CAR T-cells as living drugs for cancer treatment

Background and Objective: The adoptive transfer of T cells generated with chimeric antigen receptor (CAR) emerged as an exciting cancer immunotherapy for clinical efficacy in hematological and non-hematological malignancies. In this review, we discuss the current understanding of the molecular properties that lead to the development of different generations of CARs.

Methods: In this study, it was performed a systematic review of studies that CAR T-cells were used as drugs for cancer treatment. We searched about 60 articles in PubMed, Science Direct, Scopus and nature (2011-2017). Searches were conducted using the following keywords: CAR-T cells, cancer immunotherapy, cytokine release syndrome, universal T-cells, CRISPR/Cas9.

Finding: Early clinical trials with redirected T cells targeting CD19 have shown impressive results in hematological cancers. Like any new therapies, this method also encounters challenges like on and off target toxicity and most importantly cytokine release syndrome (CRS) that is associated with most clinical responses. Potential strategies to improve anticancer activity and efficacy while reducing unwanted side effects have been employed. Some of the suggested strategies, including suicide gene, inhibitory CAR, dual-antigen receptor, and the use of exogenous molecules as switches to control the CAR-T cell functions. Furthermore, the potential for genetic manipulation using the CRISPR/Cas9 system to generate universal CAR-T cells and potent T cells that are resistant to exhaustion and inhibition is explored.

Conclusion: Given the tremendous progress that has been made in the past several years, we believe the CAR-T cells hold immense promise for advancing cancer immunotherapy.

Keywords: CAR T-cell, cancer immunotherapy, cytokine release syndrome, Universal CAR T-cell, CRISPR/Cas9