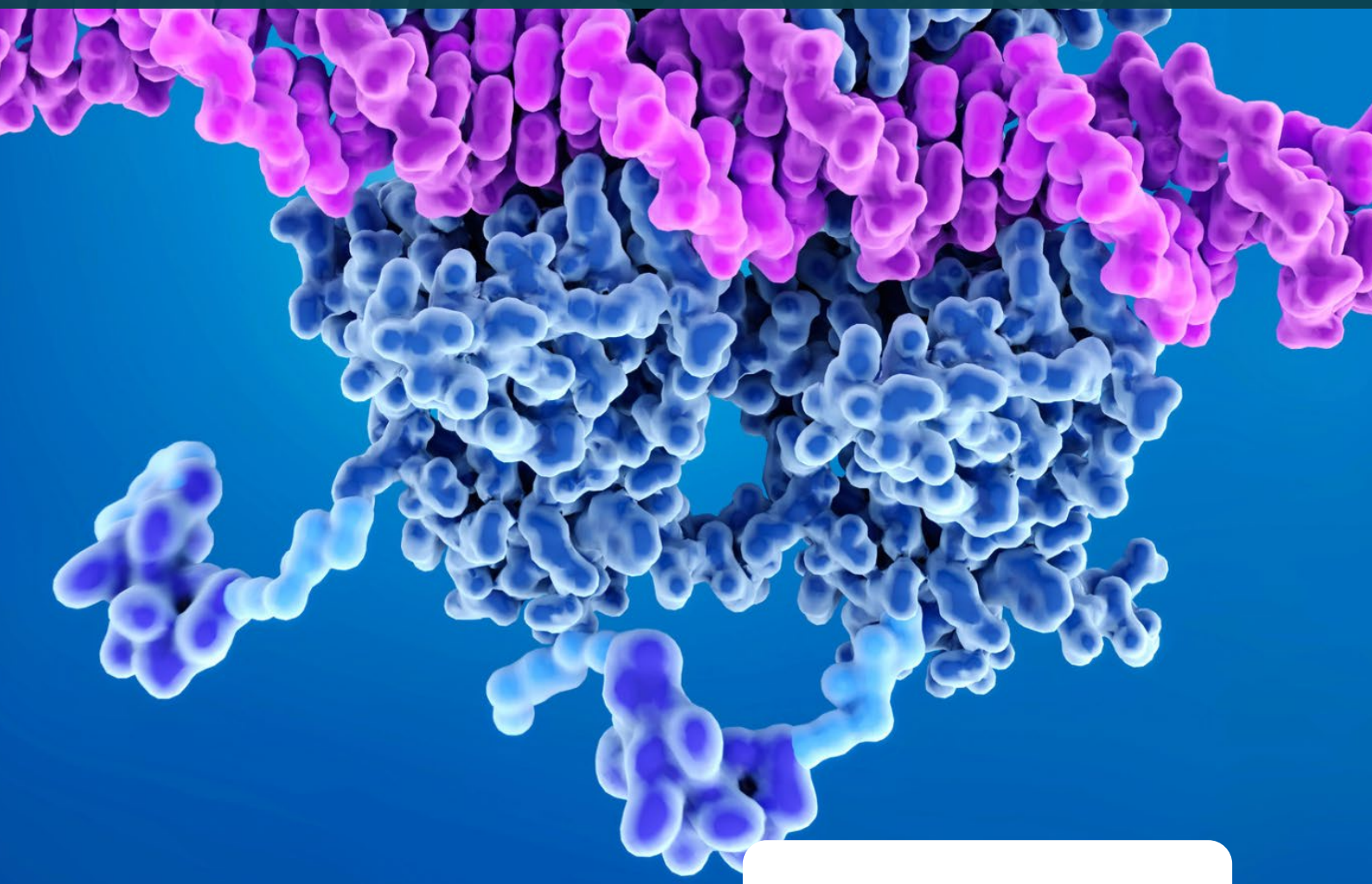
BEST PRACTICE EBOOK

Toward Precision Medicine

Transforming Clinical Research with Advanced Multiomics

Integrating multiomics technologies to revolutionise clinical research and patient care.



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Introduction

Welcome to our latest eBook! We'll delve into the transformative potential of precision medicine through the lens of advanced multiomics platforms. This eBook brings together a wealth of knowledge and cutting-edge research from leading experts in the field, summarised from their recent presentations at our Multi-Omics in Biomarker Discovery & Precision Medicine Symposium.

In this edition, we explore the innovative methods and applications of affinity proteomics, which are revolutionising the measurement of thousands of proteins, particularly in body fluids. This approach is crucial for supporting clinical decisions and population screening, moving us closer to personalised treatments based on clinical characteristics.

We also take a look at single-cell spatial analysis, where advanced techniques allow for the quantification of various genomic loci, transcripts, and proteins in single cells of intact tissues. This technology has significant potential applications in understanding disease mechanisms and developing effective therapies.

The eBook then highlights the advancements in drug discovery and development through the use of proteomics and metabolomics. By moving beyond genomics, these technologies provide a more comprehensive view dynamic factors influencing disease and drug response over time, enhancing the understanding of disease states and improving the success rates of clinical trials.

Multimodal analysis in tissue pathology is another key theme, emphasising its potential to enhance the complexity and accuracy of biomarkers used in cancer diagnosis and treatment prediction. The integration of various analytical modalities with advanced information technology is highlighted as a critical factor in achieving a synergistic effect in diagnostic value.

We also explore the development of ultra-sensitive, multi-omic, and multi-plex assays utilising novel digital microfluidic technology. This cutting-edge platform streamlines DNA, RNA, and protein biomarker analysis, providing harmonised data and reducing the complexity and cost of current technologies.

Finally, we discuss the use of spatial multi-omics data to enable precision medicine in chronic inflammatory diseases. This approach integrates quantitative histopathology with spatial biology to generate insights and support drug discovery and biomarker identification.

Overall, this edition provides valuable insights into the latest advancements in precision medicine, showcasing the potential of multiomics technologies to revolutionise clinical research and patient care. We hope it inspires you to explore these innovative approaches in your own research and clinical practice.

Tom Cohen

Senior Digital Content Editor, Oxford Global

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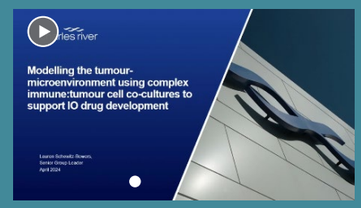

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Contents

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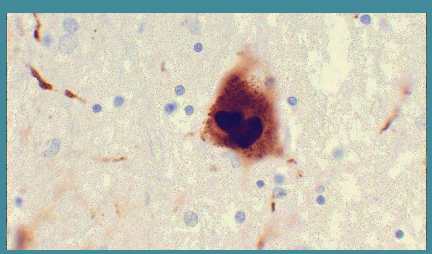
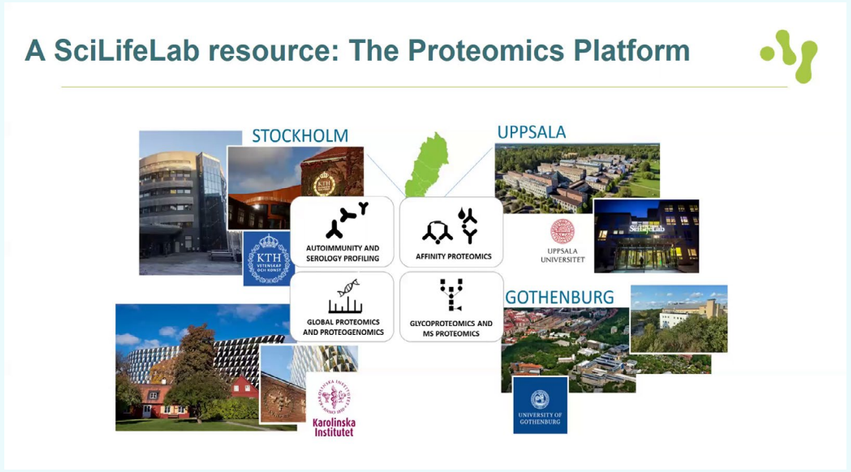


Affinity Proteomics in Precision Medicine

Claudia Fredolini, head of the Proteomic Platform at the Royal Institute of Technology (KTH) in Stockholm, focused on the methods in affinity proteomics that can be used for precision medicine. The Proteomic Platform is a comprehensive resource for scientists, hosted by KTH and other institutions such as the Karolinska Institute and Uppsala University. It includes a wide range of technologies, including mass spectrometry and affinity proteomics methods, which contribute to precision medicine, diagnostic epidemiological studies, and biology research.

The platform consists of around fifty scientists, including platform management, scientific directors, and group leaders with strong publication records. They are also advised by external experts and connected to major proteomic organisations like the European Infrastructure for Translational Medicine.



Affinity proteomics employs the use of affinity reagents to measure thousands of proteins, a task that has become possible in recent years thanks to technological advancements. These methods are particularly suited for studying proteins in body fluids, where mass spectrometry may have limitations. The platform offers various assays, including quantitative methods for screening proteins and sensitive immunoassays for biomarker validation, which are crucial for clinical applications and precision medicine.

One of the key goals is to move from the traditional “one drug fits all” approach to personalised treatments based on clinical characteristics. Non-invasive biomarkers play a significant role in this setting, supporting clinical decisions and population screening.

The platform supports biomarker research for discovery and validation, collaborating with numerous research groups annually. For example, they work with Davide Vetrano at the Karolinska Institute on studying multimorbidity in the elderly population. This involves analysing samples from over two thousand participants in the Swedish National Study on Aging and Care, identifying biomarkers associated with comorbidities.

Another study supported by the platform is conducted in Madrid, Spain, focusing on the microbiome as a target for precision medicine. This research investigates immune regulation in individuals affected by acute coronary syndrome, observing altered profiles of the microbiome and systemic inflammation.

The platform also explores the use of microsampling to simplify sample collection and support population studies. Portable devices allow individuals to collect samples in a less invasive manner, reducing the need for laboratory visits. This approach facilitates longitudinal sampling and increases participation in clinical trials and biomarker validation studies.

They are developing protocols to measure proteins in dried blood spots, using technologies like the Capitainer card, which allows for accurate quantification of biomarkers. This method eliminates the need for manual spot cutting and enables high-throughput processing, supporting large-scale population studies.

During the COVID-19 pandemic, the platform tested the feasibility of using the Capitainer card for population sampling. They sent out two thousand cards and analysed around nine hundred samples using multiplex assays. This study provided valuable insights into the presence of cellular proteins in dried blood spots and identified interesting biomarkers in individuals affected by COVID-.

In conclusion, the Proteomic Platform offers a comprehensive workflow for biomarker discovery, validation, and clinical application. They use multiplex methods for biomarker discovery and quantitative assays for clinical validation. Their goal is to support researchers in moving from discovery to verification and validation of biomarkers, ultimately contributing to precision medicine.

Single Cell Spatial Proteomic & Transcriptomics with Cleavable Fluorescent Probes

Jia Guo's presentation focused on the innovative research conducted in their lab on single-cell spatial proteomics and transcriptomics analysis using cleavable fluorescent probes. The lab aimed to develop a highly multiplexed single-cell analysis approach to quantify the identities, positions, and abundances of various genomic loci, transcripts, and proteins in single cells of intact tissues in situ.

Jia Guo began by disclosing their role as a co-founder of Spatomics and an inventor of a patented LED licensed to NanoString. The primary goal of their research was to analyse brain tissues, solid tumours, or developing embryos at the molecular level to understand their functions and progression. This approach also aimed to identify new biomarkers for diagnosis, treatment monitoring, and potential drug targets for more effective cellular therapies.

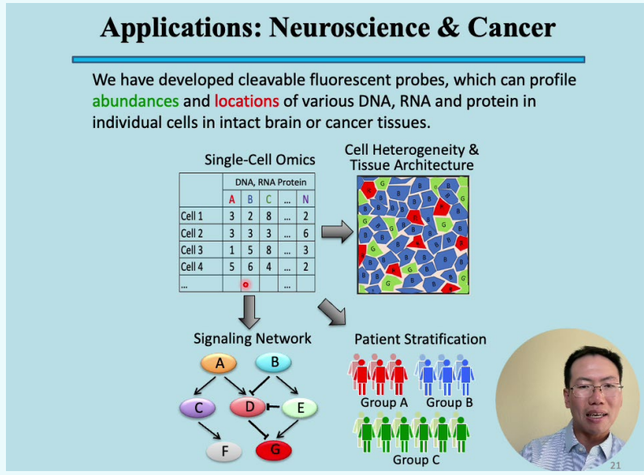
To achieve these goals, the lab developed a reiterative immunofluorescence approach. In conventional immunofluorescence, fluorescent antibodies are used to recognise targets in a specimen, which are then visualised under a fluorescence microscope. However, the lab introduced a small chemically cleavable linker between the fluorophore and antibodies. After the first cycle of staining, the fluorophores could be chemically cleaved, removing the original fluorescence signals. This allowed for multiple cycles of staining, imaging, and cleavage, enabling the quantification of a large number of different proteins in the same set of cells.

The presentation highlighted two critical requirements for this approach: effective cleavage of fluorophores in a cellular environment within a short time and ensuring that the chemical cleavage reaction did not damage the integrity of biomolecules in the cells. The lab demonstrated the cleavage efficiencies and showed that almost 98% of the original staining signals were removed within 30 minutes. They also proved that the chemical cleavage reaction did not damage the epitopes in the cells, allowing for successful staining in subsequent cycles.

The lab applied this approach to clinical samples, particularly formalin-fixed paraffin-embedded (FFPE) tissues, which often have high autofluorescence backgrounds and partially damaged biomarkers. To address this, they developed a next-generation highly sensitive in situ proteomics approach using horseradish peroxidase (HRP) enzymes conjugated to antibodies. This method amplified the signals by about two orders of magnitude compared to conventional immunofluorescence.

The presentation also covered the application of this approach to human hippocampus tissues, where they quantified nearly half a million individual neurons and classified them into subclusters based on their unique protein expression profiles. This allowed them to map the different clusters back to their original cellular locations and study the biological differences between normal and diseased tissues.

In addition to protein analysis, the lab extended their approach to RNA molecules. They conjugated fluorophores directly to oligonucleotides through a cleavable linker, allowing for cycles of staining, imaging, and cleavage to quantify a large number of different RNA molecules in the same cells or tissue samples. This method proved to be highly sensitive and accurate, even in FFPE tissues.



The presentation concluded with a comparison of their method to other multiplexed protein and RNA imaging technologies. The unique advantage of their approach was its high sensitivity due to HRP-based signal amplification. This allowed for the detection of low-expression proteins and RNA molecules in highly auto fluorescent tissues. The lab's method could routinely detect 5 to 20 copies per gene per cell in FFPE tissues and quantify hundreds of different RNA molecules simultaneously.

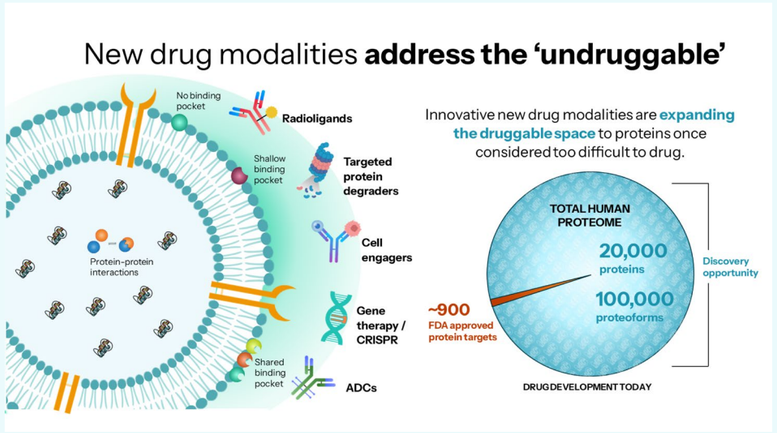
Overall, Jia Guo's presentation showcased the lab's innovative approach to single-cell spatial proteomics and transcriptomics analysis, highlighting its potential applications in understanding disease mechanisms, identifying biomarkers, and developing more effective therapies.

Moving Multi-Omics Beyond the Genome: Next-Generation Approaches to Amplify Drug Development Insights

Dr. Jonathan Usuka, CEO of Sapient, delivered an insightful presentation on the advancements in drug discovery and development through the use of advanced proteomics and metabolomics approaches. He emphasised the necessity of moving beyond genomics to accelerate drug target and biomarker discovery, and to improve clinical trial success rates.

Dr. Usuka began by highlighting the critical role of proteins in modifying disease states. He explained that most therapeutics interact with proteins, whether through ligand binding, altering cell receptors, or regulating catalytic proteins within cells. The challenge, however, has been that most proteins in the proteome have, until recently, been considered too difficult to drug. The majority of drug candidates have therefore been developed around a relatively small pool of known protein targets.

He cited emerging drug modalities, such as ADCs and targeted protein degraders, as innovations that are now expanding the 'druggable' space to allow targeting of more proteins. To advance novel medicines and improve their odds of success, it is essential to explore the broader proteome for new and better targets, as well as for biomarkers that improve our understanding of patient responses at a deeper level.



One of the key advancements in proteomics mentioned by Dr. Usuka enabling broader discovery within the proteome was high-throughput mass spectrometry. These systems can now deliver high analytical specificity along with high sensitivity and throughput to enable broader and deeper profiling across thousands of proteins at a time. He discussed how pairing this next-generation instrumentation with evolving nanoparticle enrichment techniques allow for measure of proteins at different abundance levels. High-abundant proteins can swamp the signal of low-abundant proteins, which are often the targets for drug development. Sapient's nanoparticle enrichment strategies help deplete high-abundant proteins and enrich low-abundant ones to quantify their levels in plasma, tissue, or cells.

Dr. Usuka also discussed the importance of post-translational modifications (PTMs), which create different protein forms crucial for understanding disease states and developing therapeutics. He provided examples of drugs that target PTMs, such as tyrosine kinase inhibitors and targeted protein degraders, highlighting their significance in current drug discovery and development – and noting that they can be measured via mass spectrometry.

Dr. Usuka did emphasize that genomics has been a valuable tool for target discovery and touched on the impact of genomics in personalised medicine, particularly in oncology. He cited the discovery of the KRAS mutation in lung cancer and its application to therapeutics as a significant milestone. However, he emphasised that genetic factors account for only a small percentage of disease risk, necessitating alternative methods to understand patient responses and develop new therapeutics. He also noted that RNA and protein measures are not well correlated in disease or treated states, further reinforcing the need for protein and metabolite measures that can read out these dynamic changes more accurately.

Dr. Usuka explained that to address the varied drug development gaps discussed, Sapient provides services including target identification, high-throughput screening, and the discovery of dynamic biomarkers. He provided an overview of Sapient's state-of-the-art laboratory in San Diego, where they use advanced mass spectrometry techniques to measure thousands of proteins, metabolites, and lipids from a single sample.

He further explained that simply generating data is not sufficient and stressed the importance of comprehensive data analysis to derive actionable insights. He discussed how Sapient integrates their multi-omics data with proprietary data sets, which include real-world patient outcomes, to further disease understanding and accelerate development of new treatments.

Usuka's presentation underscored the need to move beyond genomics with focus on proteomics and metabolomics to advance drug discovery and development, and ultimately, improve the success rates of clinical trials.

Advancing multi-omics biomarker discovery beyond the genome

Despite significant advances in genetic sequencing over the last decade, we still understand an exceedingly small percentage of the total human system. Across common diseases, only 15–20% of disease risk is attributable to genetics. The genome is also largely static, and given the dynamic nature of disease, we must look toward multi-omics approaches that can capture more dynamic measures of human health, disease, and drug response.

To transition to the next era of precision drug development and personalized medicine, we must be able to effectively interrogate the broader molecular landscape of proteins, metabolites, and lipids, and understand the biological associations between the different omics layers: via genomics, transcriptomics, proteomics, metabolomics, and lipidomics.

Luckily, major innovations within the last several years are finally making such analyses possible at scale and with the robustness required for meaningful discovery and translation of findings. With the rise of high-throughput bioanalytical technologies, enhanced automation, and improved AI and machine learning tools, researchers can more seamlessly and simultaneously generate, integrate, and analyze multi-omics datasets to identify meaningful correlations, develop new hypotheses, and drive groundbreaking discoveries that inform better interventions and development of effective therapeutics.

In this review, we we cover advancements specific to mass spectrometry and AI/ML software aiding improved multi-omics analyses.

Higher throughput and sensitivity

Recent transformations in mass analyzer technology have driven a step-change increase in the speed and resolution of what was traditionally considered a high specificity but low throughput analytical tool. Time-of-Flight (TOF) mass spectrometers with trapped ion mobility, for example, allow for high-speed spectral acquisition with higher sensitivity and increased coverage. This next generation of mass spectrometry systems can achieve analytical depth at scale, for both nontargeted screenings and targeted protein, metabolite, and lipid measures across thousands of samples at a time.

Improved automation

From liquid handling to digestion and cleanup, automation has sped up what were formerly complex and manual sample preparation steps while mitigating variability to improve reproducibility of mass spectrometry measures.

Broader small molecule biomarker discovery

Mass spectrometry innovations now allow for the measure of thousands of metabolites and lipids in a biosample in a single run, with the speed to process thousands of samples per day. Now truly nontargeted screenings across broad chemistries can be performed to identify the most biologically relevant signals, which may represent novel or improved biomarkers. Large-scale analyses provide the statistical power to validate these markers in a population.

Deeper coverage of the plasma proteome

Significant advancements in nanoparticle and affinity enrichment techniques are allowing for mass spectrometry-based detection and quantification of low-abundance proteins in liquid matrices which were previously masked by proteins at higher concentrations.

Capture of PTMs and proteoforms

Post-translational modifications (PTMs) and protein variants play a role in critical protein functions, and increasing evidence shows these proteoforms to be important biomarkers of disease as well as drug targets. Mass spectrometry is uniquely able to measure PTMs and proteoforms, in additional to whole canonical proteins, given that it sequences individual peptides.

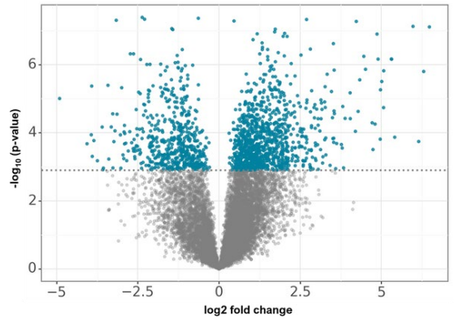
Computational software gains

Mass spectrometry can now generate multi-omics data at a much faster rate, and computing capacity has scaled to allow for this data to be made actionable. Today, advanced computational software, AI, and ML tools are capable of rapidly integrating these large-scale datasets to uncover drug targets, biomarkers, and biological insights to guide drug programs.

Case in point: Target identification in the newly “druggable” space

Historically, drug target selection has focused on a relatively small fraction of the human proteome. While the human body contains an estimated 20,000 proteins, with only about 4,000 have been considered “druggable”. However, innovative therapeutic modalities like ADCs and protein degraders are changing this landscape, able to access difficult-to-drug proteins as well as the more than 100,000 proteoforms in the proteome.

Using mass spectrometry-based discovery proteomics, we can assay more than 12,000 protein groups in tumors vs. normal human tissue, revealing a vast number of significantly changed proteins that could represent viable drug targets,



For example, the above study found that ~30% of the 12,000+ proteins measured are differentially expressed at an FDR < 0.05 in tumor samples.

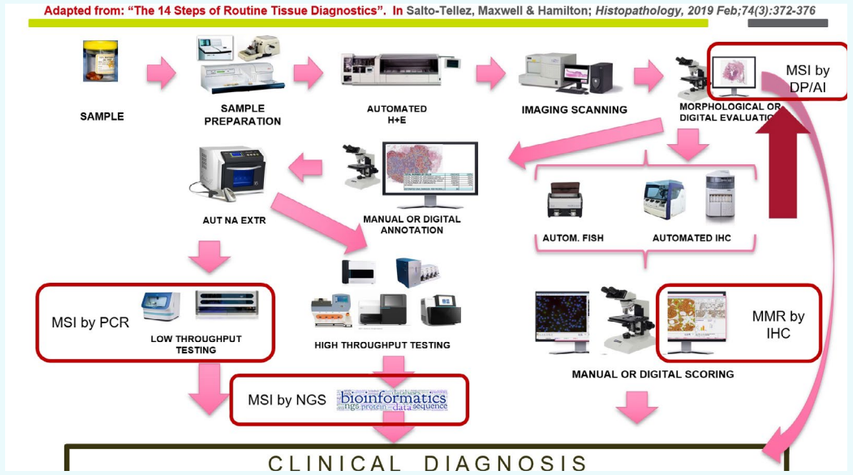
Learn more about how mass spectrometry is being developed to identify novel drug targets at sapient.bio/target-identification.

Multimodal Analysis Towards Biomarker Complexity

Manuel Salto-Tellez delivered a comprehensive presentation on the significance of multimodal analysis in tissue pathology, emphasising its potential to enhance the complexity and accuracy of biomarkers used in cancer diagnosis and treatment prediction. He began by introducing the concept of multimodal analysis, highlighting its ability to match the biological complexity of cancer with equally complex biomarkers.

Salto-Tellez provided a historical perspective on the evolution of tissue pathology, tracing its journey from the adoption of immunohistochemistry laboratories nearly fifty years ago to the more recent integration of genomic analysis and digital pathology. He posed a critical question about the next disruptive technology or analytical approach that could further improve patient outcomes. Despite the advancements brought by these technologies, he noted that the benefit of genomic analysis to patients remains modest, and the precise value of artificial intelligence (AI) in diagnostics is still being explored.

He emphasised the need for biomarkers with technical or analytical complexity to match the biological complexity of diseases like cancer, particularly in immuno-oncology. Salto-Tellez discussed the development and characteristics of successful digital pathology tools, which should be intuitive, meaningful, quantitative, and correlate with clinical outcomes. He highlighted the use of AI in analysing histological features, quantitating biomarkers, and predicting molecular status from images without nucleic acid analysis.



Salto-Tellez described the importance of a quality management system for developing tissue-based AI tools, including good machine learning practices and regulatory reviews. He provided examples of AI applications in pathology, such as analysing microsatellite instability and generating explainable results, demonstrating the potential of AI in clinical diagnostics.

He identified challenges in multimodal analysis, such as accessing hospital information in real-time and accrediting analytical tools, while emphasising the need for integrated diagnostics. Salto-Tellez concluded that the future of tissue pathology might lie in the comprehensive analysis of existing information systems, including digital images, to provide holistic integrated diagnostics.

Throughout the presentation, Salto-Tellez underscored the importance of integrating various analytical modalities with advanced information technology to achieve a synergistic effect in diagnostic value. He highlighted the need for real-time access to hospital information and the computational technology required to create effective multimodal analytical tools.

Salto-Tellez also discussed the potential of AI in clinical trials, noting that current attempts to create AI tools often come too late in the process. He advocated for bringing AI analysis upfront to maximise its benefits. He shared insights from collaborations with experts like Jakob Kather, emphasising the importance of using real-world data and clinical trials in validating new AI tools.

In his closing remarks, Salto-Tellez expressed gratitude to the laboratories at Queen's University of Belfast, ICR, and Royal Marsden for their contributions to the data presented. He left the audience with the idea that the future of tissue pathology might not involve a new disruptive technology but rather a comprehensive analysis of the diverse information systems available in hospitals.

Overall, Salto-Tellez's presentation provided a thorough overview of the current state and future potential of multimodal analysis in tissue pathology, highlighting the critical role of AI and integrated diagnostics in advancing cancer diagnosis and treatment.

Development of Ultra-Sensitive, Multi-Omic and Multi-Plex Assays Utilising a Novel Digital Microfluidic Technology

Nate Siegfried's presentation provided an in-depth overview of the company's innovative technology for biomarker analysis. Nate Siegfried, with a background in biophysics and RNA folding, shared his journey from his postdoctoral fellowship at UNC to his work in the lab of Mike Ramsey, which ultimately led to the founding of Codetta Bio. He also discussed his experience in industry, where he led the development of a therapeutic drug monitoring test from inception through FDA clearance.

The presentation began with an introduction to Codetta Bio's cutting-edge technology which stands out as a new biomarker discovery tool. Siegfried highlighted the unique capabilities of their custom microfluidic-based platform, which streamlines DNA, RNA, and protein biomarker analysis on a single platform and in a single analysis run. This efficiency is further enhanced by the platform's unprecedented flexibility, allowing new biomarkers to be easily added to multiplex panels. The technology's noise-cancelling feature eliminates background signals, a common issue in multiplex PCR assays and immunoassays, enabling modular design and highly sensitive assays.

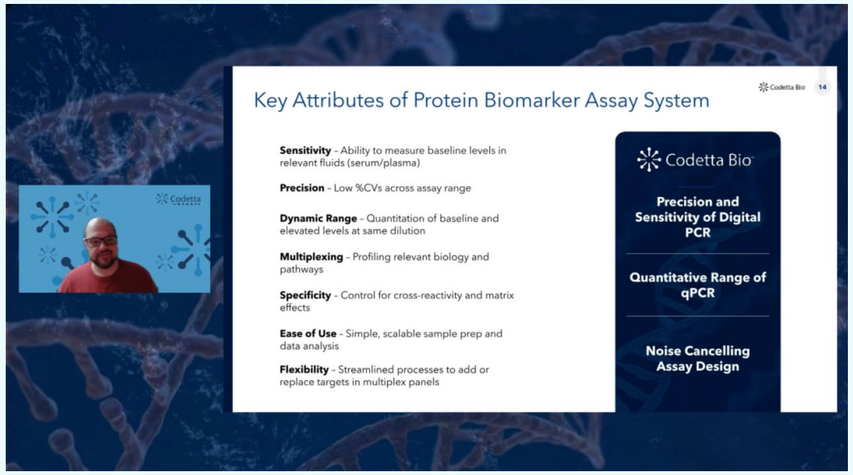
Siegfried explained that the platform combines the properties of digital and quantitative PCR on a single analysis chip, allowing for quantitation over a very broad dynamic range. This technological advancement enables the production of harmonised data in approximately two hours using a single instrument. He also introduced the Technology Access Programme (TAP), inviting attendees to explore how Codetta Bio's technology could drive their research forward.

The presentation then addressed the challenges of achieving harmonised multi-omic data with current technology. Siegfried pointed out that multiple instruments are typically required, each introducing different workflows and necessitating additional samples and precious material. This process is often complex, time-consuming, and costly, with instruments located in different labs. The inconsistency across instruments and methods complicates data integration, making it challenging to achieve harmonized, comparable insights and potentially introducing biases that obscure critical multi-omic insights.

In contrast, Codetta Bio's platform allows for the simultaneous analysis of DNA, RNA, and protein targets in multiplexed arrays, producing data in hours from a single instrument. This streamlined process provides sensitive and selective data from standard assay workflows, with harmonised data input and output handled in the exact same way. Siegfried emphasised the advantages of their platform, including reduced hands-on time, faster turnaround times, and the elimination of the need for overnight incubations.

Siegfried then delved into the technical details of their workflow, explaining how they begin with a slurry of dye-encoded beads, each bearing a specific capture molecule. The beads are mixed with the sample, allowing specific capture to occur, and the sample matrix is washed away. For protein targets, a secondary antibody carrying a DNA tag sequence forms an immunocomplex with its target antigen. The beads are then placed into the microfluidic chip, where each sample lane contains around 250,000 microwells per sample. Signal generation occurs in the tail portion of these wells, with positive signal beads producing glowing tails.

The noise-cancelling feature of their technology, which eliminates background signals, was further explained. Siegfried described how their beads serve to eliminate background noise, allowing for highly sensitive and specific assays. He also highlighted the platform's ability to quantitatively measure samples in both the very low concentration digital range and the more concentrated analogue range. This dual modality enables measurement over a very wide dynamic range.



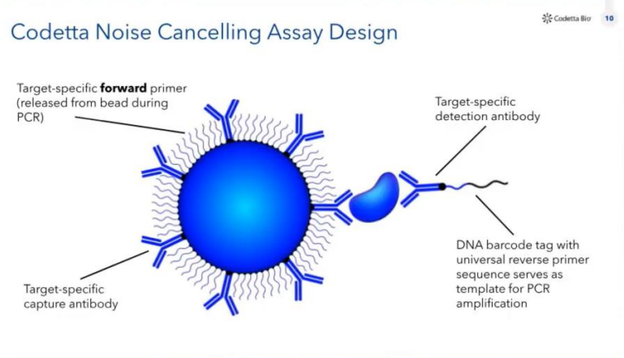
Siegfried concluded the presentation by showcasing the multi-omic capability of Codetta Bio's platform, which allows for the simultaneous detection of protein and nucleic acid targets on the same platform for the same sample. This capability enables truly integrated multi-omics analysis, providing a more comprehensive view of biological processes. He invited attendees to join their Technology Access Programme and explore how Codetta Bio's technology could help drive biomarker discovery.

Development of Ultra-Sensitive, Multi-Omic and Multi-Plex Assays Utilizing a Novel Digital Microfluidic Technology

Director of Assay Development, Nate Siegfried, presented on Codetta's new tool for biomarker discovery, and discussed how their technology drives new capabilities. He highlighted some examples of data produced from the platform, and provided context on how you could think about leveraging this technology in YOUR lab

"Our strategy is to develop an integrated platform that redefines multi-omics and sets a new standard of capability in the mid-plex translational research and clinical markets."

- Jacques Corriveau, *CEO of Codetta Bio*



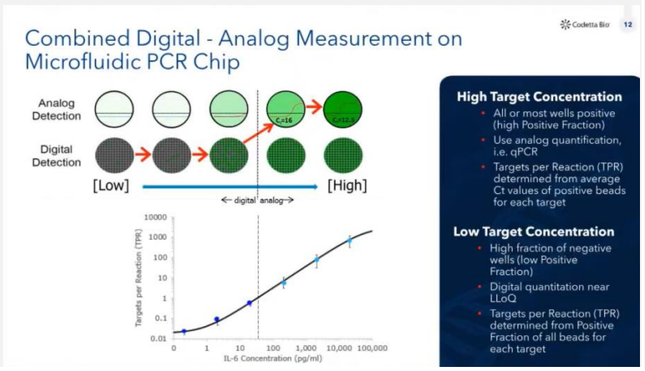
Noise Cancelling Assay Design

On the surface of each protein bead, we have immobilized a specific antibody, along with a specific forward primer. That primer matches the DNA tag found on the detection antibody for that target, but not any other. Since each target has a detection antibody with a unique tag sequence, productive PCR can only occur when the correct detection antibody is paired with the matching target bead. Off-target, non-specific binding events can't produce amplicon, thereby "turning off" the noise that is commonly a problem in multi-plex immunoassays, and allowing enhanced sensitivity.

Combined Digital & Analog Measurement

Another unique feature of Codetta's technology is the ability to quantitatively measure samples in both the low-concentration digital range, as well as the more concentrated analog range.

By combining these two modalities, we can measure samples over a very wide dynamic range; this is data we collected for IL-6 over 6 logs.



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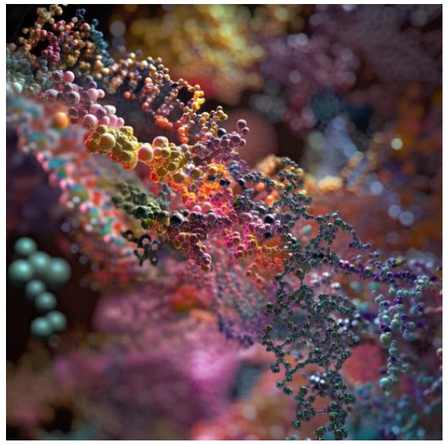
Introducing Sonata Services

Just as a classical **sonata** brings together two instruments to create a seamless composition, **Codetta Bio Services** unites the precision and depth of nucleic acid and protein analysis. This integrated approach enables researchers to explore and analyze key molecular components side by side, **creating a symphony of data and insights that drive discovery.**

With Codetta Bio Sonata Services, you can seamlessly integrate multiple dimensions of biological analysis into a single, cohesive performance. Much like a sonata balances contrasting movements, our platform **harmonizes complex data from both proteins and nucleic acids**, elevating your research to new levels of precision, clarity, and efficiency.



4-Plex Cytokine Assay
(IL-2, IL-4, IL-6, IL-7)

Researchers studying immune responses, inflammation, or conditions like COVID-19 can leverage our state-of-the-art technology to experience ultra-sensitive cytokine detection. Utilizing a unique combination of digital PCR and qPCR methods, our platform delivers an unprecedented dynamic range. Our novel noise-canceling assay design eliminates background signals found in today's multiplex assays.

For more information visit: codettabio.com/services

Codetta Bio Omics Assay
(IL-2, IL-4, IL-6, IL-7 + 2 custom nucleic acid targets)

The Codetta platform stands out as the first to provide an integrated solution for simultaneous analysis of **proteins and nucleic acids** from the same sample.

Using specific affinity reagents—capture antibodies for proteins and capture oligos for nucleic acids—our system ensures consistent and unified data output, simplifying research workflows and enabling comprehensive insights across multiple analytes.

The Codetta Bio Omics Assay lets you evaluate key cytokines across multiple indications and assess gene expression of your choice within the same plasma sample.

Dual Immune Activation Panel
(IL-2, IL-7 + 4 nucleic acid targets)

Our specialized assay offers comprehensive monitoring of immune activation, function, and recovery, delivering critical insights across diverse areas of research and treatment, including:

- Cancer Immunotherapy Monitoring
- Autoimmune Disease Research
- HIV Treatment and Immune Recovery
- Vaccine Development
- Immune Response Assessment

For broader omics insights, researchers have the option to assess gene expression alongside corresponding protein levels from the same sample.

Inflammatory Disease Biomarker Development Using Omics Approaches

Priyank Patel's presentation was an insightful exploration into the use of spatial multi-omics data to enable precision medicine in chronic inflammatory diseases. The presentation was divided into four sections, beginning with an introduction of the speaker, followed by an overview of the multi-omic technologies used, the challenges faced in spatial analysis, and the approach to addressing these challenges by building a spatial analysis paradigm. The final section showcased a vignette about the characterization of mucosal inflammation using this approach.

Priyank Patel, a senior scientist in the Molecular Histopathology and Spatial Biology group, focused on studying chronic inflammatory diseases such as interstitial lung disease, inflammatory bowel disease, and systemic sclerosis. The team integrated quantitative histopathology with spatial biology to generate insights and support drug discovery and biomarker identification. They used a variety of staining methods, from traditional H&E and colorimetric immunohistochemistry to spatial proteomics and transcriptomics, to probe human FFB tissues for mRNA or protein expression.

The presentation highlighted the use of various non-spatial and spatially resolved technologies to generate insights for specific projects. Starting with single-cell RNA sequencing, which provided a full transcriptome readout but was not spatially resolved, the team moved on to Visium, which offered spatial resolution but not at a single-cell level. For true single-cell resolution, they used NanoString's CosMx instrument, which was spatially resolved but limited to 6000 Plex mRNA panels. The team used these transcriptomic platforms for exploratory studies and hypothesis generation. Once a hypothesis was in place, they switched to the Lunaphore's Comet platform, a special proteomics platform that allowed them to probe for 38 proteins in the same tissue section for hypothesis validation.

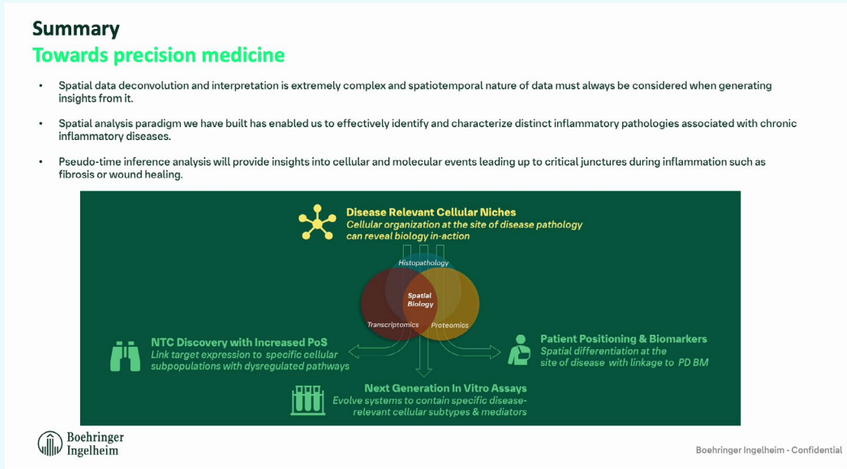
The data discussed in the presentation came from two sources: a small snippet generated from the Comet instrument and a larger dataset from a publication where authors performed 1000 Plex CosMx panels on FFP tissues from healthy donors and patients with UC and CD. The team used this dataset extensively for methods development.

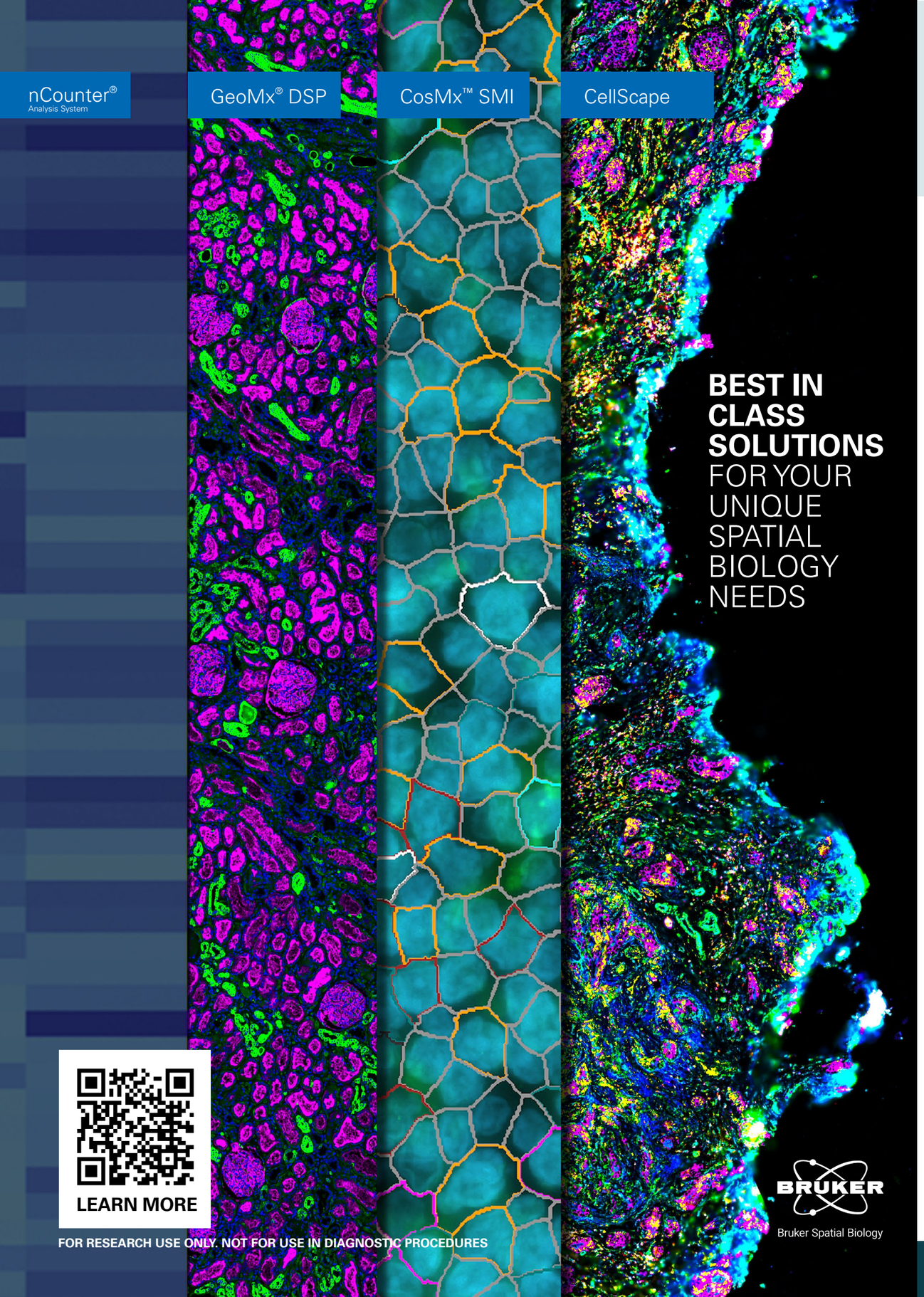
The presentation detailed the team's first experience analysing high-dimensional data with the Lunaphore's Comet platform, where they designed a 38 Plex IC panel to study innate immune response in mucosal inflammation using human IBD FFPE tissues. They began their spatial analysis journey by asking specific questions about the proximity of macrophages expressing their target of interest to epithelial cells during inflammation. Through quantitative analysis, they showed no statistical difference in proximity between uninflamed and inflamed mucosa.

The team faced challenges in effectively interpreting spatial data, leading them to build a hierarchical model of inflammation. This model considered different distance scales for cellular communication and tissue architecture. They identified distinct pathologies of inflammation within tissues and built a pseudo-time progression to understand the events and key drivers of inflammatory diseases. The hierarchical model allowed them to study cellular proximity, microenvironments, pathway enrichment, and more.

The presentation also covered the team's approach to characterising different hierarchical levels of tissue and understanding the cellular and molecular processes required to maintain homeostasis of uninflamed mucosa. They used spatial analysis to identify inflammation-associated niches and study their composition and contribution to inflammation. The team created signatures to build a pseudo-time progression or trajectory analysis, representing the progression from uninflamed mucosa to mild inflammation, chronic inflammation, and ulceration.

In conclusion, the presentation emphasised the complexity of spatial data deconvolution and interpretation and the need to avoid bias or artifacts. The team integrated histopathology, spatial transcriptomics, and proteomics to create a comprehensive view of spatial biology, supporting activities such as increasing the probability of success for portfolio projects, building disease-relevant in vitro models, and identifying biomarkers for patient positioning. The presentation ended with a Q&A session, where Priyank Patel answered questions from the audience.





Advancing Precision Medicine: The Role of Spatial Biomarkers

In her presentation, Espy Anguiano from Bruker Spatial Biology discussed the significant role and value of spatial biology and biomarkers in advancing precision medicine, particularly in the field of immuno-oncology.

Anguiano began by introducing the concept of spatial biology and its importance in precision medicine. She emphasised that while spatial biomarkers can be applied to various diseases and therapeutic settings, the focus of this presentation was on immuno-oncology. Anguiano provided a brief background on the subject before delving into the main topic of spatial biomarkers, highlighting the technologies offered by Bruker Spatial Biology.

The presentation outlined the advancements in cancer treatment over the past decade, largely due to the development of targeted therapies and associated biomarkers. Anguiano explained that the success of cancer treatment depends on multiple factors, including the type of therapy, the stage of the disease, and the expression of specific biomarkers. She noted that while immunotherapy has revolutionised cancer treatment, its response rates remain variable, ranging from 15% to 60%.

Anguiano highlighted the importance of biomarkers such as PD1 expression, tumour mutational burden (TMB), and microsatellite instability (MSI) in predicting responses to therapies. However, she pointed out that not all tumours benefit from these markers, and the development of resistance mechanisms and toxicity effects remain significant limitations. Anguiano emphasised the need for improved biomarker discovery approaches to better understand resistance mechanisms and uncover novel therapeutic strategies.

The presentation then shifted to the concept of spatial profiling, which generates protein or RNA expression data from distinct tumour compartments, thereby minimising bias and providing more accurate biomarker measurements. Anguiano explained that spatial profiling allows for more precise biomarker measurements and helps understand where biological processes are occurring within tissues. She introduced Bruker's suite of technology platforms designed for spatial biology, including GeoMx, CosMx, and CellScape.

Anguiano illustrated the value of these technologies through key case studies, demonstrating how spatial biomarkers have advanced precision medicine. She discussed a study by Merck that identified an 18-gene expression signature, known as the tumour inflammation signature (TIS), which predicts response

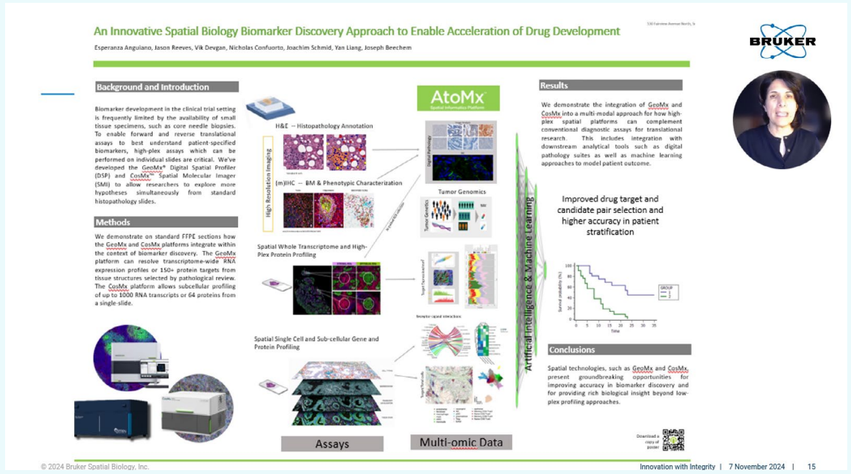
to PD1 blockade. Anguiano explained that bulk gene expression introduces confounding bias, but spatial profiling can resolve critical biomarker expression differences in spatial context.

The presentation also covered the technological platforms offered by Bruker Spatial Biology. The GeoMx platform is designed for high-throughput multiomic tissue profiling, while CosMx is a high-sensitivity subcellular spatial imager for transcriptomic phenotyping and single-cell analysis. CellScape is a flexible and robust spatial imager for single-cell spatial protein analysis. Anguiano emphasised that these platforms are highly synergistic and complement each other, providing comprehensive biomarker analysis.

Anguiano highlighted several studies that have made groundbreaking discoveries using spatial biomarkers. One notable study reported the association of B cells with immuno-oncology treatment response, revealing that tertiary lymphoid structures are biomarkers of response in IO therapy, particularly in melanoma. She stressed the importance of validating biomarkers discovered in small-scale studies through larger cohort studies to create real impact in precision medicine.

The presentation concluded with a discussion on the future of spatial biology, emphasising the need for standardization and best practices in spatial biology studies. Anguiano mentioned a recently published Best Practices article aimed at establishing guidelines for conducting spatial biology studies. She also highlighted the role of artificial intelligence and machine learning in advancing spatial biology and precision medicine.

Anguiano ended the presentation by expressing optimism about the future of spatial biology and its potential to transform precision medicine. She thanked the audience for their attention and looked forward to answering any questions.



Report Conclusion

The future of multiomics platforms for biomarker discovery and precision medicine is exceedingly promising. As spatial biology technology advances, multiomics platforms offer comprehensive ways to analyse tissue samples at unprecedented levels of detail. These platforms synergize to provide high-throughput, subcellular, and single-cell spatial analyses, significantly enhancing our understanding of disease mechanisms. The integration of spatial profiling allows for precise biomarker measurements, revealing critical insights into the location and role of biological processes within tissues.

Moreover, the application of artificial intelligence and machine learning is set to further revolutionize this field, enabling the analysis of complex data sets and the discovery of novel biomarkers. The establishment of guidelines and best practices will ensure the robustness and reliability of spatial biology studies. With these advancements, multiomics platforms will undoubtedly play a pivotal role in advancing precision medicine, leading to more effective and personalized therapeutic strategies.

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