Table of Contents

Company .......................................................................................................................... 3

Inflammation Background and Services ................................................................. 4

Neuroinflammation ....................................................................................................... 5

Artherosclerosis ........................................................................................................... 5

Post-Surgical Inflammation ....................................................................................... 6

Autoimmune Disorders ............................................................................................... 7

Conclusion ..................................................................................................................... 8
Myriad RBM, Inc. is a CLIA-certified biomarker testing laboratory that solves complex drug development and diagnostic challenges with innovative products and services. With more than a decade of experience developing and validating multiplexed immunoassays, we provide services for the identification and quantification of important biomarkers.

Our Multi-Analyte Profile (MAP) services can quantitatively measure hundreds of proteins from just a single drop of blood serum or plasma. The ability to provide accurate data on this scale, from such small sample volumes, is made possible thanks to our expertise in multiplexed immunoassay design and development combined with the automated improvements implemented to optimize the Luminex technology.

Briefly, samples are electronically logged, manually plated alongside controls, then run on a robotic system that performs all of the volume critical steps including dilutions, standard curves, and combination of reagents, before each sample is read on a Luminex instrument (more detailed information can be found in our QC white paper). The automation and rigorous application of these methods distinguishes our services in terms of precision and efficiency.
Inflammation: Background and Myriad RBM Services

Chronic inflammatory processes are associated with a remarkable range of human diseases including numerous cardiovascular, pulmonary, neurodegenerative, and autoimmune disorders. Advances in our understanding of inflammatory biomarkers and their role in disease offer tremendous clinical value. Myriad RBM’s multi-analyte profiling (MAP) technology provides comprehensive, quantitative and sensitive measurement of dozens of protein biomarkers involved in inflammation pathways, including cytokines, chemokines, and acute-phase reactants. Our biomarker panels have been featured in over 140 publications covering a vast spectrum of research characterizing the immune response, from biomarker discovery and validation, to clinical studies on disease prognosis and therapeutic response.

Chronic Obstructive Pulmonary Disorder (COPD)

Chronic obstructive pulmonary disorder (COPD) is characterized by progressive and irreversible airway obstruction resulting from tissue damage related to a chronic abnormal inflammatory response in the lungs. COPD is currently the fourth leading cause of death worldwide\(^1\) and thus there is great interest in the identification and validation of novel biomarkers for use in both diagnostic tests and development of new therapeutics. Our MAP services have been a central component of multiple studies investigating the levels of circulating inflammatory markers in COPD patients\(^2^4\). In a recent example, Cockayne et al. used our biomarker panels to simultaneously assess the concentration of 126 proteins in serum samples from 140 COPD patients with varying levels of disease severity\(^2\). The authors identified 7 biomarkers that showed significant differences across the COPD patient groups. Figure 1 shows the increase in levels of EN-RAGE and sRAGE with respect to COPD severity. These findings reinforce the central role of systemic inflammation pathways in COPD and identify the RAGE pathway as a potential therapeutic target.

**Figure 1:** Increased serum EN-RAGE and decreased serum sRAGE are associated with COPD disease severity. Log2 transformed levels of EN-RAGE (A) and sRAGE (B) are plotted for each subject for non-smoking controls (NS), smoking controls (S), GOLD I and II (mild/moderate COPD) and GOLD III and IV (severe/very severe COPD) groups.

Cockayne et al. 2012
Neuroinflammation

Inflammation in the central nervous system (CNS) is marked by microglial activation, the subsequent release of pro-inflammatory mediators, blood-brain barrier permeability, and eventually leukocyte invasion. In a chronic state, this neuroinflammatory response leads to neuronal damage and is thought to be prominently involved in multiple neurodegenerative disease processes, including Alzheimer’s (AD), Parkinson’s, and Huntington’s diseases. Our multiplexed immunoassay panels have been successfully incorporated into multiple studies that highlight the link between inflammation and neurodegenerative disease \(^5,6\). For example, a longitudinal study by the Texas Alzheimer’s Research and Care Consortium used our HumanMAP® panel to simultaneously assess the levels of 34 inflammatory biomarkers in 197 patients with AD and 203 control subjects \(^5\). Using principal component analysis, the authors found a highly significant association between elevated levels of inflammation and the earlier onset of disease (Figure 2), suggesting the presence of a pro-inflammatory endophenotype associated with Alzheimer’s disease. Future research elucidating the different roles of these inflammatory mediators in AD pathology may uncover a host of novel potential therapeutic targets.

Atherosclerosis

Atherosclerotic cardiovascular disease is the leading cause of death in the United States. Previously thought to be a lipid storage disease, extensive research has now characterized atherosclerosis as a chronic inflammatory disorder, with inflammatory processes playing a critical role throughout all phases of disease progression. Considerable interest has since been focused on pathways of inflammation in the search for potential cardiovascular disease biomarkers. A pair of studies demonstrates the utility of our multiplexed immunoassay panels in the identification of inflammatory biomarkers that may have diagnostic or predictive clinical value \(^7,8\).

In the first of these studies, Tantry et al. used our services to assess inflammation markers in plasma samples from 171 patients with various stages of coronary artery disease (CAD) \(^7\). The authors found a statistically significant increase in a number of specific inflammation markers in patients with progressive CAD as compared to patients with asymptomatic stable CAD, including C-reactive protein (CRP), RANTES, interleukin-1α, -4, -7, -10, soluble vascular cell adhesion molecule (sVCAM) and macrophage inflammatory protein1-α (MIP-1α) (Figure 3). As these markers were specifically elevated in patients with more advanced CAD, the findings may help identify those at high risk for disease progression or a potentially life-threatening ischemic event.
**Figure 3:** Biomarker profile in the different stages of coronary artery disease. RANTES, IL-8, CRP and MIP-1α are increased in patients with progressive CAD. Biomarker levels expressed as mean ± SEM. Tantry et al. 2010

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**Autoimmune Disorders**

Autoimmune disorders affect 50 million Americans, and represents an important and growing area of research on inflammatory biomarkers\(^\text{10}\). While a number of pro-inflammatory biomarkers associated with autoimmune disorders have been identified, there is a strong need for new clinical response markers to guide clinicians in tailoring treatments to individual patients. A number of studies have used the HumanMAP panel to identify a distinct biomarker profile of drug responders in a clinical trial\(^\text{11-13}\). In one recent study, the authors assessed changes in 107 biomarkers in rheumatoid arthritis patients undergoing treatment with golimumab (Simponi\(^\text{®}\)), a human monoclonal antibody to tumor necrosis factor (TNF-α). The authors found multiple markers that were significantly altered after 4 weeks of drug treatment, including more than a dozen inflammatory markers (**Figure 4**).
Importantly, a subset of these proteins showed promise as biomarkers for predicting clinical response to golimumab. These markers showed a greater decrease from baseline to week 4 of the study in patients who were drug responders at week 14 as compared to non-responders. Additionally, changes from baseline to week 4 in some of the same biomarkers showed strong associations with multiple clinical measures. This study underscores the tremendous value of biomarkers that can predict early-stage drug responses, allowing clinicians to more efficiently adjust treatments to individual patients.
**Conclusion**

Together these studies highlight the unique advantages of using Myriad RBM’s powerful multiplexed immunoassays to simultaneously detect and quantify a large number of analytes within a single study. The identification and characterization of inflammatory biomarkers and their role in disease processes will continue to make major contributions to our understanding and treatment of these disorders. Myriad RBM strives to be a leading provider of assays for biomarkers of inflammation.


