Novel molecular target and approach(es) for the bidirectional modulation of T-cell function

Tech ID: 33302 / UC Case 2023-767-0

BRIEF DESCRIPTION

Researchers at UC Irvine have identified and tested a molecular target that regulates T cell function during chronic viral infection and cancer. The molecular target is one of the high mobility group proteins (HMGB2). HMGB2 is a DNA binding protein that regulates transcriptional processes, meaning that its modulation will have profound effects on T cell differentiation and ultimate function by altering the expression of many genes.

SUGGESTED USES

Treatment of:

·Viral infections

·Cancer

·Autoimmune diseases

·Vaccines

FEATURES/BENEFITS

·Novel and previously unexplored function of HMGB2 in restoring T cell function during viral infection, cancer, and autoimmunity.

·HMGB2, as a DNA binding protein, is known to modify chromatin structure and regulate gene transcription; may represent an important approach to enhancing current therapies, including the use of check point inhibitors, for restoring T cell function.

FULL DESCRIPTION

Chronic infections, cancers, and autoimmune disorders all result in the progressive development of dysfunctional T cells that are either exhausted (chronic infections and cancer) or hyperactive (autoimmunity). T cell exhaustion occurs due to the expression of inhibitory receptors (a.k.a. immune checkpoints) because of persistent high antigenic load. It is both a physiological mechanism designed to limit immunopathology during chronic disease and a major obstacle for anti-tumor immune responses. The development and implementation of FDA-approved immune checkpoint inhibitors (nine in total) has resulted in significant improvements in disease outcomes for various cancer patients. These immune checkpoint inhibitors work by targeting the inhibitory receptors that limit the effectiveness of exhausted T cells and, rendering them unable to perform their cytotoxic functions. However, not all patients and types of cancer respond to this therapeutic approach and there are instances of relapse in patients whose cancers do respond, highlighting the need for more effective therapies.

In essence, immune checkpoint inhibitors work by removing the brakes on the immune system as opposed to directly stimulating immune function. Researchers at UC Irvine have identified a role for the molecular target

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OTHER INFORMATION

CATEGORIZED AS

» **Medical**

» Disease: Autoimmune and Inflammation

» Disease: Cancer

» Disease: Infectious Diseases

» Gene Therapy

» New Chemical Entities, Drug Leads

» Stem Cell

» Therapeutics

» Vaccines

RELATED CASES

2023-767-0

HMGB2, whose mechanism of action more directly stimulates immune function. Using viral and tumor models to assess the differentiation and stemness of T cells, they were able to show that HMGB2 is upregulated and sustained in T cells after chronic viral infection, then downregulated after viral clearance. They've also shown that HMGB2's expression in T cells is required for anti-tumor responses. With genomic approaches, the inventors suggest that HMGB2 works by increasing the accessibility of genes required for survival of progenitor (or stem) exhausted T cells, thereby driving the differentiation and maintenance of an exhausted T cell pool. This novel discovery may have profound implications for T cell-targeted therapies in cancer, viral infection, and autoimmune disease.

STATE OF DEVELOPMENT

In vitro and *in vivo* studies

OTHER INFORMATION

Publications: Accepted, In Press Nature Communications

PATENT STATUS

Patent Pending

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Applied Innovation

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