MJFF PARTNERING PROGRAM

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

Durin Technologies, Inc.
Robert G. Nagele, PhD (Lead PI)

Organization and Team Overview

Durin Technologies was established as a N.J. C-Corporation in March of 2010, originally with the goal of designing and developing minimally-invasive blood-based diagnostics for the early detection and staging of Alzheimer's and Parkinson's diseases (PD). The technology is based upon the work of Professor Robert Nagele at the University of Medicine and Dentistry of New Jersey and has been exclusively licensed by the company. The team includes Dr. Nagele as Founder and Chief Scientific Officer, Benjamin Belinka, PhD, as CEO, and a technical staff.

Opportunity Overview

The concept – using autoantibodies as diagnostic biomarkers for early detection of disease

Durin's diagnostics are based upon the recent discovery by Dr. Nagele that all humans, regardless of the presence or absence of disease, have thousands of autoantibodies in their blood, many of which appear to be involved in the clearance of body debris generated by normal day-to-day wear and tear. When a disease arises, additional debris is generated which is specific to the organ/tissue/cells affected by the disease. As a result, blood levels of those autoantibodies tasked with clearing this debris are dramatically and selectively increased. The increased production of disease-specific autoantibodies changes one's autoantibody profile in a predictable way, and we have shown that these changes are common among individuals with the disease and readily detectable using human protein microarray technology. Importantly, the method is directly linked to the pathology and is sensitive enough to detect the disease at the very earliest stages, in many cases even before clinically detectable symptoms appear. Early detection allows early treatment during the window of time when such treatments can be most effective. It also allows early enrollment into clinical trials and monitoring of patient progression during these trials as well as while being cared for by their physicians. Lastly, and importantly, it will provide a good measure of therapeutic efficacy, as beneficial effects that reduce disease pathology should also reduce production of disease-specific debris and result in a measureable reduction in the corresponding disease-specific autoantibodies that are being used as diagnostic indicators.

A multi-disease diagnostic with unprecedented accuracy that requires only a single drop of blood

We have completed and published two proof of principle studies (see citations below) showing that panels of as few as 10 identified autoantibody biomarkers can be used to diagnose Alzheimer's disease and PD with greater than 95% accuracy using a single drop of blood. Importantly, since nearly all diseases generate disease-specific debris and, thus, result in the production of disease-specific autoantibodies, we believe that we have developed a multi-disease diagnostic strategy. Also, since we have found that only 10-20 autoantibody biomarkers are required to detect the presence of a specific disease and a single protein microarray can house as many as 25,000 protein targets, our long-term goal is to develop a single protein microarray that can simultaneously screen for many diseases in one blood test that uses a single drop of blood. If realized, this could potentially revolutionize the way disease diagnostics are done.

1. Nagele E, Han M, Demarshall C, Belinka B, Nagele R. (2011) Diagnosis of Alzheimer's disease based on disease-specific autoantibody profiles in human sera. PLoS One. 6(8):e23112.
2. Han M, Nagele E, Demarshall C, Acharya N, Nagele R. (2012) Diagnosis of Parkinson's disease based on disease-specific autoantibody profiles in human sera. PLoS One. 7(2):e32383.
3. Acharya NK, EP Nagele, M Han, NJ Coretti, C DeMarshall, MC Kosciuk and RG Nagele. (2012) Neuronal PAD4 expression and protein citrullination: possible role in production of autoantibodies associated with neurodegenerative disease. J. Autoimmunity 38(4):369-80; on line at http://dx.doi.org/10.1016/j.jaut.2012.03.004.
4. Nagele EP, Han M, Acharya NK, DeMarshall C, Kosciuk MC and Nagele RG (2012) Natural IgG autoantibodies are ubiquitous in human sera, and their number is influenced by age, gender, and disease. Submitted for publication.

For additional information, please contact: ResearchPartnerships@michaeljfox.org

Details of MJFF Grant

The goal of our study funded by the Michael J Fox Foundation (MJFF) was to determine if our diagnostic strategy of utilizing autoantibodies as diagnostic biomarkers for full-blown PD as described in Han et al. (2012) (see above citation) could also be used for early detection of PD. To test this, we analyzed sera obtained from MJFF's DATATOP collection which came from well-characterized patients at a very early stage of PD who had not yet received any treatments for their condition. The DATATOP collection has 2,000 aliquots of serum from approximately 500 subjects. Each serum sample was analyzed with human protein microarrays containing nearly 10,000 potential human protein targets and a panel of autoantibodies that can be used as diagnostic biomarkers for early stage PD was identified and tested.

Results and Potential Next Steps

This study has just been completed. Results and conclusions are as follows:

1. We are excited to report that we have successfully identified autoantibodies that can be used to detect and diagnose early-stage PD with greater than 90% overall accuracy.

2. We also discovered that printing lot-specific differences among protein microarrays contribute to a reduction of potential sensitivity and specificity. Using human serum autoantibody patterns generated from protein microarrays pooled from three different microarray printing lots, we detected early-stage PD with sensitivity of 91.5% and specificity of 90.0% (82 early PD, 50 controls). By contrast, data from consecutively printed microarray sister lots showed a sensitivity of 96.4% and specificity of 85.7% (64 early PD, 42 controls). Thus, we believe that achieved values for sensitivity and specificity for early detection of PD will improve even further when samples are run within a single microarray lot. An easy alternative is to minimize lot-specific differences by increasing the volumes of printed proteins.

3. The ability to recognize and distinguish early- vs. later-stage PD by this method opens the door to more precisely "staging" PD, which is a major goal of the MJFF since it will greatly facilitate clinical trials on potential therapeutics as a measure of drug efficacy.

Current work, plans and requirements

At this time, the company has nearly completed a parallel study aimed at early detection of Alzheimer's disease at the mild cognitive impairment (MCI) stage. The next step for PD diagnostics is to carry out a larger study which both validates early detection of PD and also seeks to identify panels of autoantibody biomarkers that can clinically stage the disease. The latter is important for monitoring PD patient progression while under treatment, both in clinical trials and in their doctor's offices. In addition, as mentioned briefly above, we also anticipate that beneficial effects of treatment or efficacy will be detectable using our strategy, stemming from the fact that the drug-mediated reduction of PD pathology and the debris generated by it should be accompanied by reduced levels of the identified autoantibody biomarkers that are detectable using our system.

Durin Technologies is currently seeking partners to help to further refine and validate the efficacy of its diagnostic kit design and to obtain the additional data needed for submission to and subsequent marketing approval from the U.S. Food and Drug Administration. Upon successful completion of our planned studies, regulatory filing is expected to occur 18-24 month after new financing is arranged. Our plan is to follow the same path for each subsequent disease diagnostic that is rolled out. A relatively simple diagnostic test requiring only a single drop of blood can be incorporated into annual physician examinations and will provide for early-stage treatment of this neurodegenerative condition at a stage when pharmaceutical intervention can provide the greatest degree of benefit. The per unit cost for each diagnostic kit can be as low as a few dollars and mass production can be easily accomplished.

Intellectual Property Status

Patents for this technology have been filed with the University of Medicine and Dentistry of New Jersey, and this technology has been licensed exclusively by Durin.