

Report on the ISCT Australia and New Zealand Region Virtual Meeting 2021

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It was a privilege to co-chair the ISCT Australia and New Zealand (ANZ) region virtual meeting on the 26th of February 2021. I am delighted to summarise a few of my personal highlights for the *Telegraft* readership.

The annual ISCT ANZ meeting is typically held around November each year. In previous years, delegates have taken pleasure in the traditional face-to-face format and are treated to a beautiful Australian spring. However, in the year 2020, this was not possible due to travel restrictions imposed by the global COVID 19 pandemic. Thus, for the first time, we met virtually. I had the honour of opening the meeting with a traditional Acknowledgement of Country to welcome our virtual attendees scattered across the many lands of the Australian continent. This welcome was extended to our neighbours in Aotearoa and our distinguished international guests from the North American continent.

In the first talk of the plenary session, distinguished international speaker Prof. Michel Sadelain discussed the advancements and challenges of CAR T-cell therapies. He described the new directions his team is undertaking in CAR T-cell engineering to address CAR T-cell therapy complications such as toxicities and resistance mechanisms. We learned about the clever methods his team use for precise insertion of therapeutic transgenes into genomic safe harbors via gene editing, CAR T-cell signal calibration, and epigenetic enhancements. We also heard of a novel target search for surface molecules commonly upregulated in senescence-associated pathologies.

Prof. Carl June told us a remarkable story of the first CLL patient infused with CAR T-cells who was disease-free for 10 years until succumbing to COVID-19 earlier this year. The legacy he left behind is a decade long collection of valuable data providing evidence for significant research findings. This included tracing the lineage of CAR T-cells responsible for tumour burden eradication back to a single cell and a chance discovery that epigenetic editing can improve persistence and prevent CAR T-cell exhaustion. This finding led to a new area of CAR T-cell engineering that includes multiple gene editing events. We learned of the complexities of cytokine storms following CAR T-cell infusion and ways to overcome post-infusion complications.

In the first half of the regulatory session, Meenu Mathur from the Therapeutic Goods Administration (TGA) provided updates on Therapeutic Goods Orders (TGO). Of particular note was the split of the current TGO 88 standard for donor selection, testing and minimising infectious disease into two TGOs:

- TGO 108 - minimisation of transmission of infectious disease agents
- TGO 109 - general manufacturing/quality requirements for biologicals

Peter Wenzel from the Office of The Gene Technology Regulator (OGTR) provided an overview of the Australian regulatory landscape for Genetically Modified Organisms (GMO) in Australia, focusing on clinical trials. Tim Strabala from the New Zealand Environmental Protection Authority (EPA) presented an overview of the approval and determination pathways for GMOs and medicines in New Zealand.

At each annual ISCT ANZ meeting, the regional LRA committee prepares and hosts a "grill the regulator" discussion. The representatives from local regulator bodies receive a set of provocative hypothetical scenarios for debate and comment. I have enjoyed listening to this traditional event in past meetings, and this year, the discussion did not disappoint!

During the lunch break, I had the opportunity to browse through poster presentations. I enjoyed the three-minute video format with a narrated slide presentation and the online chat function for follow up questions. I accessed the exhibitor booths via a visually pleasing graphic interface and found it easy to navigate. Although I prefer face-to-face contact, I appreciated the platform's functionality to be able to rapidly search and download content of interest.

In the first afternoon session, A/Prof. Emily Blyth from the Westmead Institute for Medical Research provided an overview of adoptive cell therapy strategies using antigen-specific T-cells to minimise infectious complications in patients following allogeneic haemopoietic stem cell transplant. We heard of improvements in manufacturing technology and demonstrated clinical efficacy with the final product's limited toxicities, including 3rd party viral-specific T-cells. Dr. Rachel Perret from the Malaghan Institute of Medical Research provided an overview of the lentivirus production and GMP manufacturing facility in Wellington, New Zealand. We also heard encouraging preliminary results for the phase I dose-escalation trial of autologous anti-CD19 CAR T-cells for relapsed and refractory B-cell lymphomas.

Prof. Melissa Little presented the current challenges of rebuilding a kidney from a single cell in the first talk of the program's final session. Prof. Little and her team generated multicellular human kidney organoids from human pluripotent stem cells and applied these human models to disease modelling, drug screening and regenerative medicine. The team is developing novel approaches for the scale-up of tissue generation and moving closer to the application of iPSC-derived kidney organoids for tissue regeneration. The final invited speaker presentation of the day entitled "*In vivo* and *ex vivo* clinical gene therapy: Are we there yet?" was delivered by Prof. John EJ Rasko. We heard of extraordinary clinical success of the *in vivo* gene therapy for blood clotting disorders exemplified by Prof. Rasko's haemophilia A and haemophilia B patients who no longer require clotting factor injections. Similar success was observed in the *ex vivo* gene therapy clinical trial for beta thalassemia. So, are we there yet? Prof. Rasko cautioned us that we are not, as in the past few months, reports came in for two cancer cases identified in the Bluebird

Bio beta thalassemia study. A single cancer case was reported in the Uniqure's haemophilia B study. Investigations are ongoing following these preliminary serious adverse event reports.

The first-ever virtual ISCT ANZ meeting was a success thanks to the fantastic contributions of our distinguished invited speakers and the generous support from the conference sponsors. I look forward to future face-to-face ISCT ANZ meetings, but until then, I am stocking up on my favourite coffee beans for the early morning ISCT 2021 New Orleans program.

All the best from down under.

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Brief Summary (30-50 words):

Zlatibor Velickovic, PhD summarises his highlights from the first-ever virtual 2021 ANZ Regional Meeting. These highlights include advancements in CAR T-cell therapies as well as reports from gene therapy clinical trials.