Accelerated Cure Project for MS

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Accelerating research towards a cure for multiple sclerosis

New technology for MS diagnostics

IQuity is a start-up company, and ACP Repository partner, that is developing diagnostic methods for several diseases, including autoimmune disease. They recently launched a novel, blood-based diagnostic test for multiple sclerosis (MS), which could have a significant impact on the efficiency of diagnosis of the disease, allowing patients to be diagnosed and treated before significant tissue damage occurs. The Accelerated Cure Project's Repository samples have played an important role in the development of this technology, which can reduce the time for diagnosis to 7 days, a significant improvement over current diagnostic methods. Existing diagnostic methods consist of evaluation of clinical symptoms, analysis of cerebrospinal fluid and magnetic resonance imaging of the brain and spinal cord.

This new diagnostic test is based on a novel technology that allows the analysis of the activity of a patient's genes in a single drop of blood and gives a 90 percent accuracy rate in identifying disease. This "gene activity signal" can identify the presence or absence of disease at the cellular level. The technology was initially discovered and developed at Vanderbilt University by Dr. Tom Aune and his research team. IQuity, based in Nashville, Tennessee, has licensed the Vanderbilt technology and developed it further resulting in a tractable blood test called IsolateMS™. This work has been funded by $2 million in seed money from the National Institutes of Health.

IQuity's new diagnostic test detects levels of specific molecules, called ribonucleic acids (RNA), in human cells. Proteins form the "building blocks" for human tissues and also regulate cell and tissue function in health and disease. Proteins are encoded by our genes. When individual genes are "read", the DNA code is transcribed ("expressed") into RNA. Some of these RNAs, called messenger RNAs (mRNAs), are "translated" into proteins including structural, enzyme and regulatory proteins. Other RNAs (regulatory RNAs) function as molecules that control the expression of genes. Both classes of RNA have been shown to exhibit distinct variations in expression that are characteristic of health and disease. MS has its own unique expression pattern that correlates with disease stage.

The IQuity diagnostic test is designed to provide a profile of RNA expression in MS which as Chase Spurlock, IQuity's CEO, has described, "…paints a molecular portrait of what's going on in an individual's cells at a given point in time, which can provide a picture of the presence of a disease." Dr. Spurlock explained further, "For diseases like multiple sclerosis, RNA signatures are detectable at the earliest stages of the disease before extensive tissue damage is observed using more traditional diagnostic methods. Through machine learning, we were able to create computer algorithms that are capable of analyzing the RNA markers in a patient's blood sample, enabling providers to more accurately and quickly determine whether a patient does or does not have the disease." To learn more about iQuity's unique diagnostic tool for providers in the autoimmune field, visit https://www.news-medical.net/news/20170320/Linking-RNA-to-autoimmune-diseases.aspx

It is interesting to consider what role these diagnostic RNAs might play in the MS disease process. As mentioned earlier, many of the RNAs identified through Dr. Aune's work are messenger RNAs, which encode regulatory and other proteins that are known to perform specific functions in the inflammatory cascade and the immune response. A publication from this work showed that the RNA profiles were "highly dynamic as a subject progresses from *clinically isolated syndrome, through clinically definite MS to MS disease of some duration."[1]

More recent work from the Vanderbilt group, using additional ACP Repository samples, has identified regulatory RNA disease markers that are now being phased into IQuity's diagnostic tests. These molecules control the expression of genes, and show distinct and consistent changes in MS disease[2].

These regulatory RNAs are particularly interesting when considered in the context of what are called "MS susceptibility loci." These are variant sites within the human genome that have been previously identified in a specific type of genetic study called genome wide association (GWAS). Over 200 genetic markers have been identified in DNA samples isolated from over 47,000 patients (including ACP's Repository donors) that are "associated" with disease. Some of these GWAS-identified loci encode proteins that are involved in the immune and inflammatory responses. Interestingly, the majority of these loci do not fall within protein coding genes. One possible explanation for this is that these non-coding MS variant loci may encode RNAs that regulate, directly or indirectly, the expression of genes that encode the protein molecules that constitute the immune and inflammatory responses.

Consistent with the ACP policy of requiring that data be returned, some of the Vanderbilt data has been received by us, with more to come. This returned data is available on an "open source" basis to all investigators and has already been provided to several scientists who are performing further analyses on the data. These data are also being used by investigators to "dig deeper" into the patient samples that were used by Dr. Aune and his team. This additional research will provide an even greater understanding of patient gene activity during the MS disease process.

Every year 15,000 new MS and 45,000 clinically isolated syndrome diagnoses occur in the U.S. The ACP team is proud to have played a part in the groundbreaking discoveries of Dr. Aune and his team at Vanderbilt that enabled the launch of an exciting, new MS diagnostic blood test.

*Clinically isolated syndrome (CIS). A first episode of neurologic symptoms that lasts at least 24 hours and is caused by inflammation and/or demyelination.

1. Tossberg et al. Journal of Clinical Informatics 2013, 3:18
2. Aune et al. Journal of Autoimmunity 2017, 81:99