

Selected Aspects of the Neuroimmunology of Cell Therapies for Neurologic Disease

Perspective

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Abstract

Neurologic disease remains a cause of incalculable suffering, a formidable public health burden, and a wilderness of complex biology and medicine. At the same time, advances in basic science, technology, and the clinical development toolkit bring meaningful benefit for patients along with realistic hope for those whose conditions remain inadequately treated. This perspective focuses on cell-based therapies for neurologic disease, with particular emphasis on neuro-immunologic disorders and on the immunologic considerations of cell therapy for nonimmune conditions. I will consider the use of chimeric antigen receptor (CAR)-T effector cells and regulatory T-cell therapies for autoimmune conditions. I will briefly discuss the immune aspects of pluripotent stem cell (PSC)-derived neuronal therapies. With apologies for the omission, we do not discuss mesenchymal stem cells, glial progenitor cells, or CAR-NK cells, primarily for space limitations.

Cell therapies rank among the more impressive technological and clinical advances in contemporary medical research. Their main practical effect has been exerted in treating hematologic malignancy, with particular efficacy in B-cell tumors such as acute lymphoblastic leukemia, lymphoma, and myeloma.¹ As a natural evolution, this therapeutic approach was extended to autoimmune conditions implicating B cells, including those that affect the central and peripheral nervous systems.^{1–4} Last year, the topic was authoritatively reviewed in this journal.^{5,6} In part, the present article seeks to build on, and update, those publications.

CAR-T Cells

CAR-T cells use antigen recognition elements derived from immunoglobulins (Igs) and expressed as single-chain fragment variable (scFv) constructs, which incorporate the antigen-recognition domains of Ig heavy and light chains as fusion proteins that are engineered to fold, so as to enable high-affinity binding to antigenic targets. For expression at the plasma membrane, CAR-T constructs include transmembrane domains. Signaling competence of scFv in CAR-T cells is endowed by coupling to the CD3- ζ chain, with addition of the intracellular components of costimulatory elements such as CD137/4-1BB. Together, this engineering affords CAR-T cells with high-affinity antigen recognition and downstream signaling that confers proliferative capacity, effector function, and persistence in the recipient for the durable therapeutic effect. Similar to immunoglobulin, the CAR-T receptor is not limited by MHC restriction for antigen recognition.

The role of B cells in multiple sclerosis (MS), once rather neglected, has become an unavoidable topic, in substantial part due to unexpected, dramatic success treating relapsing pathology of MS with CD20 antibodies.⁷ After decades of effort, the multiplicity of functions of B cells in MS remains under investigation because the canonical property—antibody

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Clinical Aspects Of Neuroimmunology

Xiang Xie



Clinical Aspects Of Neuroimmunology:

Neuroimmunology in Africa Willias Masocha,Roberto Furlan,Richard Idro,2023-05-29 *Recent Advances in Psychiatry from Psycho-Neuro-Immunology Research: Autoimmunencephalitis, Autoimmune-Encephalopathy, Mild Encephalitis* Karl Bechter,David Brown,Souhel Najjar,2019-08-12 Growing evidence derived from cerebrospinal fluid CSF neuropathological imaging genetic and epidemiological studies link neuroinflammation and immune dysregulation to a subset of individuals with a variety of severe mental disorders SMDs including affective and non affective psychotic disorders Further the recent discoveries of neuronal surface antibodies NSAs in autoimmune encephalitis AE presenting with diverse neuropsychiatric disorders such as psychosis and cognitive decline among many others provides further support to the notion that CNS autoimmunity and neuroinflammation can contribute to the neurobiology of psychiatric disturbances Further these immune mechanisms may contribute to a subset of patients currently diagnosed as having treatment resistant SMDs such as schizophrenia and major depressive disorder Additionally mounting data indicate that various infections can serve as an immunological trigger of aberrant immune responses presumably by causing release of excess neural antigen thereby giving rise to NSAs or aberrant immune cellular responses to give rise to primary or secondary psychiatric disorders such as schizophrenia and those associated with AE respectively Collectively these findings support the mild encephalitis hypothesis of SMD The significant overlap among AE associated psychosis systemic autoimmune disorder associated psychosis and psychotic disorders associated with pathological processes involving inflammation and immune dysregulation has also prompted some authors to adopt the term autoimmune psychosis AP This term reflects that this psychosis subtype is mechanistically linked to complex neuroimmune and inflammatory signalling abnormalities that can be responsive to early immunomodulatory treatment It also suggests that a subset of AP might represent an incomplete or forme fruste subtype of AE presenting with dominant or pure psychiatric symptoms mimicking primary psychiatric illnesses Because data indicate that delayed diagnosis and treatment may lead to permanent sequelae early recognition of AP utilizing neurodiagnostic workup e g CSF analysis neuroimaging and EEG and its early treatment with appropriate immunotherapy are paramount to a meaningful recovery This eBook will provide an overview of the current knowledge and research areas from epidemiology risk factors and diagnosis to the management of these conditions in this rapidly emerging field helping to bridge the gaps in knowledge that currently exist in the disciplines of Psychiatry Neurology and Neuroimmunology [Health Science Books, 1876-1982](#) ,1982 **Clinical Neuroimmunology** Syed A. Rizvi,Jonathan F. Cahill,Patricia K. Coyle,2019-10-24 This comprehensive up to date book is designed to make recent developments in neuroimmunology accessible to medical professionals in the field The field of neuroimmunology is complex and rapidly evolving especially with the current improvements in targeted biologic therapies This resource concisely offers clear explanations of these scientific and clinical advancements Divided into five parts the book begins with an in depth introduction to neuroimmunology and the principles of

immunotherapy Section two consists of eight chapters devoted to multiple sclerosis including discussions on the clinical features of the disease as well as symptom management and diagnosis Subsequent chapters then dive into other central nervous system inflammatory disorders such as neuromyelitis optica autoimmune encephalopathies and immunological aspects of cancer Following this are two chapters that examine distinct aspects of autoimmune disorders of the peripheral nervous system Finally the book closes with a review on the neurologic manifestations diagnostic approaches and treatments of the various systemic rheumatic diseases Following its successful predecessor edition *Clinical Neuroimmunology Multiple Sclerosis and Related Disorders Second Edition* is positioned to be an invaluable asset to neurologists residents and fellows internists and general practitioners who treat patients with neurologic disorders and other systemic autoimmune diseases

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