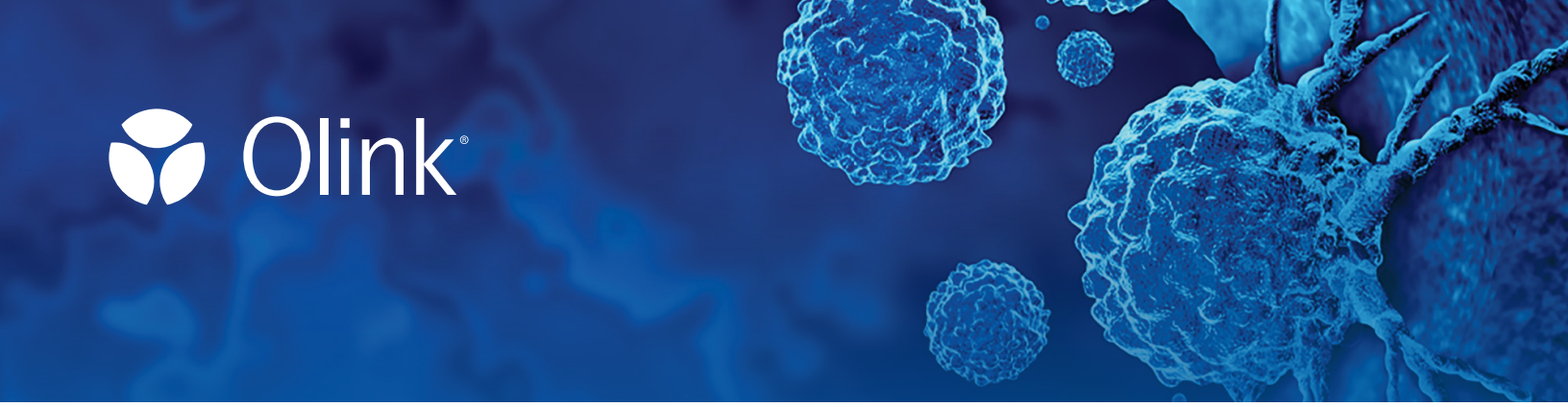

Enabling Unprecedented Analysis of Precious Samples in Oncology and Immuno-oncology

Precious samples, such as fine needle aspirates, cerebrospinal fluid, and tumor biopsies, 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.

Breast tissue

→ Lundberg P, Abrahamsson A, Kihlberg J, et al. **Low-dose acetylsalicylic acid reduces local inflammation and tissue perfusion in dense breast tissue in postmenopausal women. (2024) Breast Cancer Research**, DOI: 10.1186/s13058-024-01780-2

Breast tissue microdialysis samples

→ Ekstrand J, Abrahamsson A, Lundberg P, et al. **Breast density and estradiol are associated with distinct different expression patterns of metabolic proteins in normal human breast tissue in vivo. (2023) Frontiers in Oncology**, DOI: 10.3389/fonc.2023.1128318

→ Lundberg P, Forsgren MF, Tellman J, et al. **Breast density is strongly associated with multiparametric magnetic resonance imaging biomarkers and pro-tumorigenic proteins in situ. (2022) British Journal of Cancer**, DOI: 10.1038/s41416-022-01976-3

→ 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

Exhaled breath particles

→ 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

Aqueous humor

→ Wierenga A, Cao J, Mouthaan H, van Weeghel C, Verdijk R, van Duinen S, Kroes W, Dogrusöz M, Marinkovic M, van der Burg S, Luyten G, Jager M. **Aqueous Humor Biomarkers Identify Three Prognostic Groups in Uveal Melanoma. (2019) Investigative Ophthalmology & Visual Science,** DOI: 10.1167/iovs.19-28309

Fine needle aspirates

→ Röbeck P, Franzén B, Cantera-Ahlman R, et al. **Multiplex protein analysis and ensemble machine learning methods of fine needle-aspirates from prostate cancer patients reveal potential diagnostic signatures associated with tumor grade. (2023) Cytopathology**, DOI: 10.1111/cyt.13226

→ Franzén B, Viktorsson K, Kamali C, et al. **Multiplex immune protein profiling of fine-needle aspirates from patients with non-small-cell lung cancer reveals signatures associated with PD-L1 expression and tumor stage. (2020) Molecular Oncology**, DOI: 10.1002/1878-0261.12952

→ Franzén B, Alexeyenko A, Kamali-Moghaddam M, Hatschek T, Kanter L, Ramqvist T, Kierkegaard G, Auer G, Landegren U, Lewensohn R. **Protein profiling of fine needle aspirates reveals subtype-associated immune signatures and involvement of chemokines in breast cancer. (2018) Molecular Oncology**, DOI: 10.1002/1878-0261.12410

→ Franzén B, Kamali-Moghaddam M, Alexeyenko A, Hatschek T, Becker S, Wik L, Kierkegaard J, Eriksson A, Reddy Muppani N, Auer G, Landegren U, Lewensohn R. **A fine needle aspiration-based protein signature discriminates benign from malignant breast lesions. (2018) Molecular Oncology**, DOI: 10.1002/1878-0261.12350

Biopsy lysates

→ Han J, Correa da Rosa J, Agarwal A, et al. **Modulation of Inflammatory Proteins in Serum May Reflect Cutaneous Immune Responses in Cancer Immunotherapy. (2023) JID Innovations**, DOI: 10.1016/j.xjidi.2022.100179

→ Han J, Agarwal A, Young J, et al. **Proteomic profiling of a patient with cutaneous melanoma metastasis regression following topical contact sensitizer diphencyprone and immune checkpoint inhibitor treatment.(2022) Scientific Reports**, DOI: 10.1038/s41598-022-27020-1

→ Ramqvist T, Näsman A, Franzén B, Bersani C, Alexeyenko A, Becker S, Haeggblom L, Kolev A, Dalianis T, Munck-Wikland E. **Protein Expression in Tonsillar and Base of Tongue Cancer and in Relation to Human Papillomavirus (HPV) and Clinical Outcome. (2018) Int. J. Mol. Sciences**, DOI:10.3390/ijms19040978

Tumor single cell suspension

→ Natoli M, Hatje K, Gulati P, et al. **Deciphering molecular and cellular ex vivo responses to bispecific antibodies PD1-TIM3 and PD1-LAG3 in human tumors. (2022) Journal for ImmunoTherapy of Cancer,** DOI: 10.1136/jitc-2022-005548

Plasma extracellular vesicles

→ Viktorsson K, Hååg P, Shah CH, et al. **Profiling of extracellular vesicles of metastatic urothelial cancer patients to discover protein signatures related to treatment outcome. (2022) Molecular Oncology,** DOI: 10.1002/1878-0261.13288

→ Chandran V, Welinder C, Månsson A-S, Offer S, Freyhult E, Pernemalm M, Lund S, Pedersen S, Lehtiö J, Marko-Varga G, Johansson M, Englund E, Sundgren P, Beltin M. **Ultrasensitive immunoprofiling of plasma extracellular vesicles identifies syndecan-1 as a potential tool for minimally invasive diagnosis of glioma. (2019) Clinical Cancer Research**, DOI: 10.1158/1078-0432.CCR-18-2946

Cerebrospinal fluid

→ Li M, Chen J, Yu H, et al. **Cerebrospinal fluid immunological cytokines predict intracranial tumor response to immunotherapy in non-small cell lung cancer patients with brain metastases. (2023) OncoImmunology,** DOI: 10.1080/2162402X.2023.2290790

Skin tape strips

→ Techner J-M, Hooper MJ, Evans S, LeWitt TM, Paller AS, Guitart J, Lu KQ, Zhou XA. **Skin Tape Strip Proteomics in Mycosis Fungoides Identifies Tumor-Associated Biomarkers. (2023) Journal of Investigative Dermatology, 143(3):517-520.e12.** DOI: 10.1016/j.jid.2022.07.025

Mouse plasma, serum, tumor lysate and breast tissue microdialysis samples

→ Englund DA, Jolliffe AM, Hanson GJ, et al. **Senotherapeutic drug treatment ameliorates chemotherapy-induced cachexia. (2023) JCI Insight**, DOI: 10.1172/jci.insight.169512

→ Kerzeli I, Lord M, Doroszko M, et al. **Single-cell RNAseq and longitudinal proteomic analysis of a novel semi-spontaneous urothelial cancer model reveals tumor cell heterogeneity and pretumoral urine protein alterations. (2021) PLOS One**, DOI: 10.1371/journal.pone.0253178

→ Taylor M, Hughes A, Walton J, Coenen-Stass A, Magiera L, Mooney L, Bell S, Staniszewska A, Sandin L, Barry S, Watkins A, Carnealli L, Hardaker E. **Longitudinal immune characterization of syngeneic tumor models to enable model selection for immune oncology drug discovery. (2019) Journal for Immunotherapy of Cancer,** DOI: 10.1186/s40425-019-0794-7

→ Ekstrand J, Abrahamsson A, Lundberg P, et al. **Breast density and estradiol are associated with distinct different expression patterns of metabolic proteins in normal human breast tissue in vivo. (2023) Frontiers in Oncology,** DOI: 10.3389/fonc.2023.1128318

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 fine needle aspirates or micro-biopsies 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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