

In this issue we will present the technology behind Newborn Screening (NBS), focusing on Tandem Mass Spectrometry (MS/MS). MS/MS is credited with popularizing NBS because it made screening efficient and economical. A single sample analysed by MS/MS can detect the presence of ~80 analytes, comprising over 40 disorders (as opposed to doing individual screens for each metabolic disorder).

The following information is summarized from an article "[A Layperson's Guide to Tandem Mass Spectrometry and Newborn Screening](#)" written by Dr. Donald Chace, one of the primary investigators who developed the NBS application of Tandem Mass Spectrometry. Dr. Chace certified Dr. Cariappa (Chief Scientist, NeoGen Labs) in MS/MS technology.

### • What is a Mass Spectrometer?

A Tandem Mass Spectrometer (MS/MS) is one of several types of analytical instruments known as mass spectrometers. They are used to analyze thousands of compounds such as those present in our bodies. Mass spectrometers can be thought of as instruments that weigh molecules. Of course, molecules are extremely small and cannot be weighed in the traditional sense on a scale.

### • What is a "Tandem" Mass Spectrometer?

A Tandem Mass Spectrometer can be thought of as 2 mass spectrometers in series connected by a chamber that can break a molecule into pieces perhaps like a puzzle. This chamber is known as a collision cell. A sample is "sorted" and "weighed" in the first mass spectrometer, then broken into pieces in the collision cell, and a piece or pieces sorted and weighed in the second mass spectrometer.



### • Why do we need to use a MS/MS?

The blood samples screened contain hundreds of compounds in them, but we are interested in measuring only a few dozen compounds that have diagnostic significance. MS/MS methodology ensures that the sensitivity and specificity of the detection is close to 100%.

### • How is MS/MS used in a NBS Laboratory?

The compounds in the blood of infants that we test using tandem mass spectrometry are known as amino acids (AA) and acylcarnitines (AC). Amino acids are the building blocks of proteins providing structural and enzymatic activity. Carnitine is a transportation system for fats in and out of the cell's energy factory, the mitochondria. When a fat is attached to carnitine it is called an acylcarnitine. We often identify

acylcarnitines by the size of the fat molecule attached to it. For example, an important medium sized fat attached to carnitine, measured in the disorder MCAD (Medium Chain Acyl-CoA Dehydrogenase) deficiency, is an eight carbon fatty acid known as octanoyl carnitine (C8). The MS/MS weighs this molecule and the other acylcarnitines and tell us how much is present.

### • Why are the Measurements of AA and AC Important?

In a metabolic disorder, specific enzymes that help facilitate the breakdown of AA or the conversion of fat to energy do not function. If an enzyme is not functioning, the breakdown of a compound to waste products does not occur. In other instances, products are not produced that are important in generating fuel for the cell. Because the compound cannot be metabolized, it will accumulate in the blood and tissues. The compound in excess thus becomes a poison (eventually crossing the blood brain barrier and causing mental retardation).

NeoGen Labs MS/MS methodology, using specialized software, proprietary cut offs (based on a 3.5 million baby database) and expert medical interpretation, can determine if there is too much of the compound in blood, 24 hours after birth onwards. Pre-symptomatic detection of abnormal concentration of metabolites, in the first few weeks of life, allows for the most beneficial treatment outcomes.

### September 2008 Statistics (~800 Samples)

- 1 case of MMA/PA
- 2 case of VLCADD
- 1 case of TSH
- 1 case of G6PD

### Diets

We have been working with SHS and have requested them to stock a small supply of diets at NeoGen Labs to treat MSUD and VLCADD. These are the two IEMs we have been seeing more frequently in the past few months. The intent is to help start treatment immediately while arrangements are being made for a long term supply

### Screening Panels

- **First Step** (Over 50 IEMs for Rs. 3975)
- **First Step MS/MS** (45 IEMs, includes Fatty Acid Oxidation Disorders, Amino Acid Disorders, and Organic Acid Disorder panels for Rs. 3250)
- **First Step Bio** (5 IEMs which include CH, CAH, G6PD, GALT and Cystic Fibrosis for Rs.1500).

As always, we look forward to your feedback. Let us know what you would like us to cover in future issues.

Thomas Mookken

T: +91 99006 55115 E: [mookken@neogenlabs.com](mailto:mookken@neogenlabs.com)

[www.neogenlabs.com](http://www.neogenlabs.com)