PREDICTION OF THE 2024 MEDICINE NOBEL PRIZE

BUI DAC CHI MD

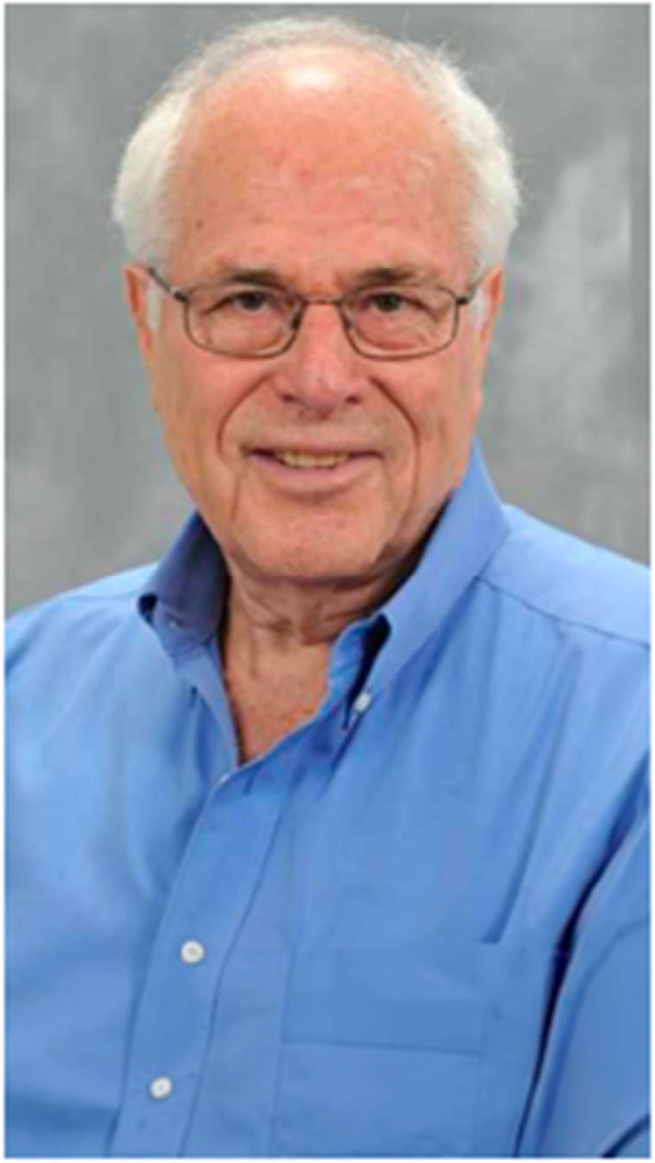
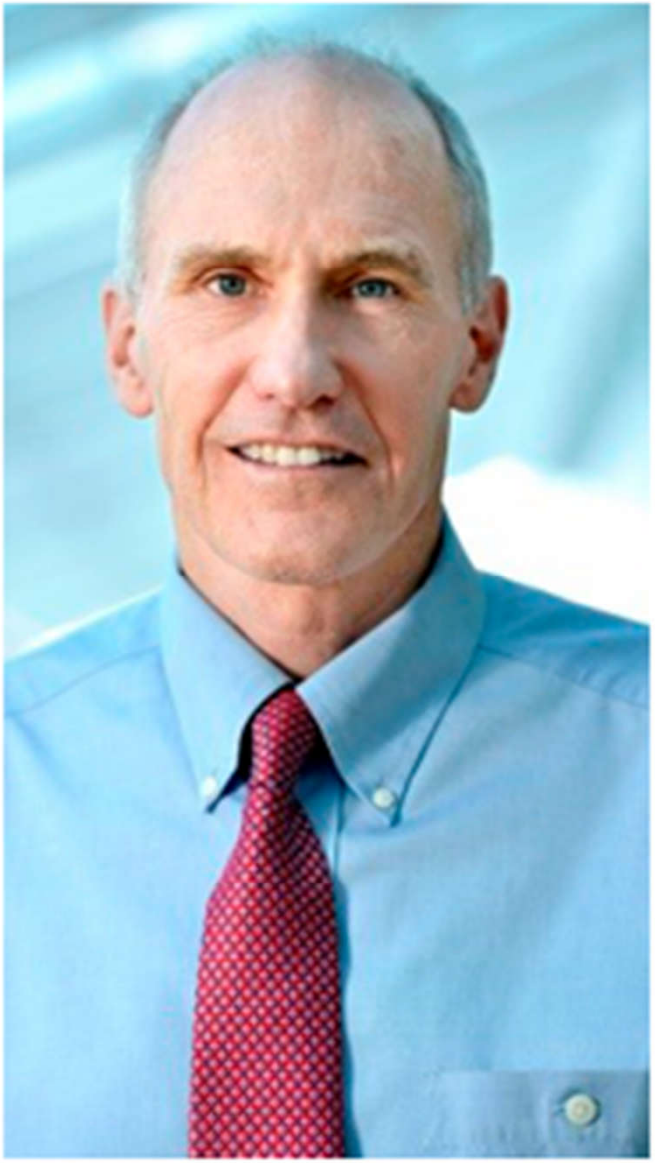
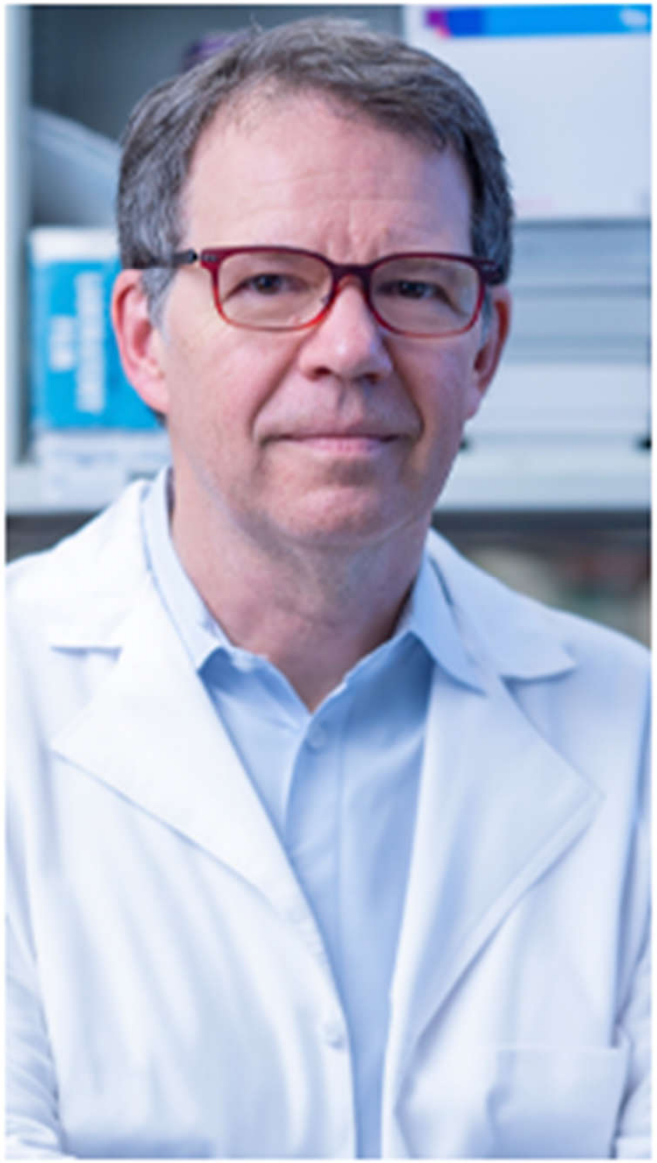
MEDIC CLINIC SAIGON

The 2024 Medicine,Nobel prizewill beawarded to the CAR Tcell therapyin which each patient's T cells are modified to target and to kill their cancer cells.Three pionneers:

1.zelig Eshhar MD,Ph D(at the WeizmannInstitute of Science,Israel)

,,,,,,,,,,,,,2.Michel Sadelaine MD,PhD(at the Memorial Sloan Kettering Cancer Cfnter,USA)

3.Carl JuneMD(at the penn'sPereman School of Medicine,USA)

shhar, Carl June, Michel Sadelain

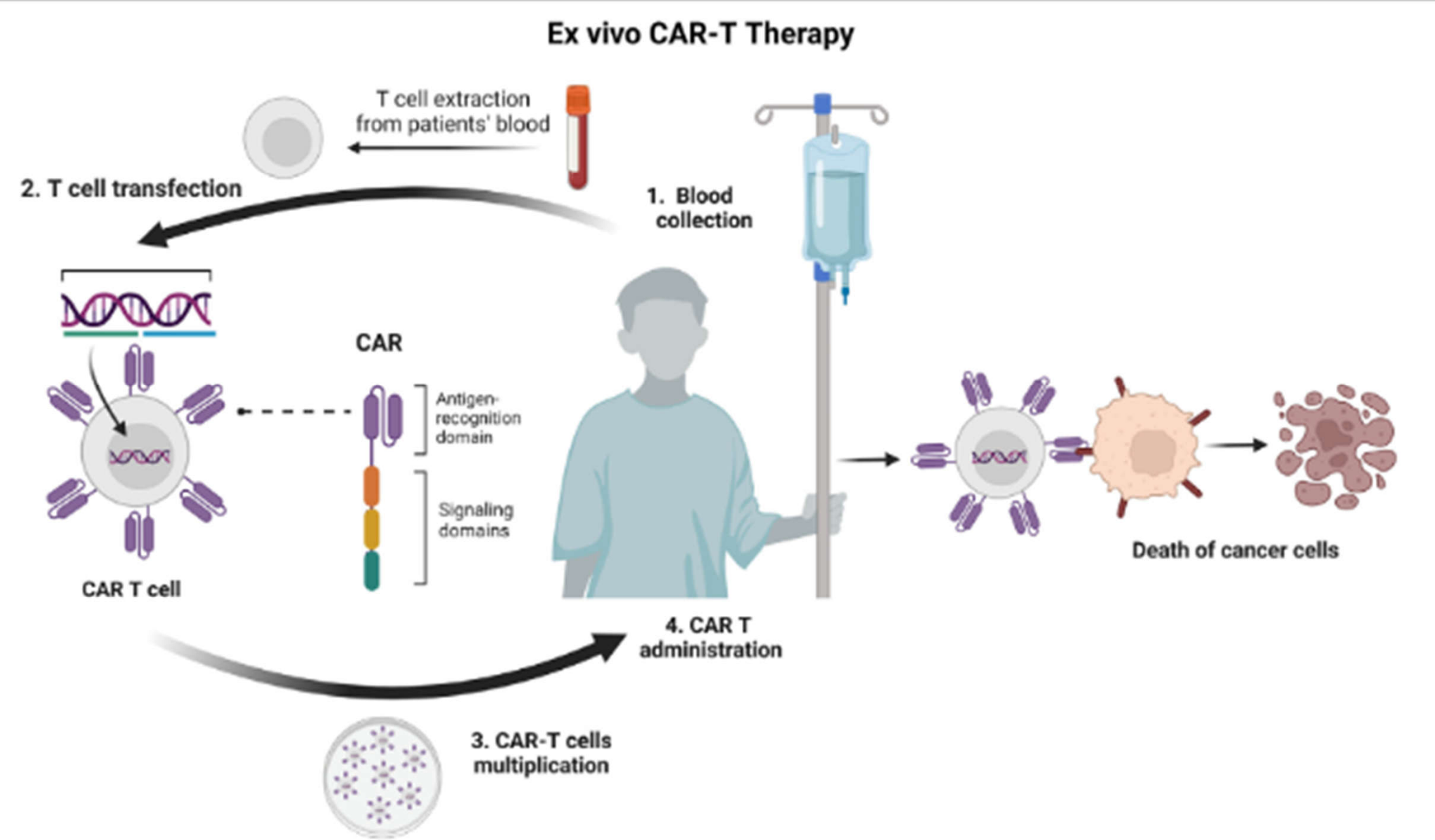


***Fig. 2:* Process of *ex vivo* CAR T therapies.** *Ex vivo* CAR T-cell therapy involves isolating a patient's or healthy donor's T-cells via leukapheresis, genetically modifying them with a CAR construct designed for specific cancer antigens. These modified cells are then cultured and expanded. The expanded and modified T-cells are reintroduced into the patient via infusion. Activated CAR T-cells recognise and destroy cancer cells expressing the targeted antigen, potentially providing long-term immunity against cancer recurrence.

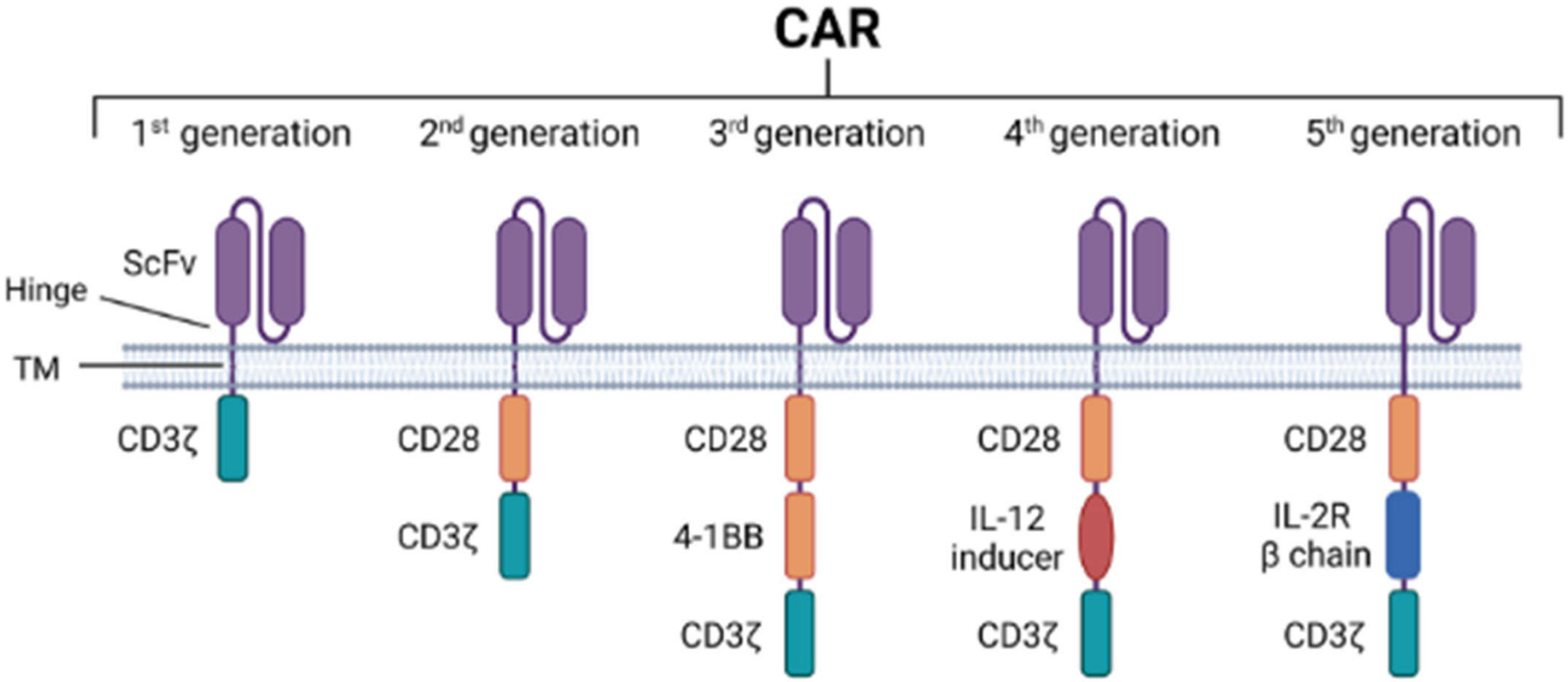


***Fig. 1:* Overview of CAR structure.** All five generations of CAR constructs share common structures with 4 domains: an extracellular domain targeting tumour-specific antigens (ScFV), a hinge region, transmembrane domain (TM), and finally an intracellular domain. As demonstrated, the structure of CAR intracellular domain indicates CAR generation as well as its functional activity. For instance, the CD3ζ domain initiates essential signal transduction pathways necessary for T-cell activation, proliferation, cytokine production, and cytotoxicity. Meanwhile, the CD28 and 4-1BB domains function as co-stimulatory signals, augmenting T-cell activation, persistence, and functionality. The IL-12 inducer domain is employed to prompt cytokine release within the tumour microenvironment, and the IL-2R beta chain mimics IL-2 signalling, enhancing CAR-T cell survival, proliferation, and persistence.

Advancements and challenges in developing *in vivo* CAR T cell therapies for cancer treatment

Thuy Anh Bui,[a,b,e] Haoqi Mei,[a] Rui Sang,[c] David Gallego Ortega,[a,d,e] and Wei Deng[a,c,]*

[a]School of Biomedical Engineering, University of Technology Sydney, Ultimo, NSW 2007, Australia
[b]Whitlam Orthopaedic Research Centre, Ingham Institute for Applied Medical Research, Liverpool, NSW 2170, Australia
[c]Graduate School of Biomedical Engineering, ARC Centre of Excellence in Nanoscale Biophotonics, Faculty of Engineering, UNSW Sydney, NSW 2052, Australia
[d]Garvan Institute of Medical Research, The Kinghorn Cancer Centre, Darlinghurst, NSW 2010, Australia
[e]School of Clinical Medicine, Faculty of Medicine, University of New South Wales Sydney, Kensington, NSW 2052, Australia

Summary

The Chimeric Antigen Receptor (CAR) T cell therapy has emerged as a ground-breaking immunotherapeutic approach in cancer treatment. To overcome the complexity and high manufacturing cost associated with current *ex vivo* CAR T cell therapy products, alternative strategies to produce CAR T cells directly in the body have been developed in recent years. These strategies involve the direct infusion of CAR genes via engineered nanocarriers or viral vectors to generate CAR T cells *in situ*. This review offers a comprehensive overview of recent advancements in the development of T cell-targeted CAR generation *in situ*. Additionally, it identifies the challenges associated with *in vivo* CAR T method and potential strategies to overcome these issues.

Expanding the Scope of CAR T Cell Therapy

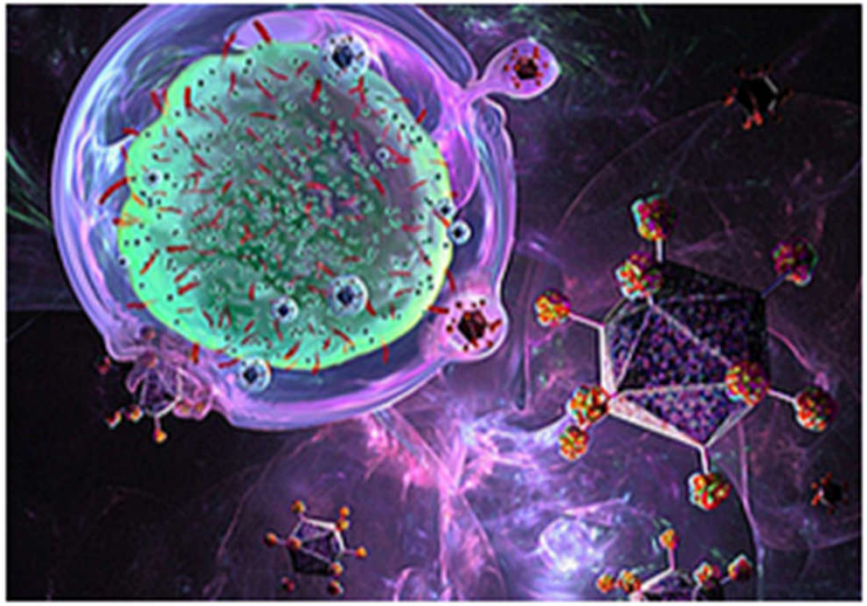


Image: Keith Chambers / Science Photo Library

Interdisciplinary Discussion

Date: Monday, 8 to Tuesday, 9 April 2024

Location: Leopoldina, Jägerberg 1, 06108 Halle (Saale) und C

The onset of Chimeric Antigen Receptor (CAR) T cell therapy marks a revolutionary development in the field of immunotherapy, achieving notable success since its approval in 2017 for treating B cell malignancies. Designing a patient's own T cells to specifically identify and eradicate tumor cells has successfully treated individuals with previously incurable hematologic cancers.

While CAR T cells are currently predominantly utilized in anti-tumor therapy, their initial conceptualization aimed at a broader objective of targeting membrane antigens, opening the door to numerous potential applications. Subsequent studies have explored the application of CAR T cells in non-malignant pathologies, encompassing autoimmune diseases, infectious diseases, and more recently, conditions such as cardiac fibrosis and cellular senescence.

VIDEOS OF THE EVENT ON YOU

Videos on the Leopoldina Yo

FURTHER INFORMATION AND

The interdisciplinary discussi
an training event with the Sax
Medical Association and is air
sionally interested public.
Registration is closed.

THE END