POST EVENT PROCEEDINGS

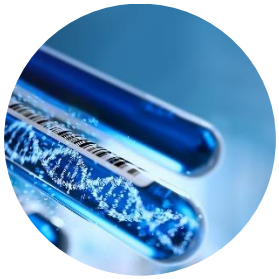
Biomarkers 2023

27 - 28 February 2023 | Manchester, UK

Earlier this year, Oxford Global was proud to present **Biomarkers 2023**, uniting senior-level experts to provide a focussed forum for thought-provoking discussion and to gain insights from the key figures in the biomarkers community.

Over 400 attendees engaged with esteemed pharmaceutical & biotech representatives as well as thought-leaders from academic & research institutions onsite and benefited from attending over 90 presentations to gain a forward-looking perspective on the latest technologies and strategies impacting biomarker research across multiple applications and therapeutic areas.

We are delighted to present you with concise and insightful summaries of presentations delivered by prominent thought leaders in this comprehensive post-event proceedings document.



CONTENTS

DAY ONE, TRACK ONE:

Identification & Validation In Oncology And Immuno-Oncology

Urine As A Source For Biomarker Analysis

Alexandra Sevko, Director, Translational Research, Prokarium

Alexandra Sevko, Director of Translational Research at Prokarium, has extensive experience in immuno-oncology, spanning over 20 years. She has worked in various laboratory settings, including clinical diagnostic labs, academic labs, and the industry. Her passion lies in leveraging different approaches to improve cancer treatment outcomes and enhance patients' quality of life.

The focus of her current work is a genetically attenuated Salmonella Typhi strain that is being explored for its potential in bladder cancer treatment. This strain can induce localized inflammation without systemic spread or prolonged survival, making it a promising candidate. The motivation for this research stems from the high cost and limited availability of Bacillus Calmette-Guérin (BCG), the standard treatment for non-muscle invasive bladder cancer.

Alexandra highlights that a single intravesical dose of this Salmonella strain could potentially elicit a strong immune response, making it a cost-effective alternative to BCG. Additionally, its facultative anaerobic nature allows it to accumulate in hypoxic tumor areas. The primary mode of action is believed to be immune stimulation, and the use of pathogenic bacteria differs from traditional microbiome therapy.

Urine is a valuable source for biomarker analysis in bladder cancer research. It provides insights into immune and inflammatory responses, immune memory formation, cancer recurrence, and drug response. Urine collection is non-invasive and easy, making it a convenient choice for such studies.

Alexandra discusses the challenges of maintaining sample quality during urine collection, transportation, and analysis, focusing on flow cytometry and proteomics. She presents data on the viability of urine samples after 24 and 72 hours of refrigeration, emphasizing that it's possible to analyze urine leukocytes by flow cytometry even after refrigeration.

In terms of proteomics, Alexandra mentions the absence of a golden standard for bladder cancer immunotherapy protein markers. Various panels have been proposed, but none have gained universal acceptance. She also raises

questions about normalizing protein biomarkers in urine samples, as systemic factors and local inflammation can complicate the normalization process.

In summary, Alexandra Sevko's presentation covers her extensive experience in immuno-oncology, the potential of a genetically attenuated Salmonella strain for bladder cancer treatment, the benefits of using urine as a biomarker source, and the challenges associated with maintaining sample quality and normalizing protein biomarkers in bladder cancer research.

The Balancing Act Of Predictive Biomarker Validation And Companion Diagnostic Development

Clare Balendran, Vice President, Head of Translational Development, Novo Nordisk

Clare Balendran, Vice President and Head of Translational Development at Novo Nordisk, discussed the challenges of developing predictive biomarkers and companion diagnostics in the context of drug development. She highlighted the discrepancies between the idealized, textbook approach to biomarker and diagnostic development and the realities of the drug development process.

Balendran emphasized several key reasons for this mismatch, including the need for interventional studies in novel target areas, high attrition rates in early drug development, and the pressure to streamline drug development timelines. She also noted a preference for broad, non-selected programs in many therapeutic areas outside of oncology.

To address these challenges, Balendran stressed the importance of proactive planning and preparing for diagnostic development, even if it cannot be implemented immediately. She underscored the need for alignment between the diagnostic and clinical teams and the importance of building a strong biomarker hypothesis based on target biology.

Balendran also discussed the significance of understanding regulatory requirements and engaging with health authorities to discuss viable strategies for clinical studies. She emphasized adaptability in the face of changing circumstances, as data, science, and project dynamics can evolve during drug development.

In conclusion, Clare provided valuable insights into the complexities of developing predictive biomarkers and companion diagnostics, particularly in non-oncology areas. Her presentation highlighted the importance of strategic planning, alignment, and adaptability to navigate these challenges effectively.

FS222, A Novel CD137/PD-L1 Tetravalent Bispecific Antibody, Modulates the Preclinical Tumor Microenvironment by Activating CD8+ T Cells Resulting In Tumor Growth Inhibition

Daniel Jones, Senior Scientist, F-Star Therapeutics

Daniel Jones, a Senior Scientist at F-Star Therapeutics, discussed FS222, a CD137/PDL1 tetravalent bispecific antibody. This molecule holds promise for cancer treatment due to its unique binding capabilities, impacting CD137 and PDL1.

The presentation highlighted how FS222's technology offers four binding sites, enabling potent binding and novel mechanisms of action. It aims to engage CD137-expressing cells with PDL1-expressing cells, enhancing immune responses specifically in high PDL1 areas.

The discussion delved into preclinical data, showing that FS222's potency increased with dose, without a plateau in sight. This suggested a lack of the "hook effect" seen in some drugs. Clinical trials were ongoing, with promising PK profiles and dose-dependent increases in soluble biomarkers.

Key in-vitro and in-vivo findings indicated FS222's potential for reducing tumor growth and complete regression in animal models. The presentation concluded with the importance of the biomarker strategy, shaping the clinical trial and aiding dose optimization.

Acknowledgments went to the FS222 team and, most notably, the patients participating in the trials.

Biomarkers And Beyond

Elizabeth Sheppard, Global Pricing & Market Access Director, Oncology Diagnostics, AstraZeneca

Elizabeth Sheppard, Global Pricing & Market Access Director, Oncology Diagnostics at AstraZeneca, delivered a talk discussing the role of biomarkers in precision medicine for cancer treatment. She expressed gratitude to Oxford Global for the opportunity and emphasized the importance of accuracy and precision in biomarker-based treatments, comparing it to hitting a target on a dartboard. She discussed how biomarkers have evolved over time and highlighted the significance of targeted therapies like HER2 in breast cancer treatment.

She discussed the different types of biomarkers, such as risk, diagnostic, prognostic, predictive, response monitor, and safety indicators. She

emphasized that biomarkers have revolutionized cancer treatment, increasing the success rates of clinical trials and allowing for personalized treatment plans.

She pointed out that the adoption of biomarkers faces challenges such as lab adoption, reimbursement policies, and the need for quality control to ensure accurate results. Regulatory frameworks and policy changes also impact biomarker utilization. She highlighted the rising incidence of cancer and the growing importance of biomarkers in early detection and screening. The future holds a strong pipeline of biomarker-based diagnostic methods, particularly in oncology, and their continued role in improving clinical development and patient outcomes.

Validation, Qualification, Companion Diagnostic – What Is The Difference?

Stephanie Traub, Associate Director, UCB

Stephanie Traub, Associate Director at UCB, presented on the distinctions among validation, qualification, and companion diagnostics in the context of biomarkers. Her talk stemmed from a previous biomarker analysis workshop and aimed to provide a comprehensive overview of these concepts.

Traub began by explaining biomarker qualification, defining it as demonstrating a biomarker's reliability within a specified context of use. She clarified that this process doesn't automatically make the biomarker suitable for clinical practice or in vitro diagnostics and mentioned the FDA's role in evaluating and certifying biomarkers.

The discussion then turned to assay validation, with Traub detailing the process of customizing evidence and rigor to align an assay with its intended purpose. She emphasized that the validation approach depends on factors like context of use, technology, and intended application of biomarker data.

Context of use emerged as a pivotal consideration in biomarker development, encompassing the specific purpose and application of a biomarker assay, considering factors like analytical platforms, study design, biomarker biology, and its relevance to pharmacological interventions.

Traub introduced fit-for-purpose validation as a method to adapt validation parameters based on data use, applying different levels of rigor for exploratory biomarker research or regulatory purposes.

Clinical validation's importance was stressed, involving demonstrating a biomarker's correlation with clinical or biological states in a predefined context of use to determine its real-world relevance and utility.

Companion diagnostics were highlighted as crucial tools, helping healthcare professionals assess treatment risk-benefit profiles based on a patient's biomarker status. Traub explained the development pathway from fit-for-purpose biomarker assays to companion diagnostics, requiring an active decision-making process with a focus on clinical utility.

The discussion also touched on differences in developing biomarker assays for clinical trials and companion diagnostics, with the former involving establishing a prototype assay, verifying performance, and assessing suitability for the intended patient population. In contrast, companion diagnostics require a stable, finalized assay suitable for manufacturing and ensuring diagnostic accuracy in the intended patient group.

Finally, Traub mentioned the regulatory frameworks governing companion diagnostics by the FDA and the European Medicines Agency (EMA), highlighting distinctions from regulations concerning biomarker qualification and fit-for-purpose assays.

In conclusion, Stephanie Traub's presentation provided clarity on the distinctions among validation, qualification, and companion diagnostics in the realm of biomarkers. She emphasized the importance of understanding the intended use and context of biomarker data when developing and applying these tools in drug development and clinical practice.

Towards The Identification Of Biomarkers Of NASH/NAFLD Disease Progression

Vincent Mikol, Precision Medicine Head, Sanofi

Vincent Mikol, the Precision Medicine Head at Sanofi, discussed a collaborative project focused on identifying biomarkers for predicting the progression from non-alcoholic fatty liver disease (NAFLD) to non-alcoholic steatohepatitis (NASH). NAFLD and NASH are conditions that can lead to serious liver problems, including cirrhosis and liver cancer.

Key points from his talk include:

1. **Prevalence of NAFLD and NASH**: NAFLD is prevalent in the Western world, affecting up to 20% of the general population and increasing significantly in obese individuals and adolescents. NASH is a more advanced stage of NAFLD characterized by inflammation and fibrosis.
2. **Unmet Medical Need**: NASH is a silent but dangerous condition with no approved therapies, despite its increasing prevalence and severe health implications. It is estimated to become a $35 billion market.

3. **Challenges in Diagnosis**: Diagnosing NASH typically involves invasive procedures like liver biopsies, which are late-stage and associated with risks. There's a need for non-invasive diagnostic tools.
4. **Collaborative Project**: Vincent's presentation focused on one aspect of a multi-faceted project that involved a unique collaboration between different research entities, funded by the French government and Sanofi. They had access to annotated human liver samples and data from patients who underwent bariatric surgery.
5. **Biomarker Identification**: The project aimed to identify non-invasive biomarkers to diagnose NASH and predict its progression. They screened a wide range of clinical and biological parameters, including proteins, lipids, microRNAs, and genes.
6. **Model Development**: By combining clinical and biological biomarkers, they developed scoring functions to differentiate between healthy, NAFLD, and NASH patients. Their models showed promising diagnostic accuracy with an area under the curve (AUC) of approximately 0.8.
7. **Validation**: The scoring functions were validated in multiple independent cohorts, showing good sensitivity and specificity, particularly in predicting NASH progression.
8. **Back Translation**: The project also involves translating their findings back into preclinical mouse models to validate if these models can be used for drug discovery and testing.

In summary, Vincent Mikol's presentation outlined a promising development in identifying biomarkers for NASH diagnosis and progression prediction, with the potential to improve patient care and advance drug development efforts in this critical area of unmet medical need.

Analysis Of LAG-3 To Support A Bispecific Immunotherapy Clinical Programme

James Lawrence, Senior Bioanalytical Biomarker Outsourcing Manager, F-Star Therapeutics

James Lawrence, Senior Bioanalytical Biomarker Outsourcing Manager at F-Star Therapeutics, presented an overview of F-Star Therapeutics' clinical program, focusing on FS118, a tetravalent binding antibody designed to target PD-L1 and LAG-3, which are checkpoint inhibitor targets. The presentation covered their unique antibody technology, the mechanism of action for FS118, and the importance of biomarkers in their clinical trials.

F-Star Therapeutics employs a novel antibody platform technology with tetravalent binding, featuring two binding arms and two F-cabs, providing a differentiated mechanism compared to traditional antibodies.

FS118 is a bispecific antibody that targets PD-L1 and LAG-3. The key feature of FS118 is the shedding of LAG-3, which counters acquired resistance associated with checkpoint inhibitor treatments. This allows for more prolonged and effective treatment.

Preclinical data demonstrated that FS118 outperformed the combination of individual antibodies in a mouse Casanova tumor model. Moreover, it was shown that FS118 induces the shedding of LAG-3, which is mediated by metalloproteinases (Adam 10 and Adam 17).

In clinical trials, FS118 is tested in two patient groups: CPI-resistant patients and CPI-naive patients, focusing on overcoming PD-1 resistance and preventing resistance from developing, respectively.

James Lawrence emphasized the importance of using biomarkers for FS118, particularly soluble LAG-3, as a surrogate for target engagement and for PK/PD modeling. The context of use for the biomarker was defined early on in the development process.

The biomarker assay was developed to ensure sensitivity, precision, and reproducibility. The assay was designed to measure total LAG-3 to account for both free and drug-bound forms, making it suitable for PK/PD modeling. Sample prep stability was also validated to ensure reliable results.

Clinical data showed an increase in soluble LAG-3 levels after the administration of FS118, and this effect was maintained through subsequent treatment cycles. The data supports the biomarker's use in PK/PD analysis.

In conclusion, FS118's unique mechanism of action, targeting both PD-L1 and LAG-3, offers potential benefits in overcoming resistance to checkpoint inhibitors. The biomarker assay developed for soluble LAG-3 showed promising results in clinical trials and can be incorporated into future trials to help assess treatment efficacy and inform dosing decisions. Lawrence thanked the patients and clinical teams involved in the trials for their contributions to the development of FS118.

Biomarkers In Clinical Development For Neurodegenerative Disorders

Jordi Clarimon, Lead Specialist, Clinical Biomarkers, H. Lundbeck A/S

In his presentation, Jordi Clarimon, Lead Specialist in Clinical Biomarkers at H. Lundbeck AS, discussed the importance of biomarkers in clinical development for neurodegenerative disorders. He highlighted the need for biomarkers to detect early signals, demonstrate target engagement, and support decision-making in clinical trials.

Clarimon outlined the seven categories of biomarkers identified by the FDA, which range from diagnostic and monitoring biomarkers to predictive and safety biomarkers. He emphasized the importance of reproducibility and the challenges in finding reliable biomarkers, especially in the context of neurodegenerative diseases.

The presentation also discussed the implementation of fluid biomarkers in clinical trials for neurodegenerative disorders, including Alzheimer's disease, Parkinson's disease, and Lewy body pathology. Clarimon highlighted the use of novel technologies and more sensitive assays to detect and monitor these biomarkers.

In conclusion, Clarimon stressed the significance of the context of use for biomarkers and the need for robust biomarkers for non-Alzheimer's disease proteins. He also mentioned the potential of using tissues like olfactory mucosa, submandibular gland, and skin for biomarker analysis and the promising developments in biomarker technologies.

DAY ONE, TRACK FOUR:

Digital Pathology & AI-Based Imaging For Biomarker Research

Approaches To Integrating AI Into Image Analysis

Alice Gosselin, Digital Pathology Data Scientist, Sanofi

In her presentation, Alice Gosselin, a Digital Pathology Data Scientist at Sanofi, discussed the integration of artificial intelligence (AI) into image analysis in the context of digital pathology. She highlighted the increasing complexity of data gathered from phenotypical, morphological, and spatial information in the field of digital pathology, emphasizing the need for advanced analysis methods.

Gosselin introduced the audience to the EmuCan consortium, which focuses on integrated immuno-profiling of large cancer patient cohorts, aiming to better understand the immune system in the tumour microenvironment, patient responses to treatment, and potential targets for future therapies.

The dataset used for the presentation focused on images from biopsies of patients with advanced non-small cell lung cancer, particularly utilizing imaging mass flow cytometry, which provides data on more than 40 phenotypical markers, spatial coordinates, and morphological characteristics of cells.

Gosselin explained the two key steps in the analysis pipeline: dimension reduction and clustering. For dimension reduction, the presentation introduced three approaches using autoencoders (neural networks designed to reduce data dimensions): classic, classical spatial, and spatial attention. These methods aimed to extract relevant features from the data while minimizing reconstruction errors.

The presentation also described three clustering approaches: K-means, PhenoGraph, and Spatial-SORT. PhenoGraph utilizes a nearest-neighbour graph to identify clusters, while Spatial-SORT incorporates spatial information and prior expression metrics or anchor metrics to refine clustering results.

Gosselin presented a heatmap generated using PhenoGraph with spatial attention autoencoders, illustrating the identification of different cell populations within the tumour microenvironment, including T cells, macrophages, and potential immuno-resistant regions.

In conclusion, the presentation highlighted the potential of combining dimension reduction and clustering techniques, along with spatial information, to better understand cell interactions and the mechanisms of action within the tumour microenvironment, offering insights for future treatments. Ongoing

research aims to further refine these analyses for improved biological interpretation.

DAY TWO, TRACK ONE:

Biomarker Identification & Validation: Neuroscience, NASH & Co-Morbidity

Digital Biomarker Strategies For Successful Development Of Neuroscience Targets

Jennifer Barnett, Chief Executive Officer, Monument Therapeutics

Jennifer Barnett, CEO of Monument Therapeutics, discussed the company's innovative approach to neuroscience drug development during a presentation. She began by introducing the concept of digital biomarkers, which are measures of brain function that can be assessed digitally and are correlated with both normal brain functioning and disease processes.

Barnett explained that Monument Therapeutics uses these digital biomarkers not as endpoints in clinical trials but to address a significant challenge in neuroscience drug development. Many neuroscience drugs tend to fail in clinical trials, often due to the lack of biologically specific diagnostic criteria for patient enrolment. The company uses biomarkers to identify subgroups of patients who share a common brain abnormality, allowing for more targeted drug development.

The first lead program focuses on cognitive impairment associated with schizophrenia. Barnett emphasized that while antipsychotic medication can address positive symptoms of schizophrenia like delusions and hallucinations, cognitive impairment remains a major challenge. Monument Therapeutics uses digital biomarkers to identify patients likely to respond to a novel drug that boosts nicotinic signalling, which is associated with cognitive function. The company's approach includes a fixed-dose combination of two drugs designed to improve cognitive function in a subgroup of patients with schizophrenia.

The second program addresses postoperative cognitive decline (POCD), a condition where surgery can lead to permanent cognitive impairment due to neuroinflammation. Barnett explained that Monument Therapeutics has developed a digital biomarker to identify individuals at risk of POCD. They are also developing a drug called Mt. 1980, which has demonstrated promising results in reducing neuroinflammation in preclinical studies. The drug is administered prophylactically to prevent neuroinflammation in high-risk patients undergoing surgery.

Barnett highlighted the potential applications of their work, including addressing cognitive dysfunction caused by post-COVID symptoms and chemo brain, a cognitive problem experienced by some chemotherapy patients. She concluded by emphasizing the importance of detecting and treating cognitive impairments and expressed her company's interest in collaborating with others in these areas of unmet medical need.

Biomarker Findings From Parkinson's Disease Patients Undergoing CDNF Treatment

Kira Holmstrom, Head of Biomarker Research, Herantis Pharma

Kira Holmstrom is Head of Biomarker Research at Herantis Pharma, a small biotech company based in Finland, originally a spinoff from the University of Helsinki. Their primary focus is on developing disease-modifying therapies for Parkinson's disease. Holmstrom discussed their research, which involved a Phase 1 study in Parkinson's patients and a focus on biomarkers.

Parkinson's disease is characterized by disrupted protein homeostasis, increased protein misfolding, and protein aggregation, leading to cell death and neuroinflammation. Alpha-synuclein is a prominent protein associated with Parkinson's disease. Herantis Pharma is developing a treatment based on C, D, and F, an endogenous protein involved in the unfolded protein response pathway, which regulates cellular stress caused by protein misfolding.

They conducted studies on dopaminergic neurons, both in vitro and in rodent models, demonstrating that C, D, and F can promote neuron survival by modulating the unfolded protein response. However, the treatment required an invasive delivery method, limiting its application.

In their Phase 1 study, Herantis Pharma assessed the safety and tolerability of C, D, and F, while also exploring biomarkers. They used digital biomarkers, such as bradykinesia and dyskinesia scores, imaging of dopamine transporters, and cerebrospinal fluid (CSF) biomarkers. The study showed safety and some promising effects on motor symptoms and biomarkers.

Holmstrom discussed the challenges of the invasive delivery method and presented a new peptidomimetic compound called Her96, which maintains the functionality of C, D, and F but can be administered peripherally. Preclinical studies showed it to be neuroprotective and effective in animal models of alpha-synuclein toxicity. They have received regulatory approvals to begin a Phase 1 trial with Her96.

Holmstrom emphasized the importance of biomarkers to support target engagement and efficacy in clinical trials. They are working on translating their findings into clinical efficacy and identifying key biomarkers for disease progression in Parkinson's disease.

The presentation also mentioned exploratory biomarkers related to alpha-synuclein and showed correlations between treatment biomarkers and alpha-synuclein responses. In conclusion, Herantis Pharma is actively progressing from preclinical to clinical phases in their pursuit of developing a disease-modifying therapy for Parkinson's disease.

Identification Of Clinically-Relevant Genetic Subgroups For Parkinson's Disease

Neil Humphryes-Kirilov, Associate Director of Human Genomics, C4X Discovery

Neil Humphryes-Kirilov, Associate Director of Human Genomics at C4X Discovery, discussed their work in Parkinson's disease. They use a multimodal analysis platform called Patient See that leverages genetic data to identify clinically relevant subgroups within the Parkinson's population. Traditional drug discovery in neuroscience is lengthy and failure-prone, often due to a lack of understanding of why some patients respond to treatments while others do not. They aim to investigate and stratify disease populations based on genetics to better understand drug responses.

Their approach involves comparing the genetics of Parkinson's patients to a matched healthy control group, conducting case-control analyses to identify genetic markers associated with the disease. However, they emphasize the need to move away from a univariate approach, as complex diseases involve multiple sources of genetic variation. Their platform, Patient See, employs a Bayesian approach to transform genetic data into a numerical matrix, allowing for more comprehensive analysis.

In their study on Parkinson's disease, they discovered genetic subgroups within the patient population that were distinct from the traditional risk alleles. These subgroups represented 20% to 50% of the population and appeared to influence disease progression and manifestation. Further analysis revealed unique genetic risk signatures for each subgroup, suggesting different regulatory pathways.

Collaboration with an academic group and a retrospective analysis of a failed phase three Parkinson's trial indicated that one of their genetic subgroups responded to the trial drug, while others did not. This finding holds promise for tailoring treatments to specific patient subgroups.

C4X Discovery also applies their platform to other complex diseases like ulcerative colitis, Crohn's disease, and rheumatoid arthritis, where they have identified genetic subgroups as well. They aim to gather more data to understand the genetics of these diseases further.

Overall, their platform helps identify biomarkers, understand disease biology, prioritize pathways, and discover new druggable targets for various diseases. They encourage collaboration and data sharing to advance their research efforts.

DAY TWO, TRACK TWO:

New & Emerging Biomarker Technologies & Data Analytics

Spatial And Multi-Omic Biomarkers In Age Related Diseases

Gayle Marshall, Head of Biomarkers, Medicines Discovery Catapult

Gayle Marshall, Head of Biomarkers at Medicines Discovery Catapult, discussed the importance of biomarkers and spatial capabilities in understanding the ageing process and its impact on various diseases. Marshall emphasized that ageing is a universal experience that often leads to chronic ailments, impacting physical performance and resilience. Biomarkers play a crucial role in comprehending the ageing process and its connection to diseases, with multi-omics technologies providing valuable insights. These insights can inform drug discovery programs aimed at enhancing not just lifespan but also health span.

Marshall highlighted the financial burden of ageing, with older patients consuming a significant portion of healthcare costs. She explained that ageing affects mental and physical capacity, influenced by environmental factors and events. Accelerated ageing can lead to diseases and multi-morbidity, such as arthritis, cardiovascular issues, and neurodegeneration. Despite increased lifespan, health span hasn't improved at the same rate, making it an area worth exploring to make a positive impact.

Marshall discussed a collaboration called The UK Spine, which focuses on improving the health span of patients with age-related conditions. This partnership involves academia and industry, aiming to accelerate discovery in ageing research.

She shared a study that aimed to identify a patient's biological age by analysing their blood samples. Using the nine hallmarks of ageing and a panel of around 400 genes, the study found a signature that could potentially determine biological age from plasma samples.

Marshall explained the diverse platform capabilities at Medicines Discovery Catapult, including genomics and mass spectrometry, which enable hypothesis-free analysis of biomarkers. She presented several case studies, including one involving innovative therapeutics for ageing, where specific targets were identified as age-related or disease-related.

Another case study explored the potential of repositioning existing therapeutics for aging-related issues. Bisphosphonates, commonly used for

osteoporosis, showed promise in reducing mortality following hip fractures and in other areas.

In conclusion, Marshall stressed the importance of biomarkers in understanding ageing and potential drug discovery programs. She mentioned ongoing research efforts in the United States, like the TIME study, which targets ageing with the aim of enhancing health span.

Integrating Pathology With Spatial Proteomics To Deconvolute Crohn's Disease

Priyank Patel, Senior Scientist, Boehringer Ingelheim

Priyank Patel, a Senior Scientist at Boehringer Ingelheim, discussed their approach to integrating pathology with spatial proteomics data to gain insights into Crohn's disease and explore potential therapeutic targets for the condition.

Crohn's disease is characterized by chronic inflammation driven by myeloid cells that play a significant role throughout the disease process. Patel's team aimed to understand the heterogeneity of myeloid cells during inflammation. They optimized a 40-protein marker immunohistochemistry panel and performed staining on tissues from Crohn's disease patients.

The data analysis began with the identification of unique niches within the tissue samples, leading to the identification of 14 meta-clusters with distinct pathologies. Patel explained that their analysis had two parallel streams: single-cell analysis to identify cellular heterogeneity and expression patterns of targets, and disease context analysis to characterize the pathologies associated with these meta-clusters.

Patel highlighted the expression patterns of two targets within different cell populations and meta-clusters. Target 1 was widely expressed, especially in lymphocytes and myeloid cells, while Target 2 was more myeloid-centric and less expressed in other cell types.

The next step involved examining the spatial relationships between cells expressing these targets within different pathologies. Patel showed how the localization of macrophages expressing both targets varied between inflamed and uninflamed areas of the mucosa, suggesting distinct roles in the inflammatory process.

The team then delved into the phenotypic differences of macrophages found in inflamed and uninflamed areas, identifying distinct phenotypes based on differential protein expression. They inferred that the macrophages expressing their target in inflamed areas were involved in epithelial barrier regulation.

Patel discussed ongoing work involving in vitro confirmation of their findings and the implementation of algorithms to automate pathological analysis. They also plan to integrate spatial transcriptomics and proteomics data for deeper insights.

In conclusion, Patel's presentation demonstrated their strategy to combine spatial proteomics data with pathology to gain a comprehensive understanding of Crohn's disease and identify potential therapeutic targets. The ultimate goal is to explore the functional roles of these targets in disease processes.

DAY TWO, TRACK FOUR:

Genomic & Multi-Omic Markers in Drug Discovery and Development

Mapping Cellular Interactions Via Photocatalytic-Based Proximity Labelling

Cory H. White, Principal Scientist, Merck

Cory H. White, a Principal Scientist at Merck, presented a method known as photocatalytic cell tagging during their talk. This innovative approach aims to label cells and their interactions with high precision. White explained that the surface of a cell is organized with proteins, some of which are close together due to biological relevance, such as ligands and receptors. Understanding these interactions is crucial in studying diseases like cancer and the immune system. Traditional methods, like peroxidase-based labelling, lack the required spatial resolution.

To address this, White's team developed a new approach using photocatalysts, which are activated by light. Unlike enzymes, photocatalysts are smaller and less likely to interfere with cell interactions. They offer better spatial and temporal control over labelling without introducing toxic substances.

White presented experimental results, demonstrating that photocatalytic cell tagging successfully labelled interacting cells with high spatial resolution and without harming the cells. This method could be applied to various cell systems, making it valuable for studying complex biological processes.

In one experiment, they used photocatalytic cell tagging to label interacting cells and then performed single-cell sequencing to characterize these cells. This approach allowed them to distinguish interacting cells from non-interacting cells and explore phenotypic differences.

Overall, photocatalytic cell tagging is a versatile, non-toxic, and highly precise method for studying cell interactions, making it a promising tool in biomedical research.

Genomic Analysis In Routine Cancer Care: A New Narrative On Value Frameworks And Partnership Models

Philip Beer, Chief Scientific Officer; Chair, Step Pharma; BIVDA Genomics Working Group

Philip Beer, Chief Scientific Officer and Chair of Step Pharma, discussed the state of genomics in clinical practice, particularly in the context of the United Kingdom. He highlighted the growing role of genomics and cancer biomarkers in oncology drug development and clinical practice.

He began by emphasizing the increasing use of genomic biomarkers in cancer treatment. He cited data that showed the availability of biomarker-associated therapies for various types of advanced cancer. However, he also pointed out the need for better screening to ensure that eligible patients receive these therapies, which might not be happening effectively in the UK.

Beer discussed the evolving perspective on clinical trials, particularly phase one trials, as potential therapies for cancer patients. He highlighted a meta-analysis showing that the presence of a genomic biomarker significantly increases the chances of success in phase one clinical trials.

Regarding the current status of genomics in the UK, Beer mentioned England's strong vision for the use of genomics and the reconfiguration of genomic services. However, he pointed out that despite the vision, the reality is still a work in progress. Access to biomarker testing remains a challenge, and the UK lags behind some other European countries in this regard.

Beer introduced a report being prepared by a working group that he chairs, which aims to address the challenges and opportunities of genomics in clinical practice, particularly in the UK. The report will focus on the value framework of genomics and explore models for better collaboration between the commercial sector and the healthcare system.

He concluded by envisioning a future where every patient is studied, and knowledge gained from these patients is continuously fed back into the healthcare system to adapt treatments. This self-learning healthcare system relies on the integration of genomics and biomarkers into clinical practice.

In summary, Philip Beer's presentation highlighted the increasing importance of genomics in cancer treatment and clinical trials, the challenges facing the UK in fully implementing genomics in clinical practice, and the need for collaboration and innovative models to drive progress in this field.