Plaque Array method links blood plaque components to Alzheimer's

Study on Plaxgen Alzheimer's disease blood diagnostic published in peer-reviewed journal

BY LLOYD DUNLAP

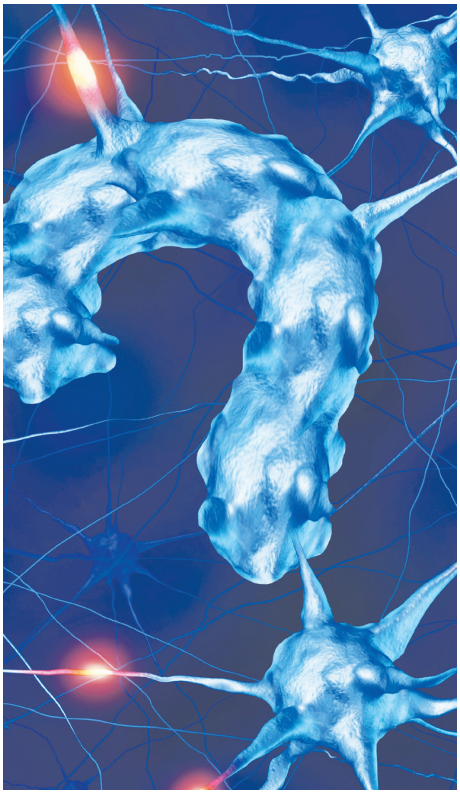
SUNNYVALE, Calif.—Plaxgen Inc., a developer of flow cytometry-based blood diagnostics for plaque-associated illnesses such as atherosclerosis and Alzheimer's disease, announced that a paper validating its Plaque Array technology for the diagnosis of Alzheimer's disease was published in the peer-reviewed journal *Clinica Chimica Acta*.

In a study titled "Plaque Array Method and Proteomics-based Identification of Biomarkers from Alzheimer's Disease Serum," researchers concluded that the Plaque Array methodology developed by Plaxgen works well for detecting amyloid beta (Abeta) and other particle formation in the blood serum of subjects clinically determined to have Alzheimer's disease (AD).

As stated in the paper's abstract, progressive accumulation of amyloid plaques in the regions of brain, carotid and cerebral arteries is the leading cause of Alzheimer's disease and related dementia in affected patients. The early identification of individuals with AD remains a challenging task reliant on symptomatic events, and thus the development of a biomarker-based approach will significantly aid in the diagnosis of AD.

The Plaque Array technique is a flow cytometry and proteomics-based method for identification of biomarkers using Alzheimer's disease serum to identify the makeup of the plaques. The technique was also effective in identifying the various components of those particles: Abeta 42, tau, cholesterol and synuclein. This could be beneficial in the development of therapeutics targeted to these specific AD pathologies. Among other findings, proteomic analysis of plaque particles showed 195 proteins bound to different plaque particles. Abeta-42 particles were shown to contain more specific serum proteins compared to cholesterol, tau and α-synuclein particles.

Thirty-five percent of AD serum samples produced a significantly higher number of total cholesterol particles compared to control, supporting the hypothesis that impaired cholesterol metabolism may play a role in vascular dementia in AD patients. There was also an 87-percent correlation between brain imaging data and Abeta-42 particle formation in the serum of subjects with mild cognitive impairment and severe AD.



Plaxgen's Plaque Array technology may help answer the question of who has Alzheimer's disease at a much earlier stage.

These results support the notion that the blood serum of patients with AD contains factors that catalyze the formation of particles that may be implicated in disease. The ability to identify these factors could be beneficial in both diagnosis and in matching therapy to disease profile. In the study, researchers also applied mass spectrometry to identify protein markers that may play a part in AD development. Approximately 76 percent of the proteins thereby identified have been previously identified with AD. Additionally, it is possible that abnormal expression or post-translational modification of these serum proteins in the affected AD subjects may contribute to accelerated plaque particle formation that could be part of the disease. The study showed this approach detected a network of proteins overlapped in abeta, tau, cholesterol and synuclein particles.

In conclusion, the Plaxgen researchers opined that "We have developed an *in-vitro* method for plaque particle detection and identified serum protein markers that are associated with AD-related plaque particle formation. With further clinical validation, this assay may provide a novel, non-invasive means for the early detection of AD."

AD is increasingly being recognized as a neurovascular disease. Major components of amyloid plaques, such as abeta and tau, are identified in both the brain and blood of AD patients. Once in the blood, they become entangled with serum components and progressively accumulate in the cerebral regions, thus contributing to AD pathogenesis.

"We are pleased that our pilot study showed the promise of this proprietary technology that uses flow cytometry, a technique more commonly utilized for cell analysis, to both detect plaques in the blood of Alzheimer's patients and to identify the components of those plaques, which will aid in diagnostic, patient stratification and drug development," said Dr. Shanmugavel Madasamy, lead study author and Plaxgen's CEO. "As reported in the study, the technique identified a meaningful number of both known and potential biomarkers for Alzheimer's in blood serum. We are evaluating the effectiveness of a subset of these markers to diagnose Alzheimer's disease precisely, and will report further data shortly."

Privately held Plaxgen is developing diagnostics in atherosclerosis, Alzheimer's disease and other plaque-related diseases, using its proprietary Plaque Array technology. Plaque Array combines flow cytometry to detect and quantify plaque particles, with mass spectrometry to identify their components, including proteins and biomarkers that could help drug developers better target treatments in multiple indications in which plaque formation plays a role. Plaxgen's Amyload test can discriminate between pathologies in AD patients by identifying the different particle types that play a role in Alzheimer's, which is important for drug development and treatment matching.

Plaxgen is a CLIA-certified medical diagnostic lab currently focused on commercializing the Atheroload test for atherosclerosis diagnosis, the StatRes Test using serum to predict a patient's response to selected statins in advance of the first prescription and the Amyload Test for Alzheimer's disease. Plaxgen holds issued and pending patents on Plaque Array technology. ■

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