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Enabling Unprecedented Analysis of Precious Samples in Neurology

Precious samples, such as cerebrospinal fluid (CSF) and mouse brain lysates, offer valuable insights and hold great potential as sources of informative biomarkers. However, their availability is limited by the invasiveness of collection procedures, the potentially challenging workflows, and/or the small volumes that can be extracted. These limitations are even more pronounced in pediatric populations. Consequently, the potential for discovering novel and clinically relevant biomarkers is significantly constrained. The Proximity Extension Assay (PEA) technology is the ideal platform for analyzing biomarkers in these precious samples. Distinguished by its ability to perform highly multiplexed protein measurements from just 1 µL of sample, PEA technology delivers unparalleled specificity and outstanding sensitivity. Herein, we highlight publications showcasing the use of PEA with a qPCR readout across various sample types obtained through invasive procedures, challenging workflows and/or in limited quantities.

Extracellular vesicles

→ Gaceb A, Roupé L, Enström A, et al. **Pericyte Microvesicles as Plasma Biomarkers Reflecting Brain Microvascular Signaling in Patients With Acute Ischemic Stroke. (2024) Stroke,** DOI: 10.1161/STROKEAHA.123.045720

→ Byappanahalli AM, Noren Hooten N, et al. **Mitochondrial DNA and inflammatory proteins are higher in extracellular vesicles from frail individuals. (2023) Immunity and Ageing,** DOI: 10.1186/s12979-023-00330-2

Chronic subdural hematomas

→ Wettervik T, Sundblom J, Ronne-Engström E, et al. **Inflammatory biomarkers differentiate the stage of maturation in chronic subdural hematomas. (2023) Journal of Neuroimmunology,** DOI: 10.1016/j.jneuroim.2023.578127

→ Abrahamsson A, Rzepecka A, Dabrosin C. **Equal Pro-inflammatory Profiles of CCLs, CXCLs, and Matrix Metalloproteinases in the Extracellular Microenvironment In Vivo in Human Dense Breast Tissue and Breast Cancer. (2018) Frontiers in Immunology**, DOI: 10.3389/fimmu.2017.01994

Cerebral microdialysis fluid

→ Dyhrfort P, Shen Q, Clausen F, Thulin M, Enblad P, Kamali-Moghaddam M, Hillered L, Lewén A. **Monitoring of Protein Biomarkers of Inflammation in Human Traumatic Brain Injury Using Microdialysis and Proximity Extension Assay Technology in Neurointensive Care. (2019) Journal of Neurotrauma,** DOI: 10.1089/neu.2018.6320

Mouse CSF

→ Shimozawa M, Bereczki E, et al. **Mitochondrial hypermetabolism precedes impaired autophagy and synaptic disorganization in App knock-in Alzheimer mouse models. (2023) Molecular Psychiatry,** DOI: 10.1038/s41380-023-02289-4

Mouse plasma

→ Liu Z, McCutcheon F, Ho H, et al. **Tranexamic acid in a mouse model of cerebral amyloid angiopathy: setting the stage for a novel stroke treatment approach. (2023) Research and Practice in Thrombosis and Haemostasis,** DOI: 10.1016/j.rpth.2023.102166

Mouse brain lysate

→ Simats A, Ramiro L, Valls R, et al. **Ceruletide and Alpha-1 Antitrypsin as a Novel Combination Therapy for Ischemic Stroke. (2022) Neurotherapeutics,** DOI: 10.1007/s13311-022-01203-0

Rat CSF

→ Lolansen SD, Rostgaard N, Barbuskaite D, et al. **Posthemorrhagic hydrocephalus associates with elevated inflammation and CSF hypersecretion via activation of choroidal transporters. (2022) Fluids and Barriers of the CNS,** DOI: 10.1186/s12987-022-00360-w

CSF

→ Del Campo M, Vermunt L, Peeters CFW, et al. **CSF proteome profiling reveals biomarkers to discriminate dementia with Lewy bodies from Alzheimer´s disease. (2023) Nature Communications,** DOI: 10.1038/s41467-023-41122-y

→ Del Campo M, Peeters C, Johnson E, et al. **CSF proteome profiling across the Alzheimer's disease spectrum reflects the multifactorial nature of the disease and identifies specific biomarker panels. (2022) Nature Aging,** DOI: 10.1038/s43587-022-00300-1

→ Gaetani L, Bellomo G, Di Sabatino E, et al. **The Immune Signature of CSF in Multiple Sclerosis with and without Oligoclonal Bands: A Machine Learning Approach to Proximity Extension Assay Analysis. (2023) International Journal of Molecular Sciences,** DOI: 10.3390/ijms25010139

→ Beaudin M, Kamali T, Tang W, et al. **Cerebrospinal Fluid Proteomic Changes after Nusinersen in Patients with Spinal Muscular Atrophy. (2023) Journal of Clinical Medicine**, DOI: 10.3390/jcm12206696

→ Maple-Grødem J, Ushakova A, Pedersen KF, et al. **Identification of diagnostic and prognostic biomarkers of PD using a multiplex proteomics approach. (2023) Neurobiology of Disease,** DOI: 10.1016/j.nbd.2023.106281

→ Rostgaard N, Olsen MH, Capion T, et al. **Inflammatory Markers as Predictors of Shunt Dependency and Functional Outcome in Patients with Aneurysmal Subarachnoid Hemorrhage. (2023) Biomedicines,** DOI: 10.3390/biomedicines11040997

→ Gaceb A, Roupé L, Enström A, et al. **Pericyte Microvesicles as Plasma Biomarkers Reflecting Brain Microvascular Signaling in Patients With Acute Ischemic Stroke. (2024) Stroke,** DOI: 10.1161/STROKEAHA.123.045720

Intracranial and systemic plasma

→ Maglinger B, Sands M, Frank JA, et al. **Intracranial VCAM1 at time of mechanical thrombectomy predicts ischemic stroke severity. (2021) J Neuroinflammation.** DOI: 10.1186/s12974-021-02157-4

Pediatric samples

→ Olvera-Rojas M, Plaza-Florido A, Solis-Urra P, et al. **Association of muscular strength and targeted proteomics involved in brain health in children with overweight/obesity. (2023) Scandinavian Journal of Medicine & Science in Sports**, DOI: 10.1111/sms.14387

→ Bao X-H, Chen B-F, Liu J, et al. **Olink proteomics profiling platform reveals non-invasive inflammatory related protein biomarkers in autism spectrum disorder. (2023) Frontiers in Molecular Neuroscience,** DOI: 10.3389/fnmol.2023.1185021

→ Abdennadher M, Inati S, Soldatos A, et al. **Seizure phenotype in CLN3 disease and its relation to other neurologic outcome measures. (2021) Journal of Inherited Metabolic Disease**, DOI: 10.1002/jimd.12366

Conclusion

The unprecedented ability to utilize 1 µL of sample for extensive protein biomarker profiling ensures that virtually no sample is too limited or too challenging to interrogate, as proven by the highlighted publications. Samples obtained from spinal taps or from animal models are a promising source of actionable biomarkers to assess risk, improve diagnoses, predict responses to treatments, and monitor disease progression and recurrence. Additionally, the low sample volume requirement benefits pediatric cases, where available volumes are limited and minimizing invasive collection is crucial. In conclusion, PEA technology not only allows maximizing data yield from each precious sample, but also enables studies that were previously inconceivable.

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