## Accelerated Cure project for multiple sclerosis

Accelerating research towards a cure for multiple sclerosis

The Continued Pursuit of Biomarkers in MS
By Farren Briggs PhD, ScM

Over the last several decades researchers have greatly increased their efforts to identify biomarkers for multiple sclerosis (MS). Unfortunately, only a few of these studies have been successfully translated into clinical tools – but with the rapid acceleration of new methods to detect proteins, gene transcripts, and other molecules, it is likely there will be great advances soon. In general, a biomarker must have a few key traits: it must **1)** be reliably measurable, **2)** be able to detect those with the trait of interest (must be sensitive), and **3)** not falsely determine those without the trait of interest as having it (must be specific; therefore low false positives).

Figure 1
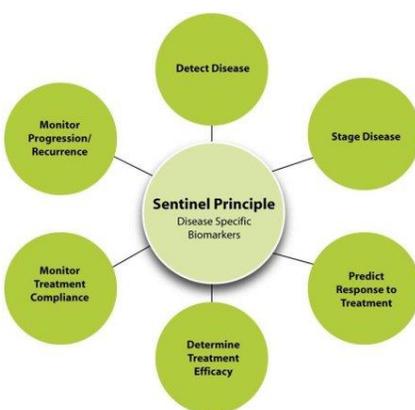
Biomarkers can play a critical role in several aspects of clinical research and hopefully, in clinical care (*Figure 1*). Of particular relevance to MS would be the ability to detect the disease (improving diagnosis), determining stage of disease (disease transition), predicting response to disease modifying therapies, and overall enhanced individual and group risk assessments. This month there were several studies reporting on research of biomarkers for various aspects of MS, but I will focus on only one study, which presented impressive findings.

This biomarker study, by Barbour *et al*, and published in the Annals of Neurology[1], had 3 research questions: **Q1)** Can we differentiate MS from non-MS? **Q2)** Can we differentiate relapsing remitting from secondary progressive MS? And **Q3)** Can we differentiate primary progressive from secondary progressive MS? The researchers sought to tackle these questions using measures on 1,128 proteins detectable in cerebrospinal fluid (CSF) from 310 individuals, who were split into a discovery and replication group. Using a suite of statistical tools, the researchers were able to near perfectly classify MS from non-MS samples using measures for 22 proteins, with an accuracy of **98%**! The non-MS samples came from healthy individuals, individuals with non-inflammatory neurological disorders, and individuals with other inflammatory neurological disorders. The 22 signals were predominantly immune-cell specific biomarkers – which is not surprising, but the specific combinations highlight new immune system relationships that are truly intriguing. Also important to note is that the biomarker set not only distinguished MS from healthy donors, but also from other neurological disorders.

The researchers were also able to do a very good job distinguishing relapsing remitting from secondary progressive MS (accuracy of **88%**). The proteins that most distinguished these stages of MS were markers predominantly released by cells in the central nervous system, especially neurons and oligodendrocytes. This reinforces the notion of the contribution of repair mechanisms and neurodegeneration (versus inflammation alone) in contributing to the change in disease course.

And last but definitely not least, primary progressive and secondary progressive MS were indistinguishable – the proteins did no better at classifying individuals in these groups than flipping a coin would have. These results are so fascinating. This, to me at least, suggests the underlying biological processes contributing to both stages of MS are not that different!

Overall, this project has highlighted multiple biological processes contributing to **<u>both</u>** MS onset and MS progression – and that CSF, though not easily accessible, holds great promise for MS biomarker development. What would be interesting is to see if others can now develop an equivalent biomarker panel for blood (which is easily accessible) using this knowledge.

1. https://www.ncbi.nlm.nih.gov/pubmed/29059494