BTN2A2

- Integrated microfluidics-based construction of anti-BTN2A2 gel droplet cell preparations for non-invasive tumor-infiltrating lymphocyte therapy
- BTN2A2, a new biomarker and therapeutic target for glioma
- BTN2A2-Ig protein inhibits the differentiation of pathogenic Th17 cells and attenuates EAE in mice
- BTN2A2 protein negatively regulates T cells to ameliorate collagen-induced arthritis in mice

Protein casein 2A2 (BTN2A2) is a costimulatory molecule first identified in antigen-presenting cells. Studies have shown the involvement of BTN2A2 in immunity. However, the exact role and the mechanism of BTN2A2 in tumors are still unclear.

Methods: First, we performed real-time PCR to measure BTN2A2 expression in glioma cell lines. Next, we performed Genes Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses to understand the mechanism of BTN2A2 in glioma. Next, we used the “ESTIMATE”, “ssGSEA” and “CIBERSORT” algorithms to analyze the correlation between BTN2A2 and immune cell infiltration (ICI). Finally, we performed immunohistochemistry, growth curve, transwell, and colony formation assays to determine the functions of BTN2A2 in glioma.

Results: Our results showed an increase in BTN2A2 expression levels in glioma tissues and cells. Next, we determined that BTN2A2 was correlated with the prognosis of patients with glioma. Then, using the ESTIMATE, ssGSEA, and CIBERSORT algorithms, we discovered that BTN2A2 was significantly associated with immune cell infiltration (ICI) in glioma. We observed an increase in BTN2A2 expression levels with an increase in the patient's tumor grade. Furthermore, BTN2A2 significantly enhanced the proliferative and migratory abilities of glioma cells.

Conclusions: Our results showed a significant increase in BTN2A2 expression levels in glioma cells and tissues. Furthermore, the prognosis of patients expressing high BTN2A2 levels was poor. Moreover, BTN2A2 was correlated with progression and ICI in patients with glioma. Together, this indicates that BTN2A2 could be a therapeutic target for patients with glioma [1)].

Pathogenic Th17 cells play a key role in the pathogenesis of many autoimmune diseases. Multiple sclerosis (MS) is an autoimmune disease of the central nervous system (CNS). Experimental autoimmune encephalomyelitis (EAE) is the commonly used animal model for human MS and is characterized by autoreactive CD4+T cells attacking autoantigens in the CNS and causing myelin sheath damage. Although the recombinant BTN2A2-IgG2aFc (BTN2A2-Ig) fusion protein has been shown to inhibit T cell functions in vitro, it's unclear whether BTN2A2-Ig affects pathogenic Th17 cells and EAE development. We show here that BTN2A2-Ig protein attenuates established EAE, as compared with control Ig protein treatment. This is associated with reduced activation and proliferation of T cells in BTN2A2-Ig-treated EAE mice. Furthermore, BTN2A2-Ig protein inhibits the differentiation of CD4 naïve T cells into pathogenic Th17 cells and reduces the expression levels of Th1/Th17 cytokines and the Th1/Th17 pathway related genes and proteins but increases the expression levels of Th2-related genes and proteins. Our studies not only provide new insights into the mechanisms by which BTN2A2-Ig affects T cells, but also have the potential to provide a new strategy to treat MS and other autoimmune diseases [2)].

Rheumatoid arthritis (RA) is an autoimmune disorder characterized by persistent inflammatory responses in target tissues and organs, resulting in the destruction of joints. Collagen type II (CII)-induced arthritis (CIA) is the most used animal model for human RA. Although BTN2A2 protein has been previously shown to inhibit T cell functions in vitro, its effect on autoimmune arthritis has not been reported. In this study, we investigate the ability of a recombinant BTN2A2-IgG2a Fc (BTN2A2-Ig) fusion protein to treat CIA. We show here that administration of BTN2A2-Ig attenuates established CIA, as compared with control Ig protein treatment. This is associated with reduced activation, proliferation, and Th1/Th17 cytokine production of T cells in BTN2A2-Ig-treated CIA mice. BTN2A2-Ig also inhibits CII-specific T-cell proliferation and Th1/Th17 cytokine production. Although the percentage of effector T cells is decreased in BTN2A2-Ig-treated CIA mice, the proportions of naive T cells and regulatory T cells are increased. Furthermore, BTN2A2-Ig reduces the percentage of proinflammatory M1 macrophages but increases the percentage of anti-inflammatory M2 macrophages in the CIA mice. Our results suggest that BTN2A2-Ig protein has the potential to be used in the treatment of collagen-induced arthritis models [3].

1)
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