Researchers say effective immunotherapy for melanoma hinges on blocking suppressive factors

11 December 2012

(Medical Xpress)—Researchers at the Moffitt Cancer Center have found that delayed tumor growth and enhanced survival of mice bearing melanoma were possible by blocking the reconstitution of myeloid-derived suppressor cells and Tregs (suppressors of anti-tumor activity) after total body irradiation had eliminated them. Blocking myeloid-derived suppressor cells and regulatory T-cell reconstitution improved adoptive T-cell therapy, an immunotherapy designed to suppress tumor activity.

The study appears in the December issue of The *Journal of Immunology*.

"Melanoma is a leading cause of cancer mortality," said Shari Pilon-Thomas, Ph.D., assistant member of the Immunology Program at Moffitt. "With few nonsurgical options for treating melanoma, immunotherapy, which focuses on the induction of immunity against cancer cells, is a promising approach. However, a major hurdle in developing effective immunotherapies is tumor-induced suppression that can limit the effectiveness of tumor-specific T-cells used in immunotherapy."

Chemotherapy or radiation can induce lymphopenia, the condition of having an abnormally low level of white blood cells. This condition is optimal for adoptive T-cell therapeutic strategies. However, after the induction of lymphopenia, suppressor populations that favor tumor progression begin reconstitution, including regulatory T cells (Tregs) and myeloid derived suppressor cells (MDSC). According to the researchers, tumor-induced suppression can stem from quickly reconstituted Tregs and MDSC.

This knowledge led to their research question, whether blocking the reconstitution of suppressor populations - such as Tregs and myeloid derived suppressor cells - could lead to better immunotherapy in mice bearing melanoma. Mice were treated with docetaxel, a chemotherapeutic drug that targets MDSC, followed by adoptive T cell therapy. In brief, the study demonstrated that when myeloid-derived suppressor cells and Treg reconstitution are blocked, immunotherapy with adoptive T cell transfer is more effective.

"It was important to understand the role of these suppressor populations after the induction of lymphopenia so that we can design more effective immunotherapeutic treatments for melanoma aimed at achieving complete tumor regression," concluded Dr. Pilon-Thomas.

More information:
www.jimmunol.org/content/189/11/5147.full.pdf

Provided by H. Lee Moffitt Cancer Center & Research Institute