_01\_RP-POS-Zipped LC-MS Data.xlsx

4b. Beck\_Lung\_01\_RP-NEG-Zipped LC-MS Data.xlsx

Raw Data: 5a. Beck\_Lung\_01\_RP-POS-Zipped LC-MS Data.zip

5b. Beck\_Lung\_01\_RP-NEG-Zipped LC-MS Data.zip