

~~**GENE MARKERS FOR SELECTING IMMUNOTHERAPIES**~~
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CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Patent Application No. 63/151,710 filed on February 20, 2021, U.S. Provisional Patent Application No. 63/196,620 filed on June 3, 2021, U.S. Provisional Patent Application No. 63/210,962 filed on June 15, 2021, U.S. Provisional Patent Application No. 63/215,838 filed on June 28, 2021, U.S. Provisional Patent Application No. 63/227,733 filed on July 30, 2021, U.S. Provisional Patent Application No. 63/250,634 filed on September 30, 2021, and U.S. Provisional Patent Application No. 63/274,342 filed on November 1, 2021, each of which is hereby incorporated by reference in its entirety.

FIELD

[0002] The disclosure relates to methods of diagnosis and prognosis, compositions for immunotherapies, methods of improving said compositions, and immunotherapies using the same.

BACKGROUND

[0003] Human cancers are by their nature comprised of normal cells that have undergone a genetic or epigenetic conversion to become abnormal cancer cells. In doing so, cancer cells begin to express proteins (including, but not limited to, antigens) that are distinct from those expressed by normal cells. These aberrant tumor antigens may be used by the body's innate immune system to specifically target and kill cancer cells. However, cancer cells employ various mechanisms to prevent immune cells, such as T and B lymphocytes, from successfully targeting cancer cells.

[0004] Human T cell therapies rely on enriched or modified human T cells to target and kill cancer cells in a patient. To increase the ability of T cells to target and kill a particular cancer cell, methods have been developed to engineer T cells to express constructs which direct T cells to a particular target cancer cell. For example, chimeric antigen receptors (CARs) and T Cell Receptors (TCRs), which comprise binding domains capable of interacting with a particular tumor antigen, allow T cells to target and kill cancer cells that express the particular tumor antigen. However, a major obstacle for adequate activity of CAR-T cells is the hostile tumor microenvironment that is comprised of immunosuppressive modulators.

[0005] There is a need to understand how attributes of CAR-positive T cells, TCR-positive T cells and other cell-based immunotherapies, patients' immunological status, and the tumor microenvironment correlate with clinical outcomes.