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BTLA and HVEM: Emerging players in the tumor microenvironment and cancer progression

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Abstract

Immunotherapy has emerged as a revolutionary cancer treatment, particularly with the introduction of immune checkpoint inhibitors (ICIs). ICIs target specific proteins that restrain the immune system from attacking cancer cells. Prominent examples of checkpoint proteins that ICIs block include PD-1, PD-L1, and CTLA-4. The success of PD-1/L1 and CTLA-4 blockade has prompted further research on other inhibitory mechanisms that could aid in the treatment of cancer. One such mechanism is the BTLA/HVEM checkpoint, which regulates immune responses in a similar manner to CTLA-4 and PD-1. BTLA, a member of the Ig superfamily, binds to HVEM, a member of the TNF receptor superfamily. While BTLA is essential for maintaining immunological self-tolerance and preventing autoimmune diseases, overexpression of BTLA and HVEM has been observed in various malignancies such as lung, ovarian, glioblastoma, gastric cancer, and non-Hodgkin's lymphoma. The function of the BTLA/HVEM checkpoint in various malignancies has been extensively studied, revealing its significant role in immunotherapy for cancer. This review study aims to explain the BTLA/HVEM checkpoint and its functions in different types of cancers. In conclusion, the development of new immunotherapies such as ICIs has revolutionized cancer treatment. The discovery of the BTLA/HVEM checkpoint and its role in various malignancies provides opportunities for advancing cancer treatment through immunotherapy.

Keywords: BTLA; HEVM; Immune checkpoint Inhibitors; Inhibitory Receptor Checkpoint; Neoplasm; TNFR superfamily.