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Th17 cells summon an immune system strike against cancer (w/ Video)

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A specific type of T helper cell awakens the immune system to the stealthy threat of cancer and triggers an attack of killer T cells custom-made to destroy the tumors, scientists from The University of Texas M. D. Anderson Cancer Center report in the early online edition of the journal *Immunity*.

The role of Th17, one of only four known types of T helper cell, opens a possible avenue for overcoming cancer's ability to suppress or hide from the body's immune system, said senior author Chen Dong, Ph.D., professor in M. D. Anderson's Department of Immunology. Dong and colleagues found that Th17 stifled development of metastatic melanoma tumors in the lungs of mice.

"While there is much work to be done, these preclinical findings imply the possibility of taking a patient's Th17 cells, expanding them in the lab, and then re-infusing them as treatment," Dong said. Development of a vaccine to stimulate Th17 cells would be another possible application.

Dong earlier discovered the existence of Th17 cells and established that they secrete the inflammatory protein interleukin-17 (IL-17). His lab showed that overexpression of IL-17 contributes to both autoimmune and inflammatory diseases.

"Th17 cells also are found in a variety of solid tumors and we wanted to know whether these cells promote cancer or play a preventive or protective role," Dong said.

Their research showed that mice made deficient in Th17 cells and then injected with a strain of melanoma that gathers in the lungs experienced aggressive cancer growth compared to mice with normal levels of Th17. At 16 days, tumors in the knockout mice had fused together and coated the lung so extensively that they were no longer countable.

Next, they tested Th17 for preventive effect, injecting Th17 cells primed with tumor-specific antigens and the melanoma cells at the same time. At 16 days, mice with Th17 had low or barely detectable levels of cancer while control mice had a heavy tumor burden in their lungs.

A third set of experiments tested a treatment effect, showing that mice injected with Th17 after they already had melanoma in their lungs had a 75 percent reduction in tumor burden compared with normal mice.

In all experiments, mice with Th17 also had higher levels of several categories of immune system cell than did those with normal or suppressed Th17.

T cells are lymphocytes, a type of white blood cell produced by the thymus equipped with receptors that recognize and bind to antigens, pieces of invading organisms presented to the T cells by dendritic cells. The bound antigen converts the T cell to T helper cells that secrete signaling molecules called cytokines to launch an appropriate immune response. Helper cells, in effect, guide the adaptive immune response.

In the *Immunity* paper, additional experiments outlined the specific pathway by which Th17 suppresses tumors:

- Tumor invasion of the lung attracts Th17 cells that secrete IL-17A.

- IL-17A in turn promotes the secretion of two chemokines, CCL2

and CCL20, which recruit leukocytes to the tumor site.

- The leukocytes include dendritic cells, which seize tumor antigens and migrate to the lymph nodes.

- There, the antigens are used to prime CD8+ killer cells, which then migrate to the lung and kill established tumors.

Source: University of Texas M. D. Anderson Cancer Center (news : web)