Webinar Summary

What is a Good Biomarker?

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Xtalks Partner:
Olink

Webinar Webpage:
https://xtalks.com/webinars/what-is-a-good-biomarker/

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Executive Summary

The webinar "What is a Good Biomarker?" explored the evolving field of biomarker research, with a focus on the pivotal role of protein biomarkers in enhancing personalized medicine and streamlining drug development. The session brought together experts from Olink, part of Thermo Fisher Scientific, who shared detailed insights into both the biological significance of proteins as dynamic indicators of health and the technological advancements that underpin robust biomarker assay development.

The speakers highlighted that while traditional genomic and RNA-based biomarkers have provided valuable information, protein biomarkers offer a direct measurement of biological activity — capturing real-time changes that are crucial for accurate disease diagnosis and treatment monitoring. This capability is especially important in complex diseases, where a single biomarker might not sufficiently capture disease heterogeneity. The discussion emphasized the transition from using individual protein markers to developing multiplexed biomarker panels, which can deliver a more comprehensive and precise view of disease subtypes, thereby advancing the goals of precision medicine.

Central to the webinar was an overview of Olink's Proximity Extension Assay (PEA) technology — a state-of-the-art platform that integrates dual antibody recognition with DNA hybridization and amplification to ensure exceptional assay specificity, sensitivity and reproducibility. The speakers walked through the rigorous 3-step, 15-factor assay verification process, detailing how extensive internal and external quality controls, interference testing and multi-site validation ensure that the assays deliver reliable, reproducible results across diverse sample types and different sites.

Furthermore, the webinar underscored the importance of a well-structured biomarker development pipeline — not only in terms of technological innovation but also in addressing critical operational challenges such as sample variability, pre-analytical factors and the need for robust statistical analyses. In addition to the technical insights, Olink's comprehensive product portfolio and supportive digital tools were showcased, illustrating how the same platform can be leveraged from early-stage discovery through to clinical translation. This integrated approach is designed to reduce development timelines and costs while increasing the likelihood of clinical success.

Overall, the webinar provided actionable insights for researchers and industry professionals looking to harness the power of protein biomarkers for improved health outcomes, reinforcing the message that reliable biomarker development is essential for the future of personalized healthcare.

Detailed Content Summary

The Evolving Role of Biomarkers in Healthcare:

The webinar opened by explaining the pivotal role of biomarkers in modern healthcare. The speakers emphasized that biomarkers are objective, measurable indicators that provide critical insights into the biological state and progression of diseases. These indicators not only facilitate early disease detection — often before clinical symptoms appear — but also enable more accurate diagnosis, prognosis and monitoring of treatment responses. This capacity to capture subtle yet significant changes in the body underscores the potential of biomarkers in personalized medicine.

In addition, the webinar drew a clear distinction between traditional genomic biomarkers and protein biomarkers. While genomic and RNA-based approaches have laid the groundwork for targeted therapies, protein biomarkers offer a more direct reflection of the body's dynamic physiology. Proteins, being the active effectors of cellular function, can undergo post-translational modifications that influence their activity and interactions. This dynamic behavior means that protein biomarkers can provide real-time snapshots of pathological processes, making them particularly valuable for understanding complex conditions. Moreover, proteins are readily measurable in accessible biological fluids such as plasma, urine and saliva, a feature that enhances their practicality for routine clinical applications and large-scale studies.

Advancements in Multiplex Protein Biomarker Signatures:

Katarina Hörnaeus, Product Portfolio Director at Olink, part of Thermo Fisher Scientific, delved into the evolution of biomarker strategies, highlighting a shift from the reliance on individual biomarkers to the implementation of multiplex protein biomarker panels. Early biomarker research often centered on single markers, which, while informative, frequently lacked the specificity needed to fully characterize multifactorial diseases. Katarina Hörnaeus noted that complex diseases, such as Alzheimer's, require a more nuanced approach because single markers like NFL may be implicated in multiple conditions, leading to ambiguous diagnostic outcomes.

Researchers can achieve greater diagnostic accuracy and enhanced resolution of disease subtypes by employing multiplex panels that assess multiple protein biomarkers simultaneously. This approach provides a comprehensive overview of disease pathology by capturing diverse aspects of the biological response. The ability to integrate data from several biomarkers allows for more precise patient stratification and tailored therapeutic strategies. As the webinar underscored, these multiplex signatures not only support early detection and monitoring but also align with the principles of precision medicine, where treatment regimens are increasingly customized based on an individual's profile.

Olink's Assay Development and Proximity Extension Assay (PEA) Technology:

A core highlight of the webinar was an in-depth discussion of Olink's innovative assay development process, which is built around the Proximity Extension Assay (PEA) technology. Lena Eriksson, Group Manager of Assay Development at Olink, part of Thermo Fisher Scientific,

detailed how PEA operates through a three-step process that begins with an immune reaction: two antibodies, each tagged with a unique DNA oligonucleotide, bind to their target protein. Once these antibodies are in close proximity, their attached DNA strands hybridize, forming a unique sequence that serves as a proxy for the presence of the target protein.

Following this, a DNA extension step takes place, which effectively "locks in" the signal, and then the process culminates in a signal amplification phase via qPCR or next-generation sequencing (NGS). This layered approach ensures high specificity and sensitivity, as the signal is only generated when both antibodies correctly recognize the target protein.

Moreover, the system is designed to be robust against common sources of interference, such as heterophilic antibodies or sample contaminants. Rigorous multi-stage screening procedures, which include assessments of dynamic range, dilution consistency and specificity, ensure that only assays meeting stringent criteria are advanced. Internal controls and external validations, including multi-site testing, further underpin the reliability and reproducibility of the PEA platform, maintaining technical variability at exceptionally low levels.

Supporting the Complete Biomarker Journey:

In the final segment, the discussion broadened to encompass the entire biomarker development continuum — from early-stage discovery to clinical translation — and how Olink's comprehensive product portfolio supports this journey. Katarina Hörnaeus explained that Olink's platform is uniquely scalable, offering both high-plex exploratory discovery panels capable of measuring thousands of proteins from minimal sample volumes, and targeted panels that can measure down to 5 proteins, delivering high quality data for clinical translation. This flexibility allows researchers to maintain a consistent approach throughout their studies, reducing the need to switch technologies as projects advance from the discovery phase to more focused, hypothesis-driven research.

Complementing the robust assay platforms, Olink provides a suite of digital tools and support services designed to streamline study design, data analysis and result interpretation. Resources such as the Olink Concordance Test, the Olink Analyze R package, interactive Shiny apps and the Olink Insight knowledge platform collectively empower researchers to manage complex proteomics datasets with ease and transparency. These integrated resources not only accelerate the transition from biomarker discovery but also help reduce development timelines and associated costs.

Overall, the comprehensive support offered by Olink reinforces the potential for biomarker-driven research to make significant contributions to personalized medicine and improved healthcare outcomes.

Featured Speakers

Lena Eriksson

Group Manager Assay Development at Olink, part of Thermo Fisher Scientific

With a strong foundation in molecular biotechnology engineering, Lena Eriksson is the Assay Development Group Manager at Olink, part of Thermo Fisher Scientific, where she has spent the past seven years overseeing the development of multiplex immunoassays using the Proximity Extension Assay technology. Her expertise includes assay selection, validation, verification and quality control method development, ensuring the production of rigorously validated, high-performance immunoassay solutions.

Katarina Hörnaeus

Product Portfolio Director at Olink, part of Thermo Fisher Scientific

Katarina Hörnaeus brings a wealth of proteomics expertise to her role as Product Portfolio Director at Olink, part of Thermo Fisher Scientific. She is responsible for the pre-configured and customizable product offerings, as well as clinical applications. Katarina's background includes working with various proteomics applications using mass spectrometry, while her prior research focused on biotransformation of xenobiotic compounds in veterinary medicine.

Quotes from the Webinar

"The Proximity Extension Assay [PEA] has overcome technological challenges in proteomics. The PEA that we use for all of our products has managed to solve many of the challenges of protein assay multiplexing." **— Katarina Hörnaeus**

"Our method (PEA with qPCR or NGS readout) is basically a three-step reaction, which is designed for scalability, but also allows for a high dynamic range." **— Lena Eriksson**

"All Olink assays undergo a rigorous three-step, 15-factor analytical verification process. There are 15,300 assays tested and 5,400+ approved." **— Lena Eriksson**

"The signal amplification using PCR allows for high sensitivity, and our broad dynamic range spans from fg/mL to mg/mL." **— Katarina Hörnaeus**

"When we run the assays, we would like the results to be repeated. We would like the same results over and over again no matter the lab or operator." **— Lena Eriksson**

"The ambition at Olink is to facilitate the entire biomarker discovery process, all the way from exploratory discovery down to clinical translation." **— Katarina Hörnaeus**

Q&A Highlights

Question 1: What are the challenges of using the supernatant from a cell simulation assay in the cell culture setup?

Katarina Hörnaeus: We actually have quite a lot of experience with that sample matrix. We have many publications, and our scientific support team has guided numerous customers using this sample type. The biggest challenge is that the protein abundance levels in this sample type may differ significantly from those in serum and plasma, for which our products are validated. Therefore, you would probably need to perform different types of dilutions on your samples before running them with the PEA technology. Our scientific support team can guide you on these dilutions, and you can also visit our website and filter publications to find other customers who have used this sample type.

Question 2: How do you remove the need for multiple replicates of samples in your panels?

Lena Eriksson: We rely on internal controls. Each sample contains internal controls that cover the three steps of our reaction, and these indicate if something is wrong with the reaction for that specific sample. Additionally, we have sample controls within the plates that provide information about how the assay varies in that run. Of course, you are always allowed to add more replicates if you wish, but that is why we don't see the need for extra replicates, as we already understand what is happening in the reaction step.

Question 3: Systemic plasma samples do not always represent the changes at different organs due to compartmentalization response, which is an indication of the need for local biomarkers. How does the Olink system perform in bronchoalveolar lavage (BAL) or perhaps in urine samples?

Katarina Hörnaeus: It works surprisingly well for these sample matrices. The answer is very similar to a previous question: our scientific support team can guide you on how to prepare these samples for optimal results using the PEA technology. We also have publications for these sample types on our website that you can review.

Question 4: Could you explain a little more about the quantitation and perhaps what a negative NPX score might mean?

Lena Eriksson: Our technique is based on PCR cycles, which are on a log scale. This means that the values can be negative because they are represented on the log scale.

Question 5: Is Olink's technology capable of detecting phosphorylated proteins — especially given their typically low abundance, transient nature and the challenges of developing high-affinity antibodies? How does the platform address these limitations, especially since it relies heavily on validated antibodies?

Lena Eriksson: Just as the person asking the question mentioned, it depends on the antibodies, which are key to our assays. The platform works well for detecting phosphorylated proteins, but

we also need to develop the assay to work effectively for these types of targets. I would say that is our current approach; however, we will ensure that we have the right signal before launching that kind of product.

Question 6: There was a slide about research questions, sample size, long-term goals and you mentioned the concept of parameters of highest importance. Could you shed a little more light on what you mean by that, more specifically?

Lena Eriksson: It's more like, is it the high-throughput screening you're doing? Are you looking for high sensitivity? What is the key factor you're after — is it detectability in certain samples? What do you know from previous experiences regarding these parameters? That's why we also try to present our assay parameters on our website, so you can review them and make an informed judgment, not only based on the antigen curves but also on where our samples fall within the measuring ranges.

Question 7: Which Olink platforms are capable of absolute quantification and which use relative quantification? For instance, for absolute quantification, do you use a full calibration curve? How many points do you use?

Katarina Hörnaeus: We have three product lines that provide absolute quantification. First, we have our Target 48 product line, which measures 45 proteins in multiplex. Then we have our Flex product line, which is a made-to-order product where you can select five to 30 different biomarkers from a library of 200, allowing you to custom-build a smaller Flex panel. Our third product line with absolute quantification is our Focus product line, which is fully customizable; you can choose biomarkers from our entire 5,000-flex library. And yes, we do full calibration curves during product development. With each kit, you run a calibrator in triplicate, and we use that data to back-calculate the results from your run against the calibration curve we produced during product development.

Question 8: How do you curate which biomarkers to add to a panel intended for research in a specific therapeutic area?

Katarina Hörnaeus: First of all, we have a broad network of key opinion leaders (KOLs) that we regularly consult for input on their specific research areas. We also have an internal team of scientific experts who work closely with our KOLs and attend conferences to stay informed about market trends and the most important biomarkers. Finally, we have a skilled data science team that uses various digital tools to curate the most relevant biomarkers for specific research fields.

Question 9: How many of the assays you screen are actually approved for use in products?

Lena Eriksson: We have screened about 15,000 assays, ending up with 5,400 approved for use in products. That means roughly 30% of the assays make it into products. For us, it is really important that these assays align with our criteria so that we can reliably measure samples and generate meaningful data.

Question 10: Is there a specific number of assays that can be included in Focus panels?

Katarina Hörnaeus: Our current Focus format allows up to 21 biomarkers in the same panel.

Question 11: What kind of matrix effects can be expected when analyzing tissue samples?

Katarina Hörnaeus: Certain sample preparation methods might introduce compounds that interfere with our technology, but we have various protocols for different tissue types. Our scientific support team can guide you if you're interested in running tissue lysates on our platform.

Question 12: Can all assays in that 5,400-library be combined into a Focus panel?

Katarina Hörnaeus: There are some limitations based on our experience and our goal of creating robust panels with a simple protocol. Our approach is not to combine proteins with two very different abundance levels. Although we have molecular techniques to shift the dynamic range to combine proteins at different abundance levels, we maintain a set level that we consider optimal for combination. Our scientific support team is happy to guide you through these discussions.

More Information

Olink®

Olink's mission is to accelerate proteomics together with the scientific community, to understand real-time biology and gain actionable insights into human health and disease.

Our innovative solutions deliver highly sensitive and accurate protein quantification, giving scientists the power to investigate complex biological processes with precision.

Contact Olink:

If you have questions following the webinar, visit https://olink.com/ for more information.

More From the Webinar:

Visit the webinar webpage for more information, including access to the recording:

https://xtalks.com/webinars/what-is-a-good-biomarker/