CAR T-REX

Welcome to the second edition of the CAR T-REX newsletter!

CAR T-REX combines innovative genome editing and non-viral gene delivery methods to engineer CAR T-cells that can overcome T-cell exhaustion in the tumour microenvironment. Our project aims to develop auto-regulated genetic circuits controlled by microRNAs in immune cells, utilising the TraffikGene® platform for high-performance non-viral gene delivery of synthetic miRNA constructs. We will select and benchmark the best-performing circuits in preclinical assays and conduct GMP-like manufacturing runs for the final CAR T-cell product.

Now, let's dive into the latest news and developments from the CAR T-REX project!

CAR T-REX Website

CAR T-REX General Assembly

We recently held our first in-person meeting in Spain at CiQUS (Universidade de Santiago de Compostela), marking a significant milestone for our team. The gathering provided an excellent opportunity to strengthen our collaboration and discuss the progress we have made during the first year of the project.

The General Assembly included a visit to the Galaria CAR T-cell manufacturing facilities at Campus Vida in Santiago. Galaria is a public company under the Galician Health Service and serves as an instrumental entity and technical service for the region. Currently, besides offering advanced healthcare services, Galaria is empowered to develop, implement, and manage healthcare infrastructure projects initiated by the Autonomous Community of Galicia.

The visit aimed to explore potential collaborations and discuss the challenges facing the field of cell and gene therapies. We had the opportunity to tour the state-of-the-art facilities and gain insights into the processes being employed for advanced therapies manufacturing. The discussions also focused on future advancements, regulatory hurdles, and the importance of partnerships in advancing the capabilities and reach of these therapies.

For more details, please read the full press release here.

Progress to date

The CAR T-REX team has recently achieved its first two project milestones related to our genetic modification activities, including optimisation and selection of the best-performing RNA guides and miRNA precursor constructs. Preliminary experiments performed by TargetGene have shown promising results from insertion into the “Driver” gene for expression of the miRNA, which will be further developed over the next phase of the project.

Furthermore, high-throughput screening experiments performed at CIQUS have identified preliminary “carrier” candidates for delivery of the genetic cargo into cells. Iterations will be performed to maximise efficiency in combination with the genetic cargo.

Partner Spotlight

TARGETGENE
Biotechnologies

TargetGene's technology & expertise
TargetGene is a therapeutics oriented gene-editing company from Israel. TargetGene's core technology is based on the T-GEE platform, its novel and proprietary ultra-precise dual-RNA guided system. T-GEE can be visualised as a pair of programmable molecular "DNA scissors" that utilise two RNA guides and an obligatory dimeric nuclease to achieve exquisite specificity. T-GEE addresses the biggest challenge of guided gene editing - off-target cleavage of unintended genes - as it is designed to be ~100,000 times more precise than CRISPR-Cas9, potentially creating a radically safer therapeutic tool. T-GEE can be used to modify the patient's own DNA, rewiring the transcriptome by precisely replacing genes, correcting genetic abnormalities or enhancing a cell type (e.g., T Cells) allowing a cure as opposed to chronic treatment.

TargetGene's role in CAR T-REX Project
TargetGene is providing the T-GEE platform and expertise in "genetic circuit rewiring" for gene editing to solve T-cell exhaustion without compromising product safety. TargetGene is developing, designing and testing all the genetic components and molecular assays necessary for implementation of safe and precise gene replacement through Homology Directed Repair (HDR). This consists of guide-pairs, HDR donor-DNA and artificial negative regulator components. These components will be transferred to the CAR T-REX partners for testing of novel delivery systems, for immunological efficacy assays and in vivo pre-clinical testing.

Interesting fact about TargetGene
TargetGene was created by Yoel Shiboleth and Dan Weinthal who were the pioneering figures behind the invention and patenting of an RNA-guided gene-editing system in 2011, predating CRISPR. Investors and their scientific consultants initially dismissed the idea as "science fiction", but obviously today, RNA-guided nucleases have become widely adopted, and indeed essential, in all fields of biology.

Connect With Us!

Stay connected with the CAR T-REX team at various conferences and events throughout the second semester of 2024. Engage with our experts, learn about our latest discoveries, and explore future collaboration opportunities.

Advanced Therapies Europe
- Estoril, Portugal
- 10-12 September
- Learn more here

Cell & Gene Meeting on the Mesa

- Phoenix, AZ, USA
- 07-09 October
- Learn more here

European Society for Gene and Cell Therapy (ESGCT)

- Rome, Italy
- 24-27 October
- Learn more here

Partner Updates

LIT Symposium 2024

From the 26th – 27th of June the team at Leibniz Institute for Immunotherapy (LIT) hosted the Third International Synthetic Immunology & Synthetic Biology Symposium in Regensburg, Germany. More than 150 participants attended a variety of talks over 2 days, including development of cancer specific cellular therapies and the growing potential of artificial intelligence in synthetic immunology. You can find out more here.

No CRISPR, no problem: 'Jumping gene' system could be bridge to complex gene editing
Read more here

A new gene editing technique derived from bacterial “jumping genes” can add, remove, recombine and invert DNA sequences, potentially overcoming some of the limitations of CRISPR.

FDA approval of the first cellular therapy for a solid (non-hematologic) cancer
Read more here

On February 16, 2024, the U.S. Food and Drug Administration granted accelerated approval for lifileucel (Amtagvi), a cellular therapy developed by Iovance Biotherapeutics. This marks the first FDA-approved cellular treatment for a solid (non-hematologic) tumor

Thanks for reading the second edition of the CAR T-REX Newsletter! We’ll be publishing new editions every six months throughout the project. Please forward it to your colleagues, and make sure to follow us on LinkedIn for further updates.

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