Dx Firm Plaxgen Moving Plaque-based Alzheimer's, Atherosclerosis Tests toward Commercialization

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NEW YORK (GenomeWeb) – Having spent the last seven years prepping its technology, proteomic diagnostics firm Plaxgen is now moving tests for Alzheimer's disease and atherosclerosis towards commercialization.

First in line is the company's Alzheimer's diagnostic, named Amyload, for which it is currently planning a validation study expected to begin in June 2015 and run through approximately January 2016, Plaxgen Founder and CEO Shanmugavel Madasamy told GenomeWeb.

The company plans to offer the test initially out of its Fremont, Calif.-based CLIA facility while simultaneously filing for US Food and Drug Administration 510(k) clearance, he said, noting that it plans to target the test to pharma firms that would use it for selecting patients for clinical trials and measuring response to treatment.

Plaxgen's cardiovascular pipeline consists of two tests, its Atheroload test for aiding preclinical diagnosis of atherosclerosis and related diseases, and its StatRes test, which is intended to aid physicians in selecting the appropriate statins for their patients.

Launched by Madasamy in 2007, Plaxgen has raised roughly $4 million from private investors to date and currently has seven employees. The company's technology is based on a combination of capture of target biomarkers using plaque arrays followed by isolation and analysis of those markers by flow cytometry and MALDI mass spec.

The firm presented a demonstration of this technology in a paper published last month in *Clinica Chimica Acta*, in which researchers including Madasamy used the platform to identify serum proteins involved in the process of plaque particle formation linked to Alzheimer's.

The plaque array process works essentially as an enrichment step, allowing researchers to search only plaque-related serum proteins as opposed to the full serum proteome, Madasamy said.

The platform starts with an array consisting of soluble plaque-forming constituents. These constituents are incubated with serum from test subjects, which leads to the formation of insoluble plaque particles as the plaque-forming constituents work as substrates for the plaque-related serum components.

The array's plaque-forming constituents are chosen to allow for isolation of the plaque particles of interest to the disease under investigation. For instance, in the case of the Alzheimer's test, the array is designed to capture plaque particles including amyloid-β 42, tau, cholesterol, and α-synuclein.

These particles are then passed on to a flow cytometer where they are separated and quantified by plaque type. They are then analyzed using MALDI mass spec to identify their protein constituents with the aim of detecting proteins involved in plaque formation that could prove useful as disease biomarkers.

In the *Clinica Chimica Acta* paper, the researchers found via their flow cytometry analysis that roughly 35 percent of AD serum samples produced significantly higher levels of cholesterol particle formation than age-matched controls. They likewise found a correlation of 87 percent between brain imaging data and Aβ42 particle formation in mild cognitive impairment, severe Alzheimer's patients, and age-matched controls.

The study also found, however, that 15 percent of the control serum samples also demonstrated Aβ42 particle formation when run on the plaque array. This, the authors noted, could suggest that these controls in fact were in the early stages of disease formation. However, no signs of disease, early or otherwise, were picked up via imaging of these subjects.

In the mass spec portion of their analysis the researchers identified 195 serum proteins linked to plaque formation, roughly 76 percent of which, they wrote, had been previously linked to Alzheimer's pathology.

Plaxgen's Amyload, Atheroload, and StatRes tests are based on the flow cytometry portion of the workflow, which, Madasamy said, the company expects will allow clinicians to detect abnormal plaque formation patterns indicative of disease earlier than existing tests.

Atheroload is intended for the detection of abnormal low- and high-density lipoprotein cholesterol particle formation. Amyload is based on the early detection and quantitation of Aβ42 and tau particles in the blood that signal the formation in the brain of the amyloid plaques thought to be responsible for Alzheimer's disease.

For Alzheimer's in particular, drug researchers and clinicians are interested in blood-based tests offering early detection as it would allow them to better select patient cohorts for drug studies and more easily monitor patient response to agents under development.

Much Alzheimer's protein biomarker research has revolved around cerebrospinal fluid levels of the Aβ42 and tau, but the disadvantage of CSF-based measurements is that they require patients to undergo a lumbar puncture. In many countries, patients tend to be reluctant to undergo this procedure, which has proven an obstacle to recruiting patients for clinical trials.

As a result, a number of companies and academic teams are pursuing blood-based protein biomarkers for Alzheimer's. For instance, last year a team of researchers from King's College London and proteomics firm Proteome Sciences identified a panel of 10 protein biomarkers that could help predict patients likely to progress from mild cognitive impairment to Alzheimer's disease.

In 2013 molecular neuropsychiatry firm Genomind signed an exclusive licensing agreement with Emory University to commercialize blood-based protein markers for the disease. Those markers

stemmed from a 2012 analysis of potential plasma protein in three separate patient cohorts done by a consortium of researchers under the Alzheimer's Disease Neuroimaging Initiative.

Plaxgen intends to apply the mass spec portion of its workflow — in combination with the flow cytometry data — to the development of additional protein biomarkers and support of drug development research, Madasamy said.

Meanwhile, company researchers are currently evaluating an Alzheimer's diagnostic based on a subset of the 195 serum proteins identified in the *Clinica Chimica Acta* study.

"It is possible that these serum proteins in the affected AD patients might directly or indirectly contribute to accelerated plaque particle formation," they wrote.