



Neurology focus

The challenges

The inaccessibility of the brain and the relative scarcity of definitive physical parameters for clinical evaluation represent major challenges when it comes to neurological conditions such as neurodegenerative diseases and chronic pain. A better understanding of the biology and the underlying pathophysiology is also required. It is important to search for better fluid-based biomarkers that give physicians effective decision making tools. There is a need for easily accessible biomarkers that can diagnose and stratify patients as well as signal when patients respond to treatment (1). Neurodegenerative diseases in particular, are also expected to increase in prevalence as people live longer than ever before.

Protein biomarkers

Although advances in brain imaging offer improved diagnostics, fluid-based biomarkers could reflect the broad range of biological activities. There is an urgent need to identify proteins that will assist in patient diagnosis that correlate with the biological response to different diseases, which can be easily measured in a non-invasive manner from samples such as peripheral blood. In the neurology field, it can also be important to examine other specialized sample matrices such as cerebrospinal fluid (CSF), brain tissue lysates or microdialysis samples. Here we will briefly review how Olink's multiplexed protein biomarker panels can address some of these issues.

Olink® technology

The proximity extension assay (PEA) successfully merges a dual-recognition immunoassay that employs pairs of matched antibodies linked to unique DNA oligonucleotides for readout by quantitative real-time PCR (qPCR), this results in a multiplexable and highly specific method where only 1 μ L of sample is needed to quantify up to 92 protein biomarkers simultaneously (2). Multiple 92-plex panels are available, covering a range of disease areas and biological processes. The figure shows the four different steps of the PEA technology.

(A) Immunoassay (B) Extension (C) Preamplification (D) Detection



Olink offers a broad range of protein biomarker discovery and validation tools, as fee-for-service or kits to run in your own lab. Olink NEUROLOGY, for example, is designed specifically for research in the neurology area, but can be complimented with other highly relevant panels such as those focused on inflammation or oncology. Olink MOUSE EXPLORATORY is also available, extending the technology for pre-clinical studies.

Example studies

Lumbar radicular pain

Studies suggest that disc herniation may be associated with an upregulation of several inflammatory molecules. One study demonstrated an inflammatory fingerprint in the serum of patients with persistent lumbar radicular pain after disc herniation (3). This fingerprint, determined using Olink technology, clearly stratified patients who did or did not develop chronic pain following surgery. This evidence enables an objective, measurable approach to a condition that is otherwise largely dependent on subjective input from patients, and giving their condition more clinical dignity. This approach could be important for future protein serum profiling of chronic pain patients with regard to prognosis and choice of treatment.

Postpartum depression

The adaptive change in the immune system function during a pregnancy sometimes causes increased levels of inflammation biomarkers in late pregnancy. According to a case-control study these biomarkers might be associated with postpartum depression. The Olink analysis enabled the screening of a wide range of inflammatory biomarkers where several that differed between groups represented novel findings (4).

Traumatic brain injury

When it comes to traumatic brain injury (TBI), it is important with an early diagnosis. One study used Olink to find biomarkers connected to different stages of TBI. The correct diagnosis of TBI, which can be a challenging diagnosis to make, would allow clinicians to implement strategies to reduce secondary brain injury at an early stage. Here, the protein CST5 was shown to be an ideal ultra-early biomarker with the

ability to not only determine the presence of the condition but also discriminate between TBI severities (5).

Alzheimer's disease

In another study, Olink was used to compare low abundance proteins in CSF of Alzheimer's disease (AD) patients and healthy controls. Initial comparisons between AD and controls indicated that many proteins were decreased in AD. Several novel candidate biomarkers emerged that differ between AD and controls, for example CD200 and WIF-1. Analysis of longitudinal CSF samples showed a decrease in the concentration of many proteins over 12 months (6).

Read more

PEA technology:

www.olink.com/technology

Protein panels and complete biomarker list:

www.olink.com/products

Publications:

www.olink.com/publications

FAQ:

www.olink.com/faq

Olink for neurology research

- Only 1 µL is needed to measure 92 proteins simultaneously
- A range of compatible sample types such as plasma, serum, CSF, brain tissue lysates and micro-dialysis fluid
- Around 1000 validated protein assays available in disease and biological process focused panels
- Includes validated and exploratory biomarkers for neurology research

References

1. [Blennow, K and Zetterberg, H. Searching for sentinels: The need for more informative fluid-based biomarkers in neurodegenerative disease, in *Advancing precision medicine: Current and future proteogenomic strategies for biomarker discovery and development*, p. 26-27. *Science/AAAS* \(2017\).](#)
2. [E. Assarsson et al., Homogenous 96-plex PEA immunoassay exhibiting high sensitivity, specificity, and excellent scalability. *PLOS ONE* 9, e95192 \(2014\).](#)
3. [A. Moen et al., Inflammatory serum protein profiling of patients with lumbar radicular pain one year after disc herniation. *International journal of inflammation*. 2016:3874964 \(2016\).](#)
4. [E. Bränn et al., Inflammatory markers in late pregnancy in association with postpartum depression—A nested case-control study. *Psychoneuroendocrinology* 79 \(2017\).](#)
5. [L. J. Hill et al., Cystatin D \(CST5\): An ultra-early inflammatory biomarker of traumatic brain injury. *Nature, Scientific Reports* 7:5002 \(2017\).](#)
6. [Unlocking the elusive mind: The role of protein biomarkers in understanding neurodegenerative disease. Speakers: Professors Douglas Galasko, Henrik Zetterberg and Kaj Blennow. *Science webinar* \(2017\).](#)

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