A Better Diagnostic for Tuberculosis: GC-MS/MS Bioanalysis for the Determination of the Biomarker D-Arabinose in Urine

Alturas Analytics, Inc. is proud to announce the collaboration with The Global Good Fund to develop a reference method for the detection of tuberculosis (TB). One of the features we often forget in a bioanalytical laboratory is just how important our innovations, methods and data are to the treatment of disease. The evolving technology of measuring specific biomarkers to monitor progression of disease or to evaluate the most effective therapeutic regimes is becoming standard practice for the contract laboratory. A recent example of the importance of bioanalysis is with the inspirational work initiated by Global Good and their vision to invent, develop and deploy viable technology to address life threatening problems impacting life in developing countries.

Tuberculosis (TB) is a global pandemic found in every country in the world and is the leading cause of infectious death worldwide. In 2011, more than eight million new cases and more than one million deaths from TB were reported. (1) Diagnosis of pulmonary TB is challenging and involves clinical assumptions with abnormal chest x-rays and identification of the TB bacteria after staining techniques from the analysis of sputum. Often in developing countries the identification of the TB bacteria is the only diagnostic procedure. This identification process isn’t sensitive or specific and often leads to false positive detection since the staining technique doesn’t distinguish between several types of bacteria. Expensive nucleic acid amplification methods are accurate but unsuitable for resource-constrained countries. GC-MS is a very different technique with significant potential for further development to an accurate, sensitive and specific method for the confirmation of TB in urine samples. Urine facilitates ease of sample collection compared to difficulties of sputum collection and the potential exposure to healthcare workers.

Over the last year Alturas Analytics, Inc. has utilized gas chromatography mass spectrometry (GC-MS) and gas chromatography-tandem mass spectrometry (GC-MS/MS) for the analysis of molecules that are challenging for traditional liquid chromatography and LC-MS. One application is the analysis of the biomarker D-arabinose from urine for confirmation of the diagnosis of TB.

The cell wall of tuberculosis is very unique and consists of a variety of lipids, lipoglycans, polysaccharides, fatty acids and other components. One of the principle components of the cell wall of the mycobacteria is lipoarabinomannan (LAM). Previous research indicates that D-arabinose is a surrogate for LAM and thus can be used as a surrogate to detect an infection of tuberculosis. (2). D-arabinose is a small, polar molecule that is not favorable for ionization with LC-MS and is not easily retained on conventional HPLC columns. Other methods to detect LAM such as immunoassays suffer from poor sensitivity or laborious steps of sample preparation.

The urine samples were extracted and derivatized and the aliquots evaporated to dryness. The extracts were then reconstituted in an organic solvent and injected onto one of our Thermo Scientific’s TSQ Quantum XLS Ultra™ GC-MS/MS systems. To separate the D-arabinose from L-arabinose, we used a chiral GC column. Previous methods required lengthy overnight derivatization steps using chiral reagents to distinguish between the D and L forms of arabinose. The GC-MS/MS method we are developing in our laboratory has a detection limit of 10 ng/mL for D-arabinose.

The method for the GC-MS/MS analysis of D-arabinose will be effective for the confirmation of TB and improves upon previous methods that required multi-step procedures and costly materials and reagents. This method will help treat TB and deliver more cost effective and rapid treatments to communities around the globe.

The Alturas team of scientists brings the depth of experience and knowledge to address your most demanding bioanalytical challenges with the outstanding customer care and attention to detail that our clients have come to expect. Please visit us online at alturasanalytics.com or call 208-883-3400 for more information regarding our services, assays and research initiatives. Whatever your bioanalytical needs, we look forward to providing you with excellence.


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