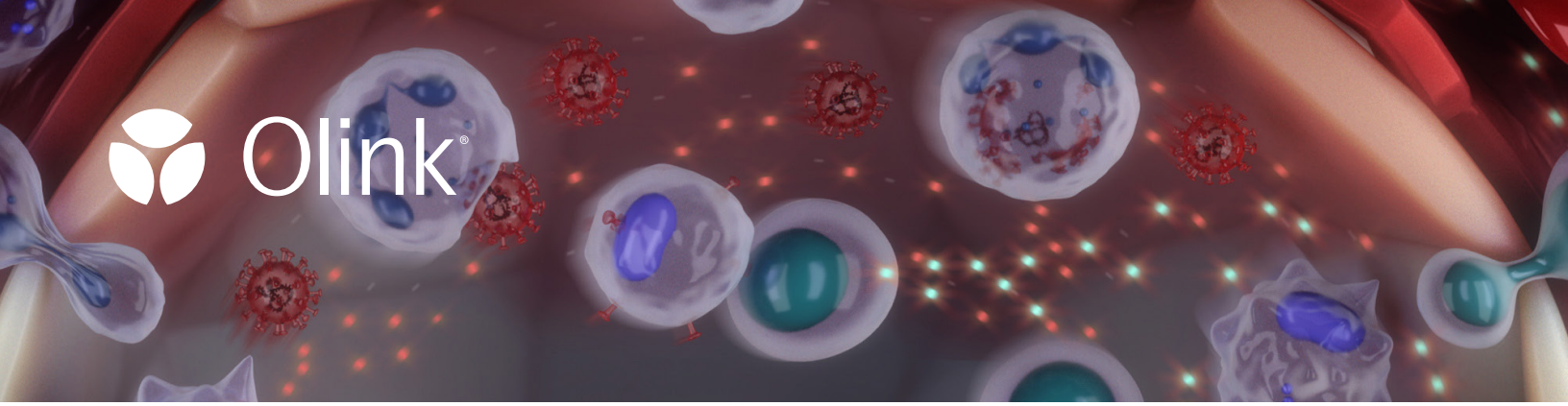

Enabling Unprecedented Analysis of Precious Samples in Inflammation and Infectious Diseases

Precious samples, such as aqueous humor, dried blood spots, and extracellular vesicles, 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.

Aqueous Humor

→ Achten R, van Luijk C, Thijs J, et al. **Non-Infectious Uveitis Secondary to Dupilumab Treatment in Atopic Dermatitis Patients Shows a Pro-Inflammatory Molecular Profile. (2023) Ocular Immunology and Inflammation,** DOI: 10.1080/09273948.2023.2182325

Bronchoalveolar lavage fluid

→ Verma A, Hawes CE, Lakshmanappa YS, Roh JW, et al. **Monoclonal antibodies protect aged rhesus macaques from SARS-CoV-2-induced immune activation and neuroinflammation. (2021) Cell Reports,** DOI: 10.1016/j.celrep.2021.109942

Dried blood spot

→ Moore CM, O'Reilly D, McCallion N, et al. **Changes in inflammatory proteins following platelet transfusion in a neonatal population. (2023) Pediatric Research,** DOI: 10.1038/s41390-023-02731-x

Extracellular vesicles

→ Maaninka K, Neuvonen M, Kerkelä E, et al. **OxLDL sensitizes platelets for increased formation of extracellular vesicles capable of finetuning macrophage gene expression. (2023) European Journal of Cell Biology**, DOI: 10.1016/j.ejcb.2023.151311

→ Sun B, Fernandes N, Pulliam L. **Profile of neuronal exosomes in HIV cognitive impairment exposes gender differences. (2019) AIDS,** DOI: 10.1097/QAD.0000000000002272

Biopsy for nasal polyps

→ Hou Y, Chen C, Li Z, et al. **Comparing Protein and Gene Expression Signature between Nasal Polyps and Nasal Fluids in Chronic Rhinosinusitis. (2023) International Archives of Allergy and Immunology,** DOI: 10.1159/000534226

Skin biopsy

→ Navrazhina K, Garcet S, Frew JW, et al. **The inflammatory proteome of hidradenitis suppurativa skin is more expansive than that of psoriasis vulgaris. (2021) Journal of the American Academy of Dermatology**, DOI: 10.1016/j.jaad.2021.07.035

→ Han J, Stratman S, Young JN, et al. **Unique protein signatures evolve during the course of a delayed-type hypersensitivity reaction in human skin. (2022) Journal of Dermatology,** DOI: 10.1111/1346-8138.16688

Synovial fluid

→ Barbarroja N, López-Montilla M, Cuesta-López L, et al. **Characterization of the inflammatory proteome of synovial fluid from patients with psoriatic arthritis: Potential treatment targets. (2023) Frontiers in Immunology,** DOI: 10.3389/fimmu.2023.1133435

→ Aulin C, Larsson S, Vogl T, et al. **The alarmins high mobility group box protein 1 and S100A8/A9 display different inflammatory profiles after acute knee injury. (2022) Osteoarthritis and Cartilage,** DOI: 10.1016/j.joca.2022.06.009

Cerebrospinal fluid (CSF)

→ Chen S, Liang J, Chen D, et al. **Cerebrospinal fluid metabolomic and proteomic characterization of neurologic post-acute sequelae of SARS-CoV-2 infection.(2023) Brain, Behavior, and Immunity**, DOI: 10.1016/j.bbi.2023.10.016

→ Stevens-Jones O, Mojzisova H, Elisak M, et al. **Paraneoplastic or not? Sirtuin-2 in anti-N-methyl-D-aspartate receptor encephalitis. (2023) European Journal of Neurology,** DOI: 10.1111/ene.15987

→ Andreasson J, Bodén E, Fakhro M, et al. **Exhaled phospholipid transfer protein and hepatocyte growth factor receptor in lung adenocarcinoma. (2022) Respiratory Research,** DOI: 10.1186/s12931-022-02302-4

→ Zhao L, Li P, Xu Z, et al. **Diagnosis of post-neurosurgical bacterial meningitis in patients with aneurysmal subarachnoid hemorrhage based on the immunity-related proteomics signature of the cerebrospinal fluid.** (2023) Frontiers in Neurology, DOI: 10.3389/fneur.2023.1166598

→ Remsik J, Wilcox J, Babady NE, et al. **Inflammatory leptomeningeal cytokines mediate COVID-19 neurologic symptoms in cancer patients. (2021) Cancer Cell, DOI:** 10.1016/j.ccell.2021.01.007

→ Koeken V, Ganiem A, Dian S, et al. **Cerebrospinal fluid IL-1β is elevated in tuberculous meningitis patients but not associated with mortality. (2020) Tuberculosis,** DOI: 10.1016/j.tube.2020.102019

→ Duran-Castells C, Llano A, Kawana-Tachikawa A, et al. **Sirtuin-2, NAD-Dependent Deacetylase, Is a New Potential Therapeutic Target for HIV-1 Infection and HIV-Related Neurological Dysfunction. (2023) Journal of Virology,** DOI: 10.1128/jvi.01655-22

→ Palada V, Siddiqah Ahmed A, Freyhult E, et al. **Elevated inflammatory proteins in cerebrospinal fluid from patients with painful knee osteoarthritis are associated with reduced symptom severity. (2020) Journal of Neuroimmunology,** DOI: 10.1016/j.jneuroim.2020.577391

Pediatric samples

→ Brodeur KE, Liu M, Ibanez D, et al. **Elevation of IL-17 cytokines distinguishes Kawasaki disease from other pediatric inflammatory disorders. (2023) Arthritis & Rheumatology,** DOI: 10.1002/art.42680.

→ Sîrbe C, Badii M, Crişan T, et al. **Detection of Novel Biomarkers in Pediatric Autoimmune Hepatitis by Proteomic Profiling. (2023) International Journal of Molecular Sciences,** DOI: 10.3390/ijms24087479

→ Jongsma MME, Costes LMM, Tindemans I, et al. **Serum immune profiling in pediatric Crohn's disease demonstrates stronger immune modulation with first-line infliximab than conventional therapy and pre-treatment profiles predict clinical response to both treatments. (2023) Journal of Crohn's & Colitis,** DOI: 10.1093/ecco-jcc/jjad049

→ Nyström N, Prast-Nielsen S, Correia M, et al. **Mucosal and plasma metabolomes in new-onset paediatric inflammatory bowel disease: correlations with disease characteristics and plasma inflammation protein markers. (2022) Journal of Crohn's & Colitis,** DOI: 10.1093/ecco-jcc/jjac149

→ Van Hoeve K, Seyed Tabib NS, Dreesen E, et al. **Infliximab Concentrations during Induction Are Predictive for Endoscopic Remission in Pediatric Patients with Inflammatory Bowel Disease under Combination Therapy. (2021) Journal of Pediatrics,** DOI: 10.1016/j.jpeds.2021.08.079

→ Ungaro R, Hu L, Ji J, et al. **Machine learning identifies novel blood protein predictors of penetrating and stricturing complications in newly diagnosed paediatric Crohn's disease. (2020) Alimentary Pharmacology & Therapy,** DOI: 10.1111/apt.16136

→ Brunner P, He H, Pavel A, Czarnowicki T, Lefferdink R, Erickson T, Canter T, Puar N, Rangel S, Malik K, Estrada Y, Krueger J, Guttman-Yassky E, Paller A. **The blood proteomic signature of early-onset pediatric atopic dermatitis shows systemic inflammation and is distinct from adult, longstanding disease. (2019) Journal of the American Academy of Dermatology,** doi: 10.1016/j.jaad.2019.04.036

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.

Non-invasive, low-volume samples like dried blood spots and invasive yet valuable ones like cerebrospinal fluid (CSF) hold promise as sources of actionable biomarkers to enhance diagnosis, predict treatment responses, and monitor disease progression. 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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1475, v1.0, 2024-03-13