OPEN ACCESS Freely available online

ISSN: 2684-1614
Journal of Tumour Research & Reports

Commentary Article

Overcoming Immune Resistance in Diffuse Large B-Cell Lymphoma: Targeting Escape Mechanisms for Effective Immunotherapy

Robert Jackson*

Department of Human Oncology, Howard University, Washington, USA

DESCRIPTION

Diffuse Large B-cell Lymphoma (DLBCL) is the most common type of non-hodgkin lymphoma, accounting for approximately 30% of all cases. DLBCL is characterized by aggressive growth and heterogeneity, making it a formidable challenge in clinical management. While significant progress has been made in understanding the pathogenesis and developing targeted therapies, treatment resistance and relapse remain major obstacles. Recent studies have shed light on the role of immune escape mechanisms in DLBCL, explaining the limitations of immunotherapy in achieving long-term remission.

Understanding immune escape mechanisms

DLBCL is known to exhibit a complex interplay between tumour cells and the immune system. Immune escape mechanisms, whereby cancer cells evade recognition and elimination by the immune system, contribute to tumour progression and treatment resistance. Several key mechanisms have been identified in DLBCL, including:

Downregulation of antigen presentation: DLBCL cells can reduce the expression of Major Histocompatibility Complex (MHC) molecules and antigen presentation machinery, impairing their ability to present tumour antigens to cytotoxic T cells. This hampers the recognition and elimination of tumour cells by the immune system.

Dysregulation of immune checkpoints: Immune checkpoints, such as programmed cell Death Protein 1 (DP-1) and Cytotoxic T-Lymphocyte-Associated Protein 4 (CTLA-4), play a crucial role in regulating immune responses. DLBCL cells exploit these pathways to inhibit T-cell activation and evade immune surveillance.

Induction of tumour-associated immunotolerance: Tumour microenvironment components, such as regulatory T cells (Tregs), Myeloid-Derived Suppressor cells (MDSCs), and immunosuppressive cytokines, promote an immunotolerant milieu that shields DLBCL cells from immune attack. These suppressive elements inhibit the effector functions of immune cells and promote tumour growth.

Resistance to cytotoxic t-cell-mediated killing: DLBCL cells can develop mechanisms to resist cytotoxic t-cell-mediated killing. This includes alterations in the expression of death receptors, upregulation of anti-apoptotic proteins, and secretion of immunosuppressive factors.

Overcoming immune escape mechanisms

The identification of immune escape mechanisms in DLBCL provides insights into potential strategies to overcome treatment resistance. Several therapeutic approaches are being explored to restore and enhance the anti-tumour immune response in DLBCL patients.

Immune checkpoint blockade: Targeting immune checkpoint pathways, such as PD-1 and CTLA-4, using monoclonal antibodies has shown promising results in other hematological malignancies. Clinical trials investigating immune checkpoint blockade in DLBCL are underway, either as monotherapy or in combination with chemotherapy or other immunotherapies.

Chimeric Antigen Receptor (CAR) T-cell therapy: CAR T-cell therapy involves modifying patients' own T cells to express receptors that recognize tumour-specific antigens. Despite remarkable success in relapsed/refractory DLBCL, immune escape mechanisms can lead to relapse or resistance. Combining CAR T-cell therapy with other immune modulators may help improve efficacy and durability.

Bispecific antibodies: Bispecific antibodies are designed to engage T cells and tumour cells simultaneously, facilitating immune recognition and elimination. Various bispecific antibodies targeting CD19 and CD20 antigens, as well as immune checkpoints, are under investigation for DLBCL treatment.

Correspondence to: Robert Jackson, Department of Human Oncology, Howard University, Washington, USA, E-mail: jacksonrt@gmail.com

Received: 24-May-2023, Manuscript No. JTRR-23-22043; **Editor assigned**: 26-May-2023 JTRR-23-22043 (PQ); **Reviewed:** 12-Jun-2023, QC No. JTRR-23-22043; **Revised:** 20-Jun -2023, Manuscript No. JTRR-23-22043 (R); **Published:** 28-Jun-2023, DOI: 10.35248/2684-1614.23.8:197

Citation: Jackson R (2023) Overcoming Immune Resistance in Diffuse Large B-Cell Lymphoma: Targeting Escape Mechanisms for Effective Immunotherapy. J Tum Res Reports.8:197.

Tumour vaccines and dendritic cell therapy: Vaccines that stimulate an immune response against tumour-specific antigens are being explored in DLBCL. Dendritic cell-based therapies, which harness the antigen-presenting capacity of dendritic cells, are being investigated to improve antigen presentation and T-cell activation.

Combination therapies: Combining different immunotherapeutic approaches, such as immune checkpoint blockade with CAR T-cell therapy or targeted agents, has the potential to overcome multiple immune escape mechanisms simultaneously. Rational combinations tailored to individual patients' immune profiles are likely to yield better outcomes.

Immune escape mechanisms pose significant challenges in the treatment of DLBCL, limiting the efficacy of immunotherapy. However, with a deeper understanding of these mechanisms, novel therapeutic strategies are being developed to overcome immune resistance. Combining different immunotherapeutic modalities, targeting multiple escape mechanisms, and personalizing treatment based on the immune profile of each patient hold promise for improving outcomes in DLBCL.