POST EVENT PROCEEDINGS

NextGen Omics US 2023

30 - 31 March 2023 | Boston, USA

Oxford Global were pleased to share with you the 2023 programme of **NextGen Omics US: In Person**. The event featured 3 outstanding programmes covering the latest innovations, developments, and opportunities of the omics market: **8th Annual Next Generation Sequencing & Clinical Diagnostics Congress**, **8th Annual Single Cell & Spatial Analysis Congress**, and the **8th Annual Genome Editing Congress**. This key omics-focused event returned with an engaging programme featuring cutting-edge presentations and interactive sessions such as roundtables, panel discussions and workshops. Providing a unique opportunity to maximize your event experience, you had the chance to participate in engaging discussions and meetings delving into some of the main areas of the industry: NGS workflows, clinical genomics, spatial technologies & bioinformatics, single cell tools & clinical applications, and novel genome editing tools & therapeutic applications.

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.

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Keynote Address:

Computational Biology – The Next Revolution in ssCancer Diagnostics

Mark Gustavson, Senior Director, Translational Medicine, Oncology R&D, AstraZeneca

In his presentation on Computational Pathology, Mark Gustavson highlighted how this field represents the next revolution in cancer diagnostics, following the advancements in molecular pathology and genomics. Computational pathology goes beyond traditional digital pathology by utilizing image analysis and machine learning techniques to provide objective and quantitative data, which enables more accurate and reliable diagnostic information.

The talk emphasized the historical progression in pathology, starting from the ability of pathologists to visually observe and understand tissue morphology and protein expression. With the advent of molecular pathology and omics technologies, diagnosis and treatment have seen significant improvements. However, the current focus is on computational pathology as the third generation in this evolution, aiming to develop approved companion diagnostics using computational methods.

Gustavson introduced the Quantitative Continuous Score (UCS), a novel approach that allows for the quantification of protein expression and spatial heterogeneity within tissue samples. Traditional pathology often relies on subjective visual interpretation and categorical scoring, which can be limited and imprecise. In contrast, UCS uses artificial intelligence and deep learning algorithms to provide continuous and quantitative data, enabling more detailed and accurate analysis.

One critical application of UCS is in the assessment of HER2 expression in breast cancer patients, particularly relevant for predicting the response to antibody drug conjugates (ADCs). Traditional HER2 scoring categorizes patients into HER2-positive and HER2-negative groups, but UCS provides a more nuanced analysis by quantifying the level of HER2 expression and spatial distribution within tumor samples. This information proves vital in determining the effectiveness of ADCs, as it accounts for spatial heterogeneity and bystander activity, where not every cell needs to have a target for the treatment to be effective.

By leveraging UCS, researchers can achieve a deeper understanding of target expression, heterogeneity, and spatial distribution, enabling more precise patient stratification and improved treatment selection. Additionally, the

approach allows for benchmarking against clinical data, ensuring that cut-offs and criteria for target positivity are defined based on clinical efficacy rather than predefined categorical thresholds.

The talk also hinted at the potential of combining computational pathology with other omics data, such as mass spectrometry, to further enhance target prioritization and better characterize the tumor microenvironment.

Overall, computational pathology promises to revolutionize cancer diagnostics by providing pathologists and clinicians with advanced tools for quantification and spatial analysis, ultimately leading to more personalized and effective cancer treatments.

Day One Track One: Single Cell Omics & Multi Omics Analysis: Current & Emerging Tools And Data Analysis

Moving the Needle From Low Ng- To Sub-Ng – Level Samples And From Small Cell Populations To Single Cells in Enabling Technologies For Proteomics And Glycomics Profiling

Alexander Ivanov, Associate Professor, Northeastern University

Alexander Ivanov's presentation delved into advancements in proteomics and glycomics profiling, particularly focusing on pushing the limits of sensitivity to work with extremely low sample amounts and even single cells. The main idea was to decrease flow rates in liquid phase separation to improve the signal in mass spectrometry detection. By doing so, the ionization efficiency could be increased, ionization suppression reduced, and ions transferred more efficiently to the mass spectrometer.

Various separation modalities were explored, such as polymerized monolithic columns, porous layer open tubular columns, and capillary electrophoresis. Interfaces like the Morini interface were utilized to enhance transfer efficiency and reduce noise, leading to improved identification results.

The experiments demonstrated substantial gains in signal-to-noise ratios and identification results, enabling analysis of samples as small as low nanograms and even individual cells. This technology opens up new possibilities for single-cell analysis, shedding light on cellular heterogeneity and unique proteomic profiles.

Furthermore, the presentation highlighted the development of top-down proteomics approaches, analyzing intact proteins from cells without the need for digestion. This allowed for a comprehensive analysis of proteoforms and modifications, providing valuable insights into cellular processes.

Additionally, Alexander Ivanov's team explored the analysis of glycans using capillary electrophoresis coupled with mass spectrometry. The research achieved quantification of glycans at the single-cell level, further expanding the scope of the study.

The talk emphasized the potential impact of these advancements in the field of proteomics and glycomics, with possibilities for studying a wide range of biological molecules with unprecedented sensitivity and resolution. Future

directions include further optimization of the technology and the exploration of various cell types and phenotypes to broaden its applications.

SIMBA – Building Interpretable Regulatory Maps Using Graph Embedding On Single Cell Multiomics Data

Luca Pinello, Associate Professor of Pathology, Harvard Medical School and Massachusetts General Hospital

In Luca Pinello's presentation, SIMBA, which stands for "Building Interpretable Regulatory Maps Using Graph-Embedding On Single-Cell Multiomics Data," is introduced as a computational tool that addresses the challenges of integrating single-cell multiomics data. The advent of single-cell technologies has enabled the profiling of various molecular features at unprecedented resolution, including gene expression, chromatin accessibility, DNA methylation, and more.

The core question Luca Pinello addresses is how to effectively leverage this rich data to gain insights into gene regulation and cellular heterogeneity. To achieve this, he proposes building a regulatory map that optimally integrates the different matrices representing various molecular features. The map aims to organize cells based on their similarities, much like the common practice of clustering cells to identify distinct populations.

However, SIMBA goes beyond traditional clustering approaches by incorporating graph embeddings. These embeddings represent important features and their relationships on the regulatory map. By doing so, the map gains an additional layer of information, allowing researchers to study not only the cells' spatial arrangement but also the relevance and impact of specific features on gene regulation.

Luca draws an analogy between the regulatory map and a city map with additional metadata. Much like how a city map can show not only buildings but also schools, parks, and restaurants, the regulatory map in SIMBA can display cells and important molecular features, such as gene regulatory elements (promoters, enhancers), transcription factor binding sites, and more.

The presentation highlights that the current approach in single-cell analysis often relies on clustering to discover cellular populations and differential analysis to identify important genes. However, this approach has limitations, as clustering assumptions may not accurately represent the underlying biology. SIMBA offers a more data-driven approach by using graph embeddings to uncover relevant genes, regulatory elements, and cellular populations without the need for predefined clusters.

To demonstrate the power of SIMBA, Luca showcases several applications. One application involves identifying master regulators—transcription factors that play a crucial role in gene expression regulation—based on their proximity to target genes and binding sites in the regulatory map. Another application involves multimodal data integration, where multiple types of single-cell omics data can be integrated into a unified map, enabling researchers to study multiple molecular features simultaneously.

While SIMBA shows great promise, Luca acknowledges that weighting different modalities and fine-tuning hyperparameters may require some level of expert judgment and domain knowledge. Nevertheless, SIMBA represents a valuable tool for researchers in understanding complex gene regulatory networks, deciphering cellular heterogeneity, and ultimately advancing our knowledge of biology at the single-cell level.

From Data Integration To Biological Insights: Analyzing statuses' And scRNA-seq Data With scATACpipe for Comprehensive And Reproducible Single Cell Multi-Omics Analysis

Lihua Julie Zhu, Professor & Head of Bioinformatics Core of Molecular Cell and Cancer Biology, University of Massachusetts Chan Medical School

In the presentation by Lihua Julie Zhu, the main focus is on the analysis of scATAC-seq and scRNA-seq data, which provides valuable insights into the regulation of gene expression and the characterization of different cell types and states. The speaker emphasizes the importance of studying genome-wide accessibility, which is influenced by the interplay between histones and DNA and plays a crucial role in defining cell identity and function.

Various methods for analyzing scATAC-seq and scRNA-seq data have been developed over the years, with the speaker introducing their own comprehensive tool that integrates multiple analysis approaches into one user-friendly pipeline. The tool covers different stages of analysis, including pre-processing, quality control, downstream analysis, motif-level analysis, peak-level analysis, and gene-level analysis.

The pre-processing steps are vital for generating meaningful biological insights from the downstream analysis. The tool offers flexibility in handling different data types and allows users to correct for batch effects and other potential sources of variation.

The downstream analysis encompasses a range of techniques, including marker gene identification, differential accessibility analysis, motif enrichment analysis, and transcription factor binding analysis. These analyses help identify key regulatory elements and transcription factors that play critical roles in defining cell types and states.

One notable feature of the tool is its ability to support any organism with annotated genomes, making it applicable to a wide range of research projects. It also provides customized reports and visualizations to facilitate the interpretation of results.

Throughout the presentation, the speaker emphasizes the need for validation and careful interpretation of the findings. While the tool offers powerful analysis capabilities, it is essential to consider the specific characteristics of the data being analyzed and the biological context in which the results are obtained.

In summary, the presentation showcases a versatile and user-friendly tool for analyzing scATAC-seq and scRNA-seq data. It provides researchers with a comprehensive set of analysis modules and the flexibility to tailor the analysis to their specific research questions and datasets.

Harnessing Single Cell Transcriptomics and Spatial Biology For Cell Centric Drug Development

Giorgio Gaglia, Discovery and Validation Lead, Sanofi

In the presentation given by Giorgio Gaglia, he discusses the use of single-cell multi-omics data to decode cellular expression and regulation dynamics during mouse palate development. He highlights the significance of understanding disease in a cell-centric manner, where the balance of different cell states and cell types defines a healthy individual. To study diseases, the speaker proposes three approaches: eliminating pathogenic cells, tuning functional states, or reactivating blocked states.

To achieve these goals, he emphasizes the need for a robust and reproducible computational pipeline to process multi-omics data effectively. The speaker introduces a standardized processing pipeline called Celbridge, which enables scalability and facilitates the usage of single-cell genomics data by various researchers, ultimately contributing to the growth of a comprehensive database for single-cell analysis.

The presentation then delves into two important aspects. Firstly, the challenge of defining cell states accurately, which can vary in semantic meaning depending on the level of molecular understanding. The speaker introduces an

agile algorithm for cell type classification based on gene sets, allowing for precise and flexible cell state identification.

Secondly, the speaker explores how to connect single-cell transcriptomics to disease phenotypes using genetics and bulk transcriptomics data integration. This approach involves associating genes identified by GWAS with specific cell types to identify potentially pathogenic cells. Another strategy involves using the algorithm "SCISSORS" to connect single-cell data to bulk data and identify cells associated with disease phenotypes.

Overall, the presentation highlights the importance of a cell-centric approach in understanding diseases and demonstrates how single-cell multi-omics data can provide valuable insights into cellular expression and regulation dynamics during mouse palate development and potentially uncovering pathogenic cells in disease contexts.

Day One Track Four: Advanced Genome Editing Technologies & Advanced Animal Models

Gene Perturbation Via CRISPR-Cas9: Full Genome Pooled Screens To Single Target Knock-Out

Marco Vincenzo Russo, Scientific Manager, Memorial Sloan Kettering Cancer Centre

In the presented talk by Marco Vincenzo Russo, the focus lies on the utilization of CRISPR-Cas9 for gene perturbation. Operating within a collaborative research environment closely tied to universities, Russo and his team delve into molecular biology, genetic screening, and structural biology.

The core project revolves around investigating a compound's efficacy against cancer by understanding its mechanism of action. The method involves employing CRISPR-Cas9 technology to unveil genes linked to drug resistance.

Russo's team follows a systematic workflow, conducting genome-wide screens with custom CRISPR-Cas9 libraries to pinpoint genes responsible for resistance. These potential candidates are then subjected to rigorous functional validation experiments.

Illustrating their approach with a case study, the team zeros in on the gene K591, which is implicated in cancer progression. They employ RNA binding protein studies and in vivo experiments to confirm the gene's role in drug resistance.

The validation process extends to using specific cell lines for knockdown validation, reinforcing the identified gene's role in resistance.

Library design and generation are crucial aspects of the workflow. The team strives for precision in targeting genes, opting for guide RNAs with lower engagement in other projects to reduce off-target effects.

To ensure reliability, the team implements stringent quality control and auditing measures for clone validation. Techniques such as Western Blot and sequencing are employed to verify the outcomes.

The workflow encompasses parallel analysis and Cas9 validation to ensure data accuracy and integrity.

Looking forward, the team aims to broaden their research horizons, exploring combinations of gene editing techniques and seeking potential biomarkers for resistance.

Throughout the presentation, Russo touches on the incorporation of safe harbor control elements in their custom libraries and contemplates systematic mutation analysis for identifying specific mutations behind resistance.

Balancing the need for effective controls with experimental soundness is a consideration echoed in the presentation's Q&A session.

Ultimately, Russo's presentation highlights the powerful applications of CRISPR-Cas9 technology in unravelling the genetic underpinnings of drug resistance in cancer treatment.

Day Two Track One: Single Cell Analysis In The Clinic & In Pharma R&D

Single-Cell Transcriptomics Reveal The Impact Of Phagocytosis For Myeloid Therapeutic Targeting

Daniel Lu, Senior Scientist, Amgen

In Daniel Lu's presentation, he discussed a study that delved into the impact of phagocytosis on the targeting of myeloid cells for therapeutic purposes. He began by questioning the conventional M1-M2 macrophage paradigm, proposing that this simplistic classification might not adequately explain macrophage diversity.

Lu's study involved a unique mouse model that replicated lung adenocarcinoma conditions. By using genetically modified mice expressing specific markers and oncogenes, they traced the process of phagocytosis within lung tissue. This approach allowed them to distinguish between myeloid cells actively engaged in phagocytosis and those not participating.

Key findings included the identification of alveolar macrophages as primary phagocytic cells in the lung. The study employed advanced techniques like single-cell sequencing and trajectory analysis to map the transitions of these macrophages through various functional states.

A significant discovery was the recognition of a "FAT signature" consisting of genes linked to endosomes, phagosomes, and metabolic processes—particularly glucose metabolism. This signature was associated with enhanced metabolic activity, suggesting a link between increased metabolic usage and immune modulation.

Furthermore, the study found that the FAT signature had implications for patient prognosis, as it correlated with poorer survival rates in lung adenocarcinoma patients.

Lu emphasized the importance of a functional classification approach for accurately targeting therapeutics. He called for a unified cell classification system to better understand cell states. Ultimately, the study's findings suggest potential avenues for innovative therapeutic strategies targeting macrophage function and metabolism in cancer treat

Single Cell Analysis Of Circulating Tumor Cells To Predict Treatment Resistance

Sunitha Nagrath, Professor, University of Michigan

Sunitha Nagrath's presentation revolved around the innovative use of microfluidic and nanotechnology advancements to conduct single-cell analysis on circulating tumor cells (CTCs). Her research primarily focused on liquid biopsies, a method that involves monitoring patients' molecular characteristics through the examination of CTCs present in the bloodstream. Despite encountering challenges due to the rarity and diverse nature of CTCs, Nagrath's team developed a sophisticated microfluidic system, in collaboration with MEMS-based microfluidic technologies, to successfully isolate and analyze individual CTCs based on their size.

Nagrath highlighted the significance of studying CTCs as they provide valuable insights into disease progression and treatment resistance. Unlike traditional tissue biopsies, liquid biopsies offer real-time monitoring of evolving molecular signatures, making them a practical and promising approach.

A key challenge faced in the field is the scarcity of CTCs in blood samples, often amounting to one to ten cells per billion other blood cells. Nagrath's team tackled this obstacle by designing a microfluidic labyrinth that takes advantage of the differing inertial forces experienced by blood cells of varying sizes. This technology achieved a remarkable efficiency of over 90% in isolating CTCs from blood samples.

The presentation then delved into the specific applications of their technology. One crucial aspect was the identification of heterogeneity within CTCs, which is similar to the diversity seen in tumors. These cells exhibit a range of characteristics, from epithelial to mesenchymal phenotypes, with the potential to influence disease aggressiveness. Nagrath's team developed a label-free technology that enabled them to isolate and analyze these heterogeneous CTC populations at the single-cell level.

The presentation also highlighted efforts to investigate gene expression and mutations in CTCs. They utilized techniques such as multiplex RT-PCR, digital droplet PCR, and single-cell RNA sequencing to gain insights into differential gene expression and copy number variations. By comparing these molecular profiles to primary tumors, they were able to identify mutations and alterations that could play a role in disease progression and treatment resistance.

One particularly noteworthy finding was the interaction between CTCs and natural killer (NK) cells, which are crucial components of the immune system's surveillance against cancer. Nagrath's team discovered that CTCs with an

epithelial-mesenchymal transition (EMT) phenotype were more susceptible to NK cell-mediated cytotoxicity. This observation suggests the potential to leverage this susceptibility for targeted therapies, particularly for patients who do not respond well to conventional treatments.

The Q&A session following the presentation addressed additional topics, such as the role of CTC clusters and platelet interactions, and the expression of beta-catenin in CTCs.

Overall, Sunitha Nagrath's presentation showcased the transformative potential of single-cell analysis of CTCs, offering a comprehensive understanding of tumor heterogeneity, gene expression, mutations, and interactions with the immune system. This approach holds promise for tailoring treatments to individual patients and predicting their responses to specific therapies, especially immunotherapies.

Day Two Track 4: Genome Editing Applications In The Clinic & Therapeutics

Genome Edited Porcine Donors Supporting Xenotransplantation

Wenning Qin, Vice President of Genome Editing, eGenesis

In Wenning Qin's presentation, the focus is on genome-edited porcine donors for xenotransplantation, aiming to develop human-compatible cells, tissues, and organs. The pressing need for organ donors prompts exploration of alternatives, and porcine organs have shown promise. The molecular incompatibilities and immunological challenges between humans and pigs are substantial hurdles, and genetic engineering is crucial for compatibility.

Qin discusses various approaches, starting with early attempts in the 1990s, progressing to more recent advancements. Key areas of incompatibility include antigen synthesis, immune regulation, and retroviral activity. These areas require targeted genetic modifications for enhanced compatibility.

CRISPR-Cas9 technology is a pivotal tool in this research, enabling targeted genome editing. Precise genetic alterations are performed to humanize pig organs and suppress molecular pathways that provoke immune responses. Qin presents techniques for optimizing gene expression, such as integrating foreign genes into the genome using viral particles.

The presentation emphasizes the need for precise genetic alterations to minimize immunogenicity. Using CRISPR-Cas9, researchers create modified pig donors with targeted gene changes. These modifications are introduced into pig embryos, leading to the incorporation of human genes and the suppression of porcine-specific elements. Nanopore sequencing, Illumina short reads sequencing, and single-cell RNA sequencing are employed for accurate evaluation of the genomic alterations.

Qin's work has led to the generation of pig donors with integrated human genes, ultimately intended for xenotransplantation. The integrated genes complement human pathways, reducing the risk of rejection. The edited pigs demonstrate promising results, with extended survival times and improved compatibility.

In the Q&A session, Qin discusses challenges related to designing for humans and addresses concerns about integrating human genes. The presentation highlights the significance of genome editing in advancing the feasibility of

xenotransplantation and offers insights into the complex genetic modifications required for compatibility.

Improved Preclinical Models Using Gene Edited Miniswine

Chris Rogers, Chief Executive Officer and Chief Scientific Officer, Precigen Exemplar

Chris Rogers delivered a presentation on "Improved Preclinical Models Using Gene-Edited Mini Swine." He discussed the significance of advancing preclinical models for drug testing to enhance the drug development process. Large animal models, particularly pigs, were emphasized for their physiological resemblance to humans compared to traditional rodent models.

Rogers explained their methodology for creating gene-edited pig models, focusing on two specific cases: hypertrophic cardiomyopathy (HCM) and facioscapulohumeral muscular dystrophy (FSHD). The HCM model aimed to address the limitations of mouse models by introducing specific mutations associated with the disease using advanced gene-editing techniques. This allowed for more accurate disease mechanism studies, therapeutic testing, and toxicology evaluations. In the case of FSHD, the goal was to create an inducible model that mimics the disease progression, enabling the examination of potential therapies and disease mechanisms.

Throughout the presentation, Dr. Rogers highlighted the collaborative nature of their work, involving academic researchers and industry partners. He also touched on the ethical considerations and practical challenges of pig cloning and editing. The presentation underscored the potential of gene-edited pig models to revolutionize preclinical research, leading to improved drug development and increased success rates in clinical trials.

CRISPR-CAS9-In-Small-Molecule-Drug-Discovery-Screening

Timothy Dahlem, Director of Biology, Recursion Pharma

Timothy Dahlem presented on the topic of "CRISPR-CAS9-In-Small-Molecule-Drug-Discovery-Screening." He introduced his role as the Director of Biology at Recursion Pharmaceuticals and highlighted their mission to decode biology for improving lives. He emphasized their use of CRISPR-CAS9 technology in genomic screening and drug discovery. Recursion Pharmaceuticals collaborates with various partners in the pharmaceutical industry, leveraging a massive amount of biological data.

Timothy explained their approach to phenomics, which involves capturing holistic changes in cellular systems using genomic morphology as an endpoint.

They employ high-resolution confocal imaging combined with deep learning algorithms to generate feature vectors representing cell morphology. This allows them to analyse individual or system-level differences in biology, which can help in drug discovery.

He elaborated on their use of CRISPR-CAS9 technology in building macrophages for whole-genome CRISPR knockout screens. They apply the technique to target genes and analyse the resulting changes in cellular morphology. By creating a phenotypic map of biology, they can investigate novel targets for diseases and discover compounds with therapeutic potential.

Timothy introduced the concept of inferential screening, where they combine CRISPR knockout screens with compound profiling to infer relationships between genes and compounds. This approach enables the identification of compounds affecting novel biology and aids in deconvoluting compound effects.

He presented ongoing research involving CRISPR-mediated insertions for disease modelling and compound profiling. The research focused on understanding signalling pathways and identifying compounds that can reverse disease-related phenotypes.

In the Q&A session, Timothy addressed questions about the comparison of cellular features, the distinction between gene knockout and knockdown effects, and the potential for identifying protein localization changes.

Overall, Timothy Dahlem's presentation highlighted the innovative use of CRISPR-CAS9 technology and phenomics in drug discovery, showcasing how these techniques can aid in understanding biology and identifying potential therapeutic compounds.

Models On Editing BRCA, ATM And CHeK2 Mutations And Their Role In Drug Development

Pamela Munster, Professor, University of California San Francisco

The presentation delves into the critical role that models play in understanding and advancing cancer treatment, with a particular focus on DNA repair-associated mutations, like BRCA and ATM. These mutations are linked to vulnerabilities in the DNA repair process, making them potential targets for innovative therapies.

The speaker highlights the complexity and rapid progress in this field over the past year, underscoring the challenge of comprehending the intricate mechanisms underlying these mutations. The talk emphasizes the critical

interplay between these mutations and the broader cellular environment, which can influence the response to therapies.

One of the main points the speaker discusses is the significance of using various models to study these mutations. Mouse models are mentioned as a common approach, despite some limitations due to differences between mouse and human biology. The speaker suggests that some findings from mouse models might not always translate directly to human clinical trials, making it crucial to incorporate other models like organoids and immune competent models for a more comprehensive understanding.

The talk also delves into the impacts of these mutations on cancer susceptibility and growth. It explains how specific mutations, such as those in BRCA and ATM genes, lead to a heightened vulnerability to certain types of cancer. For instance, these mutations hinder DNA repair processes, making cancer cells more sensitive to certain treatments like PARP inhibitors and immunotherapy.

The presentation discusses the potential of gene editing techniques in this context, but it also acknowledges the challenges involved in successfully translating findings from models into clinical trials. The complexity of DNA repair mechanisms and the intricate interplay between various factors are highlighted as potential stumbling blocks.

Throughout the presentation, the speaker underscores the need for personalized treatment approaches based on patients' genetic profiles. This approach, known as precision medicine, seeks to target treatments based on an individual's unique genetic makeup to maximize effectiveness and minimize side effects.

In conclusion, the talk emphasizes the evolving landscape of cancer therapy, where models provide insights into the intricate relationships between mutations, cellular environments, and treatment responses. This understanding has the potential to revolutionize how cancer is treated, moving towards more tailored and effective therapies.

Ex-Situ Gene Modulation Of Organs For Transplantation

Paulo Martins, Associate Professor, University of Massachusetts

In Paulo Martins' presentation, the central theme revolves around the innovative concept of ex-situ gene modulation, which holds immense potential for revolutionizing organ transplantation. He begins by underscoring the urgency of finding improved methods for transplantation due to the shortage of available organs. This pressing issue is substantiated by statistical data, projecting significant growth in the global transplantation market.

The traditional methods of organ preservation, while essential, are shown to have limitations in terms of organ quality, logistical challenges, and the need for extended preservation modalities. Martins underscores the critical nature of proper organ preservation and the potential for personalized therapeutic approaches to enhance organ viability and function.

A key focus of the presentation is machine perfusion preservation, which is demonstrated as a method with considerable promise. This approach not only maintains organ functionality but also allows for real-time monitoring and assessment of organ viability. Importantly, this method opens avenues for repairing genetic mutations, rectifying damages, and promoting the overall health of organs through gene modulation.

Martins further delves into the realm of gene editing and therapy, highlighting their potential advantages. Customized therapeutic interventions through gene addition, non-viral gene integration, and various delivery techniques, including viral carriers and nanoparticles, are discussed. The aim is to optimize the distribution and effectiveness of these therapies.

The presentation extends into the realm of research advancements, showcasing efforts to induce protective factors and enhance the regulatory response in organ transplantation. While highlighting the potential benefits, Martins acknowledges the limitations of gene therapy, particularly the challenge of targeting specific molecules effectively.

Looking ahead, Martins envisions a transformative future for organ transplantation. He suggests a close collaboration between research labs and clinical settings, leading to the emergence of organ nurseries or repair centers. In this future scenario, organs could be customized, optimized, and ready for transplantation, potentially revolutionizing the field and improving patient outcomes significantly.

When The Human Genome Editing Machinery Breaks Down: Towards Developing A Stem Cell-Based Gene Correction Therapy For REG2 Deficiencies

Mara Pavel-Dinu – Instructor of Paediatrics, Stanford School of Medicine

Mara Pavel-Dinu's presentation revolved around the development of a stem cell-based gene correction therapy aimed at addressing REG2 deficiencies, which are associated with immune system disorders. She discussed the application of gene editing technology to delve into the intricacies of human immune cells carrying these genetic mutations. Her presentation highlighted the vital role played by the human genome editing machinery during the formative stages of the adaptive immune system.

The focus was on explaining the clinical expressions and observable characteristics of the disease stemming from REG2 mutations. Pavel-Dinu detailed the workings of genome editing technologies, placing particular emphasis on the widely known CRISPR-Cas9 system as a tool for rectifying the genetic defects linked to the condition.

Through the presentation, the audience was guided through the different phases of T-cell development, with a spotlight on the significance of VDJ recombination. Additionally, the crucial role of REG proteins in driving this process was outlined. The session elaborated on the various categories of inborn errors of immunity, which encompass a range of immune-related disorders. The discussion then zeroed in on the specifics of REG2 deficiencies, underscoring the diverse clinical outcomes associated with varying degrees of VDJ recombination.

The presenter dissected existing therapies designed for these deficiencies. Allogeneic hematopoietic stem cell transplantation and lentiviral gene therapy were analyzed, along with their drawbacks and limitations. To counter these shortcomings, the potential of targeted gene therapy was introduced, utilizing stem cells derived from the affected patients themselves. This approach was framed as a safer alternative, allowing for precision correction while preserving endogenous gene expression levels.

A critical aspect of the presentation was the introduction of a universal correction strategy. This strategy revolves around using optimized cDNA to rectify the mutations, aiming for a comprehensive solution that applies to various genetic variations associated with the condition. The presenter showcased the results achieved both in vitro and in vivo, demonstrating the success of the proposed method in terms of correcting the disease's characteristics and promoting the development of diverse T-cells.

Pavel-Dinu concluded her presentation by underlining the significance of focusing on rare genetic diseases. These conditions offer a unique avenue for research, enabling insights into broader disease mechanisms. She emphasized the collaborative nature of the research effort and extended appreciation to the individuals and organizations contributing to this endeavour.