Researchers discover novel way to develop tumor vaccines

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Researchers at the University of Southern California (USC) have uncovered a new way to develop more effective tumor vaccines by turning off the suppression function of regulatory T cells. The results of the study, titled “A20 is an antigen presentation attenuator, and its inhibition overcomes regulatory T cell-mediated suppression,” will be published in *Nature Medicine* on March 2, 2008.

“Under normal circumstances, regulatory T cells inhibit the immune system to attack its own cells and tissues to prevent autoimmune diseases. Cancer cells take advantage of regulatory T cells' suppressor ability, recruiting them to keep the immune system at bay or disabling the immune system’s attack provoked by tumor vaccines.” says Si-Yi Chen, M.D., Ph.D., professor of immunology and molecular microbiology at the USC/Norris Comprehensive Cancer Center and the Keck School of Medicine of USC.

“Our study provides a new vaccination strategy to overcome the regulatory T cells’ immune suppression while avoiding non-specific overactivation of autoreactive T cells and pathological autoimmune toxicities.”

The study identified a new molecular player called A20, an enzyme that restricts inflammatory signal transduction in dendritic cells. When it is inhibited, the dendritic cells overproduce an array of cytokines and co-stimulatory molecules that triggers unusually strong immune responses that cannot be suppressed by regulatory T cells. The resulting

hyperactivated immune responses triggered by A20-deficient dendritic cells are capable of destroying various types of tumors that are resistant to current tumor vaccines in mice.

“Through a series of immunological studies, we have identified A20 as an essential antigen presentation attenuator that prevents the overactivation and excessive inflammation of the dendritic cells, which, in turn, restricts the potency of tumor vaccines,” says Chen.

The immune system’s dendritic cells are the guardian cells of the immune systems and play an important role in activating immune responses to recognize and destroy tumor cells. Tumor vaccines have been designed and developed to incite the immune response to cancer cells so that the immune system can attack and destroy cancer cells. However, discovering A20’s role in restricting immune responses has led to a method for blocking tumors from using regulatory T cells for protection.

“Despite intensive efforts, tumor vaccines have been largely ineffective in causing tumor regression in the clinic,” says Chen. “The vaccination approach we developed inhibits the key inhibitor in tumor antigen-loaded dendritic cells to selectively hyperactivate immune responses and to tip the balance from immune suppression in tumor-bearing hosts or cancer patients to effective antitumor immunity.”

This approach is capable of overcoming the regulatory T cells’ suppression mechanism and will allow for a new generation of tumor vaccines to be developed. The next step is to translate these findings into a human clinical trial, says Chen.

Source: University of Southern California