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EDITORIAL

CAR-T therapy is a breakthrough for intractable autoimmune disease?

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The dramatic effects of checkpoint inhibitor therapy[1,2] and chimeric antigen receptor T (CAR-T) cell therapy[3,4,5] have attracted a great deal of global attention and have recapitulated the history of cancer treatment so far. The recent approval of two CAR-T therapies by US Food and Drug Administration marked a very significant development in cell-based cancer immunotherapy. This milestone was demonstrated by the effectiveness of eradicating hematologic cancers using CD19-specific CARs.

The success spurred development of immune cell therapies for other cancers, especially solid tumors. With regard to CAR-T therapy for solid tumors, although the clinical effects are limited, some unexpected serious adverse events have been reported and there are still many problems. The generation of novel CAR constructs for these cancer types represents a major challenge in bringing the technology 'from-bench-to-bedside'. In the review of Santos and Bernal[6], they outlined some new technologies to equip CAR-T cells to enhance efficiency while decreasing toxicity of CAR-T therapies in solid tumors. Development research on safer and more effective CAR-T therapy for solid tumors is in progress and will improve the outcome of treatment for patients with refractory leukemia and cancer in the future.

Furthermore, it was expected that this CAR-T method would be applied to intractable autoimmune diseases. In the recent article of Kansal R *et al*[7], CD19-targeted CAR-T therapy is reported to be highly promising for intractable systemic lupus erythematosus. They used murine lupus models such as in the (NZB × NZW) F1 and MRL lpr/lpr mouse. New Zealand (NZ) mouse and MRL lpr/lpr mouse are well known to be a B-lupus model and a T-lupus model, respectively. The clinical trials of anti-CD20 antibody for lupus failed because of the transient and incomplete B cell depletion. They reported that CD8+ T cells expressing CD19-targeted CARs persistently depleted CD19+ B cells, eliminated autoantibody production, reversed disease manifestations in target organs, and extended life spans in murine lupus models. For human application, there will be many issues to be solved, but at least it will lead to the elucidation of the pathogenesis of intractable autoimmune diseases.

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