Demystifying CAR-T Therapy

Biography

Dr Thomas Sau-Yan CHAN is a Consultant of the Division of Hematology at Queen Mary Hospital. He graduated in 2006 with an MBBS (Honours) from the University of Hong Kong, and embarked on his career to become an internal physician. He obtained his Fellowship in Hematology and Hematological Oncology in 2013. His current clinical and research interests include chronic lymphocytic leukemia, immunotherapies for lymphoid malignancies and infection in immunocompromised hosts.

Abstract

Chimeric antigen receptor T-cell (CAR-T cell) therapy has revolutionized the treatment landscape of hematological malignancies. With six products currently licensed by the Food and Drug Administration (FDA), CAR-T cell therapy has shown remarkable efficacy in aggressive B-cell lymphoma, multiple myeloma, B-cell acute lymphoblastic leukemia, mantle cell lymphoma, and chronic lymphocytic leukemia. However, despite its successes, hurdles to achieving therapeutic success remain, including associated toxicities and disease relapses.

Significant progress has been made in the management of the toxicity associated with CAR-T cell therapy, such as cytokine release syndrome (CRS) and immune cell-associated neurotoxicity syndrome (ICANS). However, disease relapse continues to be a critical concern. Identifying the factors that predict relapse, both patient-related and disease-related, is crucial but the mechanistic link between these clinical factors and relapse remains largely unknown.

Among the various factors under investigation, much attention is focused on the role of exhausted T-cell phenotypes, which may contribute to relapse. In real-life settings, it is likely that multiple factors interact to influence treatment outcomes.

Ongoing trials are exploring strategies to overcome these challenges. These include administering CAR-T cell therapy earlier in the disease course, investigating new targets for CAR-T cell therapy, and employing different immune cell manipulations, such as CAR-NK cells, armored CAR-T cells, or T-cells redirected for universal cytokine-mediated killing (TRUCKS). These endeavors aim to enhance the effectiveness of CAR-T cell therapy and improve patient outcomes.

In summary, our understanding of the complex mechanisms underlying CAR-T cell therapy is still in its early stages. There is much to learn in order to optimize this form of immunotherapy and extend its benefits to a larger population of patients. Continued research and clinical trials work towards advancement in CAR-T cell therapy, offering hope for improved treatment outcomes in hematological malignancies.