POST EVENT PROCEEDINGS

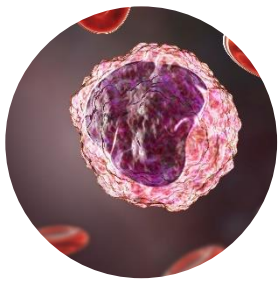
Immuno 2023

28 - 29 March 2023 | London, UK

Oxford Global were proud to present **Immuno 2023**, which united senior-level experts to provide a focussed forum for thought-provoking discussion and to gain insights from the key figures in the community.

The comprehensive programme allowed you to gain a forward-looking perspective on the opportunities and challenges impacting market growth in immuno-oncology across parallel tracks, from therapeutic strategies and modelling through to the latest clinical data. The programme included case studies across a variety of key therapeutic modalities, such as cell therapies, checkpoint inhibitors and novel antibodies, whilst further sessions allowed you to advance your understanding of topical technological innovations.

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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Day 1, Track 1: Discovery & Development: Cell & Combination Therapies

Development Of Vγ9Vδ2 T Cell-Engaging Bispecific Antibodies For Efficacious Cancer Treatment

Rob Roovers, Senior Director Preclinical Development, LAVA Therapeutics

The speaker, Rob, is a senior director of preclinical development at Lava Therapeutics. He discusses the development of a T cell-engaging antibody called "Rob v Y9v delta2 gamma2 T cell," which is designed for effective cancer treatment. Rob highlights the challenges in the field of T cell-engaging therapies, where many have not met expectations due to limited therapeutic windows, toxicity profiles, and on-target tumor-related toxicities. He presents their approach of using gamma delta T cells, specifically gamma9 delta2 T cells, which are potent cytotoxic T lymphocytes with antigen presenting capability.

Rob discusses their CD123 lead program and their efforts to develop a next-generation T cell-engaging platform that aims to retain potency, increase precision in engaging the right type of effector cells, and broaden the immune response. He explains the development of specific VHH antibodies that target the gamma delta T cell receptor and CD123, and their effectiveness in killing CD123-positive target cells while sparing normal cells.

The presentation includes data on affinity, binding, and cytotoxicity assays demonstrating the effectiveness of their T cell-engaging antibodies. Rob also presents information about their first-in-class gamma body, which targets CD1d and activates invariant natural killer T (iNKT) cells, and discusses the safety and early-phase clinical trial progress of their programs.

During the Q&A session, Rob addresses questions about the potential engagement of both gamma delta T cells and natural killer (NK) cells, as well as the activation and cytokine release profiles of gamma delta T cells when interacting with different cell types.

Overall, the presentation outlines Lava Therapeutics' innovative approach to T cell-engaging therapies and provides insights into the preclinical and clinical development of their programs.

Day 1, Track 3: Autoimmunity Mechanisms & Novel Treatments

Targeting-Oxidized-Macrophage-Migration-Inhibitory-Factor-oxMIF-In-Autoimmune-D

Michael Thiele, Chief Scientific Officer, OncoOne Research & Development GmbH

The speaker discussed macrophage migration inhibitory factor (MIF), a key regulator of adaptive and innate immunity. MIF was the first cytokine ever discovered and plays a critical role in inflammation. It acts as an upstream cytokine, triggering the release of other pro-inflammatory cytokines like TNF-alpha and interferon-gamma. MIF promotes immune cell maintenance and survival, leading to sustained inflammation in tissues. Its unique feature is its ability to overwrite the immunosuppressive effects of glucocorticoids, making it a potential drug target for acute inflammatory conditions.

However, MIF has proven elusive as a drug target due to its abundance in circulation and various isoforms. One specific isoform, oxidized MIF (OxMIF), is found in disease-related conditions due to changes in the microenvironment, making it a promising target for drug development.

The speaker presented the development of a specific monoclonal antibody, 104, targeting OxMIF. Preclinical studies showed promising results in models of glomerulonephritis, rheumatoid arthritis, and colitis, with anti-inflammatory effects comparable to dexamethasone. The team aims to submit an investigational new drug (IND) application for 104 and is looking for partners to co-develop it, with primary focus on nephritis, rheumatoid arthritis, and spondyloarthritis.

During the Q&A session, the speaker addressed questions about MIF's relationship with type 1 interferon and the potential for precision medicine strategies based on specific subtypes of diseases. They also discussed the potential for head-to-head comparisons with existing treatments like anti-TNF therapies. Additionally, the role of MIF in severe cases of COVID-19 and septicemia was mentioned as a topic of interest for further research.

Day 2, Track 1: Discovery & Development: Intratumoral Immunotherapies & Antibody Therapies

Targeting-Tumour-Associated-Macrophages-Through-Novel-Antibody-Therapeutics

Luca Cassetta, Vice President, Immunology, Macomics Ltd

In summary, Dr. Santos is the Vice President of Immunology at MEK PROMIX Limited, and he will be discussing targeting tumor-associated macrophages with novel antibody therapeutics. He co-founded Micromax and is an immunologist with expertise in human myeloid cell biology, particularly studying the role of macrophages in HIV pathogenesis. Dr. Santos worked with Dr. Jeffrey Pollard at Albert Einstein in New York, where he studied tumor-associated macrophages.

During the talk, Dr. Santos presented research on the importance of macrophages in tumor progression and metastasis. He emphasized the need to reprogram macrophages to work effectively with other immune cells such as T cells and NK cells. He discussed different waves of therapeutic approaches for targeting macrophages, including depletion, CD47-SIRPα axis targeting, and reprogramming strategies.

To identify potential targets for macrophage reprogramming, Dr. Santos used a proprietary technology platform called the Island Macrophage Discovery Platform. This platform integrates publicly available single-cell datasets and allows for the genetic modification of IPS-derived macrophages. Dr. Santos demonstrated successful editing and validation of gene targets using this platform.

Furthermore, Dr. Santos highlighted the importance of understanding the complexity of macrophages in various tumor types and the potential for using this knowledge to design more effective therapies. He also announced a collaboration with Honor Pharmaceuticals for drug discovery in immune oncology using their genome editing technology.

Overall, Dr. Santos's talk focused on the emerging role of macrophages in oncology and the potential of reprogramming strategies to improve cancer treatments.

Viral-Immunotherapy-To-Induce-Systemic-Anti-Tumor-Responses-In-Solid-Tumors

Paul Peter Tak, President and Chief Executive Officer, Candel Therapeutics

Peter Paul Tak, the president and CEO of Kindle Therapeutics, delivered a talk discussing their latest venture, a clinical platform with three investigational medicines. The first medicine, CAN2409, induces systemic immune responses through local injection and is being tested in clinical trials for lung, prostate, and pancreatic cancers. The second medicine, CAN3010, is an oncolytic virus that selectively replicates in tumors and has shown promising results in therapy-resistant glioblastoma patients. The third platform, Enlightened, uses HSV to modulate the tumor microenvironment and has a collaboration with the University of Pennsylvania to improve car T cell therapy for pancreatic tumors.

Tak presented compelling data showcasing tumor response, abscopal effects, and CDA positive T cell responses in patients with advanced lung, prostate, and pancreatic cancers. These results offer hope for patients who have exhausted other treatment options. The talk emphasized the potential breakthrough in cancer treatment, particularly in unmet medical needs and the possibility of converting "cold" tumors into "hot" tumors, expanding treatment possibilities. The clinical platform's approach demonstrated strong focus on human biology, and their strategic partnerships with academia and pharmaceutical companies contribute to the platform's success. Overall, the talk revealed an encouraging direction in cancer therapeutics with transformative potential.

Novel TNF Superfamily Antagonists

Russell LaMontagne, President & Chief Executive Officer, Boston Immune Tech

Russell Lamontagne, the CEO and co-founder of Boston Immune Technologies and Therapeutics (BTT), discussed the company's focus on developing novel antibodies targeting the TNF superfamily in their recent talk. BTT's lead candidates include TNF R2 antagonists and CD40 antagonists.

Their antibodies are unique in that they specifically target rapidly dividing or activated cells within the tumor microenvironment, ensuring selective and efficient targeting while minimizing off-target effects. They have conducted in vitro and mouse model studies, demonstrating promising results in killing tumor cells and regulating T cells.

BTT is also cautious about dosing, acknowledging that high doses might lead to monomeric binding, potentially limiting the effectiveness of their antibodies. Therefore, they plan to explore lower dosing in their phase one trial.

The company is well aware of the significance of soluble TNF R2 in aggressive tumors. While investors are more focused on targeting tumors without soluble TNF R2, BTT believes in taking a biomarker approach to identify tumors that express the oncogene and respond well to their antibodies.

BTT has a robust patent portfolio protecting their antibody technology. The company is actively seeking additional funding to advance their research, further develop their antibodies, and conduct clinical trials.

In conclusion, BTT's presentation highlights their innovative approach to developing antibodies that show promise in targeting cancer and autoimmune diseases. With their focus on selective targeting, potential combination therapies, and patient-specific approaches, BTT's research could lead to significant advancements in the field of immunotherapy.

Oncolytic-Measles-Viruses-For-Cancer-Immunotherapy

Tobias Speck, Vice President, Product Development, CanVirex

The speaker is the Vice President of Product Development at a company called Converts. He discusses oncolytic measles viruses for cancer immunotherapy devices. He holds a PhD in molecular biology and has 15 years of experience in the life sciences, specializing in immunomodulators. He presents the history of oncolytic viruses in cancer therapies, emphasizing the link between immune activation and spontaneous tumor regression triggered by viral infections.

The company he works for, Canvasback, is a spinoff from the Heidelberg University Hospital and the German Cancer Research Centre. They are developing a platform technology based on the common measles vaccine virus. The technology involves engineering the virus with additional transcription units to arm it with various immunotherapeutics, including cytokines, immune checkpoint inhibitors, and specific antibodies.

He discusses their lead candidate, Mebutseal, an oncolytic measles vector encoding the cytokine interleukin 12. They have conducted preclinical studies demonstrating its effectiveness in inducing tumor regression and durable remission in mice models.

The speaker acknowledges challenges related to pre-existing immunity against the measles vector, but they are exploring various strategies, such as dosing

and administration routes, to overcome this limitation. They are preparing for their first clinical trial and seeking funding for further development.

Overall, their approach focuses on using oncolytic measles viruses as a targeted and safe immunotherapeutic strategy to address limitations seen in current cancer immunotherapies, such as varying response rates, toxicities, and high costs.

Day 2, Track 2: Large & Small Molecule-Based Preclinical, Clinical & Translational Development

Targeting Aberrantly Expressed TSAs (aeTSAs) With Cancer Immunotherapy

Colleen Winstead, Director of Immunology, Epitopea

The speaker, who is the director of the Institute of Immunology and Immunotherapy in Birmingham, has a diverse background, having previously worked in Bristol, Cambridge, Stanford, and Mill Hill. They mentioned being "very old" but are still committed to their work.

The speaker's work revolves around antigen-specific immunotherapy, particularly for autoimmune diseases and allergies. They discuss various therapeutic approaches being explored worldwide, including the administration of peptide-coated dendritic cells, manipulating gut bacteria for antigen expression, and using nanoparticles for antigen delivery. The speaker emphasizes the importance of inducing bystander suppression, which means controlling the immune response to multiple associated antigens in autoimmune diseases.

The speaker's main focus is on epitopes, which are antigen processing-independent peptides that mimic naturally processed antigens. These peptides induce the differentiation of regulatory T cells (Treg) that express inhibitory receptors and produce interleukin-10 (IL-10), promoting a suppressive phenotype. They show evidence of epigenetic changes associated with tolerance induction and discuss successful results in animal models and small clinical studies for diseases like Graves' disease and multiple sclerosis.

During the Q&A session, the speaker addresses a question about potential non-specific immune suppression caused by their treatment and explains that they haven't observed any decrease in responses to other antigens during their studies.

Overall, the speaker presents exciting research on antigen-specific immunotherapy, emphasizing the potential for more effective and targeted treatments for autoimmune diseases and allergies.

LockBody: Selective Innate Immune Activation In The TME, With Minimal Systemic Toxicity

Niall Foy, Associate Director of Research, LockBody Therapeutics, a Centessa Company

The presentation is about a novel clinical candidate called "lB 101," which is a type of therapeutic molecule designed to activate the immune response against tumours. The molecule is a combination of antibodies that target two proteins: PDL-1 and CD47. CD47 is an immune checkpoint protein that prevents immune cells from attacking cancer cells, while PDL-1 is another protein that also hinders the immune response. The presentation explains how lb 101 works to overcome these barriers and activate an immune response against tumours.

The speaker discusses the challenges of targeting CD47 using traditional antibodies due to its widespread expression in the body, which can lead to toxic effects. lb 101 is designed to specifically target CD47 in the tumour microenvironment, avoiding systemic toxicity. The molecule has a unique hinge linker that allows it to be conditionally activated by enzymes present in the tumour microenvironment, which results in the exposure of its active binding sites.

The presentation goes on to describe the preclinical data supporting the effectiveness of lb 101. In various experiments using cell cultures and animal models, lb 101 demonstrated the ability to activate immune cells, promote phagocytosis (engulfing and destruction of cancer cells by immune cells), and inhibit tumour growth. The molecule's potential to eliminate PDL-1-positive immune cells, such as dendritic cells, was also observed, which is significant for enhancing the immune response.

The data indicates that lb 101 can effectively target both CD47 and PDL-1, leading to a stronger immune response against tumours. The molecule's ability to activate immune cells and promote phagocytosis while avoiding systemic toxicity holds promise for its potential as a novel cancer therapy. The presentation concludes by mentioning that lb 101 has received clearance for clinical trials, and the company is looking forward to further developments in this field.

Novel Approaches For Differentiating NK Cells From iPSCs

Tanya Ponomaryov, Principal Scientist, Plasticell Ltd

The speaker, Tanya Ponomaryov, introduced themselves and their background in stem cell research, starting with a PhD at the Weizmann Institute in Israel, followed by work on brain tumors at the Dan Farber Cancer Institute and haemostasis research at a UK university. They then transitioned to the industry, specifically joining a small biotech company called PlastiCell as a principal scientist. PlastiCell is located in Stevenage and uses a screening platform named "Labyrinth" to explore stem cell differentiation.

The Labyrinth platform utilizes a combinatorial cell culture approach involving solid beads or alginate beads seeded with stem cells. The cells are exposed to different media compositions with specific fluorescent tags that track their differentiation process. This process involves multiple rounds of differentiation, stopping, washing, and distributing beads to different media compositions. The aim is to create protocols for serum-free and GMP-applicable differentiation, leading to specific cell fates. PlastiCell primarily focuses on expanding hematopoietic stem cells from cord blood and peripheral blood, and they are venturing into immune oncology using induced pluripotent stem cells (iPSCs) to develop NK cells for cancer therapy.

The speaker highlighted that working with stem cells poses challenges due to their complex interactions with the surrounding environment. PlastiCell's approach involves creating a matrix and utilizing big data analysis to generate protocols for desired cell types. They've achieved success in creating megakaryocytes and platelets from iPSCs and are now working on developing NK cells for immunotherapy. Their ambition is to create an off-the-shelf NK cell product that's easier to modify and offers more control over the manufacturing process compared to using donor cells. PlastiCell's approach involves careful matrix design, validation of protocols, and characterization of the resulting cells' behaviour and functions.

The speaker acknowledged collaborations and funding that support their work, expressing openness to further challenges and partnerships. The presentation showcased their progress in using iPSCs and innovative screening methods to develop functional NK cells for cancer therapy.