**Metabotypes of Subjects with Adverse Reactions Following Vaccination: A Pilot Study**

Metabolomics Analysis: NIH Eastern Regional Comprehensive Metabolomics Resource Core (RTI RCMRC)

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**Abstract:**

An Adverse Event Following Immunization (AEFI) is an adverse reaction to a vaccination that goes above and beyond the usual side effects that are known to be associated with vaccinations. AEFIs can vary in clinical severity to very mild to incapacitating and occasionally require lost time from work or even hospitalization. In rare cases, there is an aberrant immune reaction from vaccination resulting in a potentially serious adverse event. One known serious adverse event related to the smallpox vaccine is myocarditis and/or pericarditis (myopericarditis).

Metabolomics may help identify a particular metabolic signature “metabotype” in patients who are predisposed to developing AEFI such as a systemic reaction, or myocarditis that currently is difficult or impossible to identify prior to the development of the AEFI. This proposed pilot study looks at the metabolic profiles of a specific population of subjects who received the smallpox vaccine with or without other concomitantly administered vaccines to help determine if a unique metabotype can be identified in subjects who reported systemic reactions following immunization. In addition, this proposed study will look at the metabolic profile of several subjects with subclinical or clinically diagnosed myopericarditis to determine if these subjects have a unique metabotype. The ability to identify a unique metabotype would allow a clinician to potentially mitigate serious AEFI and ultimately improve the quality of immunization healthcare. If identified, these profiles might represent novel biomarkers of risk that can supplement existing clinical decision making for risk stratification or vaccine exemptions.

**Sample Description:**

The study population included five subjects with clinically diagnosed myopericarditis (Group 1), 30 subjects with asymptomatic elevation of troponins (Group 2), 31 subjects with systemic symptoms, all following immunization (Group 3), and 34 subjects with no AEFI (Group 4), serving as controls. Two-hundred sera samples – 100 baseline (pre-vaccine) and 100 post-smallpox vaccination were analyzed by untargeted metabolomics using nuclear magnetic resonance (NMR) spectroscopy.

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

Procedures: 1. Adverse Reactions Following Vaccination NMR Procedures.docx

Study Design Tables: 2. Adverse Reactions Following Vaccination NMR Study Design Table.xls

Metadata: 3. Adverse Reactions Following Vaccination NMR METADATA.xlsm

Processed Data: 4. Adverse Reactions Following Vaccination Normalized Binned Data.xlsx

Raw Data: 5. Adverse Reactions Following Vaccination NMR Raw Data.zip

**Notes:**

Full sample preparation and analysis procedures are available in the accompanying document entitled **1. Adverse Reactions Following Vaccination NMR Procedures**.

Descriptions of abbreviations for factors are available in the Variable Dictionary in the accompanying document **2. Adverse Reactions Following Vaccination NMR Study Design Table.xls**.

The phenotypic metadata and normalized data are available in the accompanying documents: **3. Adverse Reactions Following Vaccination NMR METADATA.xlsm** and **4. Adverse Reactions Following Vaccination NMR Normalized Binned Data.xlsx** for normalized binned NMR data. Sample ID and factors can be found in the first 5 columns and other columns in the spreadsheet contain sample metadata and the normalized binned data. If the statistical program does not allow variable names to begin with a number then add a prefix to the column names, for example, bin\_8.98 instead of 8.98.

The Sample ID serves as the unique identifier (Graphical ID) of the individual samples and is used as the NMR folder name in the raw NMR data file **5. Adverse Reactions Following Vaccination NMR Raw Data.zip**.