ESACT-UK Travel Award Conference Report

ISCT 2026 Annual Meeting, Dublin

The ESACT-UK travel award enabled attendance at the ISCT 2026 Annual Meeting in Dublin, an internationally recognised meeting dedicated to the translation of cell and gene therapy from research to clinical application. The conference provided a valuable opportunity to engage with current developments across the field, present ongoing research, and expand an international professional network in a highly interdisciplinary environment. For research focused on scalable, non-viral hematopoietic stem cell (HSC) gene therapy, the meeting was particularly relevant because of its strong emphasis on manufacturing, translation, and clinical implementation.

One of the major strengths of ISCT 2026 was the structure of its scientific program. The meeting was organised around a translational framework that extended well beyond standard plenary and abstract sessions, incorporating the Translational Pathway Program, Lab Practice Essentials, corporate sessions, Global Showcase presentations, and interactive roundtables. This created a highly effective balance between strategic scientific discussion and practical sessions addressing process development, analytical methods, manufacturing workflows, and clinical translation. As a result, the meeting provided not only exposure to scientific innovation, but also a broader understanding of how advanced therapy products must be developed in a way that is robust, scalable, and aligned with regulatory and commercial realities.

Several important themes emerged across the conference. A particularly prominent one was the continued movement of the field toward scalable and clinically realistic manufacturing solutions. Across multiple sessions, there was clear emphasis on automation, closed-system processing, reproducibility, and cost-conscious development, reflecting the broader shift of cell and gene therapy from proof-of-concept science toward deployable therapeutic platforms. This was highly relevant to ongoing work in non-viral HSC engineering, where the long-term value of a platform depends not only on biological performance, but also on its manufacturability and potential to reduce cost of goods.

A second important theme was the increasing maturity and relevance of non-viral engineering strategies. This directly aligned with the presented project, “Breaking free from viruses: developing a scalable non-viral platform for HSC gene therapy using CRISPR/Cas9 and Sleeping Beauty transposon delivered via nucleofection or lipid nanoparticles.” The project investigates complementary non-viral strategies for CD34+ HSC engineering, evaluating CRISPR/Cas9 ribonucleoprotein delivery for targeted

editing and Sleeping Beauty transposon delivery for stable integration. Early findings demonstrated approximately 50% non-homologous end-joining efficiency at the AAVS1 safe harbour locus using CRISPR/Cas9 RNP nucleofection, while Sleeping Beauty minicircle transposon with SB100X mRNA achieved 82% transfection efficiency, and the LNP-based approach reached 97% encapsulation efficiency, 88% yield, and greater than 90% HSC viability across tested conditions. These results strongly supported the feasibility of high-efficiency non-viral HSC engineering and resonated with wider discussions at the meeting on the need for flexible, scalable, and more affordable alternatives to viral-vector-based gene therapy platforms.

A particularly important highlight of the meeting was selection for the ISCT 2026 Elevator Pitch Competition. This competition is designed to showcase a limited number of presenters in a short-format setting, and being selected as one of 20 participants was a significant recognition of the relevance and communication potential of the project. My presentation used a LEGO-inspired analogy to frame the concept of a modular, plug-and-play non-viral gene therapy platform, emphasising how optimisation of the delivery platform could enable more flexible payload exchange, improved scalability, and reduced cost. This format proved to be highly effective in communicating the broader translational vision of the work to a diverse audience. Following the presentation, large number of delegates reached out personally to say that the pitch was particularly strong and memorable and to express interest in learning more about the project and its wider applications. This response was especially encouraging, as it suggested that the work resonated not only scientifically, but also as a compelling translational concept.

In addition to the Elevator Pitch Competition, the project was also presented in poster format, which provided an important opportunity for deeper scientific discussion. The poster presentation allowed much more detailed engagement with delegates from academia and industry on specific aspects of the work, including delivery routes, transposon integration, HSC viability, scalability, and future functional assessment. The poster therefore complemented the short oral format particularly well: the pitch created initial visibility and interest, while the poster allowed follow-up technical conversations with those who wanted to explore the work in more depth. Together, these two presentation formats significantly increased the visibility of the project within the meeting and created opportunities for meaningful scientific exchange.

The meeting was also highly beneficial from a networking perspective. ISCT 2026 brought together 2,508 delegates from 57 countries, with representation across Europe, North America, Asia, Australia, and South America, creating a genuinely international setting for discussion and collaboration. This was especially valuable in broadening professional contacts beyond existing European networks and in gaining a wider perspective on how scientific, regulatory, and translational priorities differ across regions. Informal discussions during and after the poster session, the Elevator Pitch

Competition, and other meeting activities provided useful feedback on the presented research and opened new conversations around the development and positioning of non-viral HSC gene therapy platforms.

Overall, attendance at ISCT 2026 was an extremely valuable experience and made an important contribution to scientific development, visibility, and professional growth. The program was particularly effective in demonstrating that future progress in cell and gene therapy will depend on the integration of strong biological science with scalable manufacturing, regulatory readiness, and clear translational strategy. The opportunity to present the work in both poster format and as one of the 20 selected participants in the Elevator Pitch Competition was a particular highlight of the meeting, and the positive follow-up interest from delegates underscored the relevance and appeal of the project. The support of ESACT-UK was essential, as it enabled participation in a meeting that was scientifically enriching, professionally rewarding, and highly relevant to ongoing research in non-viral HSC gene therapy.

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Breaking Free from Viruses: Toward a Scalable Non-viral Platform in HSC Gene Therapy

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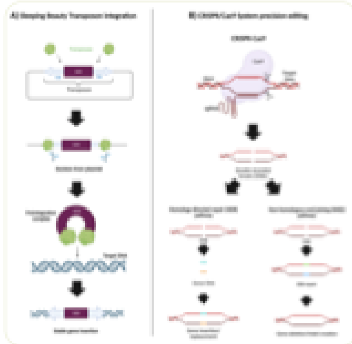
BACKGROUND

Hematopoietic stem cell (HSC) gene therapies have proven to be an effective therapeutic modality to address a range of severe genetic diseases. Despite their success in a clinical setting, there remains ongoing manufacturing challenges, such as low transduction efficiency, limited cell expansion (and consequently, low doses), and the need for large quantities of costly viral vectors.

This study focuses on the development of ex vivo HSC gene therapies using non-viral techniques. The two main approaches analysed are CRISPR/Cas9 and Sleeping Beauty transposon systems. The goal is to develop a robust non-viral cell therapy platform capable of producing larger quantities of undifferentiated, gene-modified HSCs.



METHODS & RESULTS

1 NHEJ assessment of ribonucleoprotein (RNP) complex electroporated KG1A cells

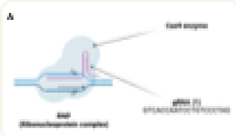
Figure 1. Non-homologous end-joining screening using CRISPR/Cas9 ribonucleoprotein (RNP) complex electroporation in KG1A cells (1).

A. Ribonucleoprotein (RNP) complex explained. Cas9 and gRNA is incubated for 10 minutes before electroporation.

B. CRISPR RNP electroporation editing efficiency assessment. The gDNA extracts were PCR amplified, and the amplicons were next generation sequenced (Plasmidsaurus/Full Circle). The NHEJ editing efficiency (calculated with CRISPRNano) are included for all samples. Non-transfected sample was used as control.

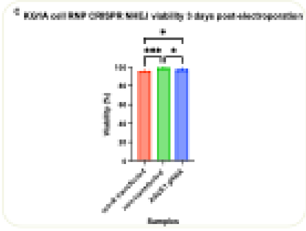
C. Viability of KG1A cells 3-days post-electroporation with CRISPR Ribonucleoprotein complex. Mock transfected and non-transfected cells are used as control.

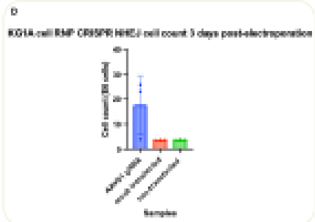
D. Total cell count of KG1A cells 3-days post-electroporation with CRISPR Ribonucleoprotein complex. Mock transfected and non-transfected cells are used as control.



B

Sample	NHEJ (%)
RNP	33.29
NT control	0





2 Comparison of RNP and Sleeping Beauty transposon electroporation to HSCs

Figure 2. Comparison of mobilised peripheral blood derived HSC electroporation with Sleeping Beauty and RNP.

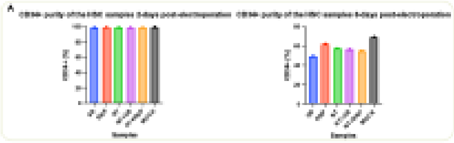
A. CD34+ Purity of HSC samples 2- and 6-days post-electroporation. BV421 fluorochrome is used for staining CD34+. Non-transduced, mock electroporated, non-transduced with sleeping beauty and non-transduced with CRISPR samples are used as control.

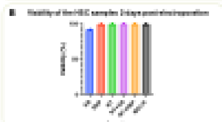
B. Viability of HSC samples 2-days post electroporation.

C. CRISPR RNP electroporation editing efficiency assessment. The gDNA extracts were PCR amplified, and the amplicons were next generation sequenced (Plasmidsaurus). The NHEJ editing efficiency (calculated with CRISPRNano) are included for all samples. Non-transfected sample was used as control.

D. HSC Venus expression analysis using fluorescent microscopy 2-days post-electroporation with SB100X system. Images were taken with 4x objective with EVOS fluorescence microscope.

E. Venus expression analysis of HSC using flow cytometry 2- and 6-days post-electroporation with sleeping beauty transposon system.





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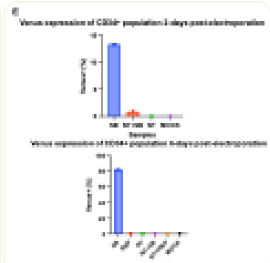
Sample	NHEJ (%)
RNP day 2	0
RNP day 6	50.30
NT control	0



3 Venus integration to HSCs using sleeping beauty transposon encapsulated in lipid nanoparticles

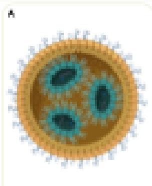
Figure 3. Screening of Venus integration to mobilised blood derived HSCs using sleeping beauty transposon encapsulated in ionisable lipid nanoparticles.

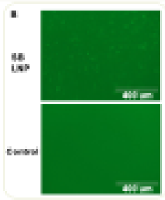
A. SB transposon MC and SB transposase mRNA packed into ionised lipid nanoparticle.

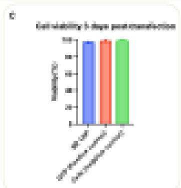
B. HSC Venus expression analysis using fluorescent microscopy 3-days post-transfection with SB100X system encapsulated into LNPs. Images were taken with 4x objective with EVOS fluorescence microscope.

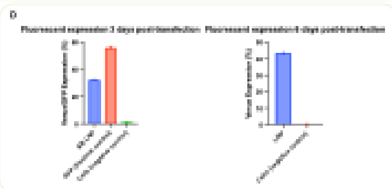
C. Viability of HSC samples 3-days post-transfection. Viability is above 97% for all samples.

D. Venus expression analysis of HSC using flow cytometry 3- and 6-days post-transfection with sleeping beauty transposon system encapsulated into LNPs. 43.4% Venus+ expression was achieved.









CONCLUSIONS & FUTURE WORK

Initial stage of small-scale comparison and development of ex-vivo HSC gene therapies using non-viral techniques was presented. The two main non-viral systems used - precision genetic engineering (CRISPR/Cas9) and transposable elements (sleeping beauty transposon) - were demonstrated for HSC cells. The systems were delivered using lipid nanoparticles and electroporation.

Next steps: Small-scale ex-vivo hematopoietic stem cell therapies will be further optimised. Through intermediate scale the final platform will be transferred to commercial scale expansion systems. The feasibility of "Switch and swap" will be analysed in different bioreactors using variety of cargo.

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REFERENCES

(1) Della Volpe. (2024). "A p38 MAPK-ROS axis fuels proliferation stress and DNA damage during CRISPR-Cas9 gene editing in hematopoietic stem and progenitor cells." Cell Rep Med 5, 101823.
(2) Holstein, M. (2018). "Efficient Non-viral Gene Delivery into Human Hematopoietic Stem Cells by Minicircle Sleeping Beauty Transposon Vectors". Molecular Therapy. Cell Press, 26 (4), pp. 1137–1153. doi: 10.1016/J.YMTHE.2018.01.012/ATTACHMENT/3816819-CD44-4331-8D16-