

Hello and welcome to the very first project newsletter for CAR T-REX - **CAR T Cells Rewired to Prevent EXhaustion** in the Tumour Microenvironment! Join us as we work towards the goal of effectively targeting solid tumours. Scroll down to learn more about the project, partners, and what's next for CAR T-REX.

CAR T-REX Overview

The Challenge: Current CAR T cell therapies have achieved impressive clinical success in the treatment of multiple haematological malignancies; yet the translation to solid tumours has been challenging, primarily owing to antigen heterogeneity, limited infiltration in tumour tissue, and T cell exhaustion or loss of function. To tackle this, we aim to develop and reprogramme novel CAR-T cells, with ability to circumvent tumour microenvironment exhaustion. The development will employ non-viral gene editing and delivery systems, steered by a Quality by Design (QbD) approach, facilitating an accelerated transition from laboratory workbench to clinical application.

The Project: Launched in June 2023, CAR T-REX is a Pathfinder Open project funded by the European Innovation Council (EIC). The project will span 4 years, with the overarching goal of developing novel, scalable GMP compliant CAR T cell therapies with enhanced effectiveness in treating solid tumours.

The Team: The CAR T-REX consortium brings together a multidisciplinary team with unique expertise and capabilities in **genome editing, non-viral gene delivery, immunology, and T cell therapy**, as well as quality-by-design (QbD) methodologies and cGMP manufacturing. Read all about the CAR T-REX partners [here](#).

Partner Spotlight



Centro Singular de Investigación
en Química Biológica e
Materiais Moleculares

USC's technology & expertise

USC has developed, in Prof. Javier Montenegro's research group, a novel non-viral gene delivery technology. USC's approach utilises synthetic cationic peptides with reactive pendants onto which different hydrophobic tails can be attached, granting access to libraries of structurally diverse peptide-amphiphile carriers. This platform enables the rapid screening of potential carrier candidates in a short time window while facilitating the extraction of structure-activity relationships and, thus, the discovery of tailor-made gene delivery vehicles.

USC role in CAR T-REX Project

USC will provide its gene delivery platform technology to the CAR T-REX consortium in order to maximise the chances of discovering a safe yet effective T-cell transfection tool suitable for the ambitious rewired CAR products aimed at in the project. The unique features that USC's technology already presents (chemical diversity of carriers, broad gene cargo scope, minimal toxicity) will be further refined and

expanded in the context of the CAR T-REX project to facilitate its applicability in challenging T-cell transfection procedures.

Interesting fact about USC

Inside USC's central building, Pazo de Fonseca, in a small but cosy space named Xardín das Pedras que Falan (which could be translated as the "Garden of the speaking stones"), sheltered from the shadow of a spectacular Gingko biloba, there is a plaque under which a time capsule is buried. This story, unknown even to many Santiago de Compostela natives, was the result of the unlikely but happy union of the University of Santiago with the collective [Sentinel Wardrobe](#). The capsule was buried on April 27, 2013, a decade ago. It was baptised back in the day as "Hermes 2047", in honour of the messenger of the gods, and will be recovered on the same date, but from the year 2047, which in binary language is written with eleven ones, as it appears on the plaque. What's in it? Who will still be here to open it when the time comes? We prefer to leave these questions in the limbo of things we don't know about the future. But, of course, we hope to be here to tell you the end of this story.



Connect With Us!

Members of the CAR T-REX team will be heading to a range of conferences and events in 2024 and would love to catch up with you for a chat. Look out for us at the events below, and feel free to [reach out](#) if you'd like to connect.



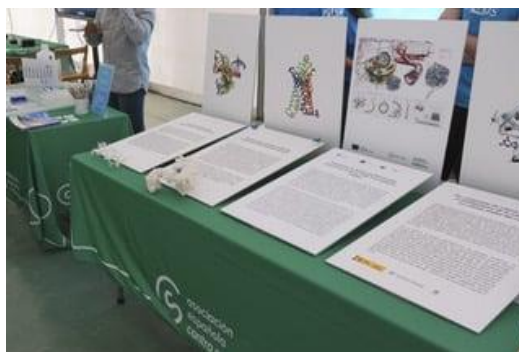
Advanced Therapies Europe

- Estoril, Portugal
- 10-12 September
- Learn more [here](#)



European Society for Gene and Cell Therapy (ESGCT)

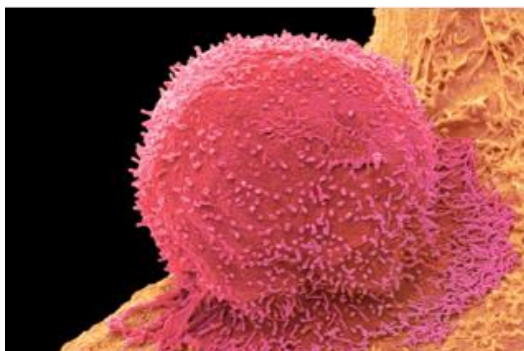
- Rome, Italy
- 24-27 October
- Learn more [here](#)



“Science for all” fair

CAR T-REX team members from USC recently participated in a science fair as part of an event organised by [Asociación Española Contra el Cáncer](#) (Spanish Association Against Cancer). The event included a parade to support cancer research in Santiago de Compostela and the “Science for all” fair, which included a panel explaining some of the research being performed for the CAR T-REX project.

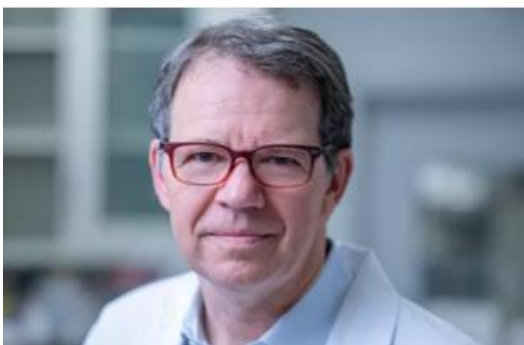
Cell & Gene Therapies: Recommended Reading



Innovative new cell therapies could finally get at tough-to-target cancers

Read more [here](#)

Researchers are engineering immune cells to take aim at solid tumors.



Disrupting a Single Gene Could Improve CAR T Cell Immunotherapy, New Study Shows

Read more [here](#)

Dr. Michel Sadelain’s lab showed that disrupting a single gene called SUV39H1 gave CAR T cells more staying power to fight cancer.

Future Plans & Call to Action

The next big step for the CAR T-REX project is to use the T-GEE platform to select the best RNA guides for CAR T cell reprogramming. These experiments are underway and we aim to have the top candidates ready for further screening in the coming months.

We’re also working on the CAR T-REX Quality by Design (QbD) strategy, which focuses on establishing pre-defined objectives and manufacturing controls to ensure the safety and efficacy of the final CAR-T product. The next steps for the QbD strategy are to establish the quality target product profile (QTPP) and devise a control strategy to ensure consistent manufacturing process performance and the desired product quality. This approach will help to fast-track our final CAR T cell therapy towards clinical manufacturing.

Thanks for reading the first 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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