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# Current state and perspectives of CAR T cell therapy in central nervous system diseases

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## Abstract

B cell-directed CAR T cell therapy has fundamentally changed the treatment of hematological malignancies and its scope of application is rapidly expanding to include other diseases such as solid tumors or autoimmune disorders. Therapy-refractoriness remains an important challenge in various inflammatory and non-inflammatory disorders of the CNS. The reasons for therapy failure are diverse and include limited access of current therapies to the CNS, as well as enormous inter- and intraindividual disease heterogeneity. The tissue-penetrating properties of CAR T cells make them a promising option to overcome this problem and to tackle pathologies directly within the CNS. First application of B cell-directed CAR T cells in neuromyelitis optica spectrum disorder and multiple sclerosis patients has lately revealed promising outcomes, expanding the potential of CAR T cell therapy to encompass CNS diseases. Additionally, the optimization of CAR T cells for the therapy of gliomas is a growing field. As a further perspective, pre-clinical data reveal potential benefits of CAR T cell therapy also in the treatment of primary neurodegenerative diseases such as Alzheimer's disease. Considering the biotechnological optimizations in the field of T cell engineering, such as the extension to target different antigens or the variation of the modified T cell subtype, new and promising fields of application for CAR T cells are rapidly opening up. These innovations offer the potential to address the complex pathophysiological properties of CNS diseases. To optimally utilize CAR T cell therapy for CNS diseases in the future while minimizing therapy risks, there is a need for further mechanistic research as well as prospective controlled trials to seriously assess the disease and patient-specific risk-benefit ratio.

**Keywords:** CAR T cells; glioma; multiple sclerosis; neurodegeneration; neuroinflammation.

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