Society for Immunotherapy of Cancer

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New research on immune based therapies for cancer presented at the SITC 26th Annual Meeting & Associated Programs

Understanding the local immune responses to cancer

NORTH BETHESDA (Friday, November 4, 2011) - Macrophages are important cells that reside in tissues and play a role in immune responses. When macrophages are in immunostimulatory (M1) form they promote protective immune responses, if macrophages are in immunosuppresive form (M2) they diminish protective immune responses. After exposure to certain substances, macrophages can shift from one form to the other. Tumor cells can release factors that shift M1 macrophages to M2 cells, diminishing an anti-tumor immune response and allowing the tumor to survive an immune attack. A study presented today at the Society for Immunotherapy of Cancer 26th Annual Meeting & Associated Programs set out to determine how macrophages "decide" whether to adopt one functional state or another when they encounter a tumor.

Yishan Chuang from Northwestern University and colleagues treated and analyzed macrophages with different immune signaling molecules found at the tumor site to determine their resulting functional states. One particular tumor-derived signal (Interleukin-10) was found to govern the outcome of this decision-making process in a manner that was not overcome by the addition of previously-identified immunostimulatory molecules. In some circumstances, both M1 and M2 macrophages were found to exist simultaneously, suggesting that macrophages may essentially "flip a coin" to decide whether to adopt one functional state or another, and the probability of choosing an immunosuppressive state is increased when Interleukin-10 is present.

This study sheds new light on our understanding of local immune responses and should help identify novel therapeutic targets and strategies for the treatment of cancer and other diseases involving chronic immune dysfunction.

New approach to treating Mantle cell lymphoma

NORTH BETHESDA (Friday, November 4, 2011) - Mantle cell lymphoma (MCL), an aggressive form of B-cell non-Hodgkin lymphoma, is incurable. High dose chemotherapy with stem cell transplant eliminates the vast majority of tumor cells, but a small minority of chemo-resistant cells ultimately grow and cause relapse. According to researchers at the Society for Immunotherapy of Cancer 26th Annual Meeting & Associated Programs, one possible approach to treatment is using a novel, personalized approach called "immunotransplant" to amplify the immune response of anti-tumor white blood cells.

J. Brody, MD from Stanford University, and colleagues developed the "immunotransplant" maneuver which uses anti-tumor immune cells (T cells) to eliminate lymphoma cells that persist post-transplant. The anti-tumor T cells are originally generated by treating the patient with an individualized lymphoma vaccine, then cryo-preserved and re-infused into the patient immediately post-transplant. A phase I/II study of immunotransplant was initiated for 24 newly diagnosed MCL patients to test the hypothesis that immunotranasplant amplifies anti-tumor T cells as seen pre-clinically.

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Researchers found that immunotransplant not only restored the anti-tumor immune cells, but actually amplified their numbers significantly in 83% of patients tested.

This study suggests that anti-tumor T cell amplification through immunotransplant could improve clinical outcomes for people with mantle cell lymphoma and other forms of cancer.

Using redirected T cells as a new form of cancer treatment

NORTH BETHESDA (Friday, November 4, 2011) - Recent studies have shown that human T cells can be re-directed to attack cancers with specific surface markers. For example, significant remissions of chronic lymphocytic leukemia have been reported using T cells engineered to express an antibody molecule on their surface. These specialized antibody-based molecules are called chimeric antigen receptors (CARs). According to research presented today at the Society for Immunotherapy of Cancer 26th Annual Meeting & Associated Programs, these "designer" T cells could represent a new approach to treating certain forms of cancer such as pancreatic cancer or ovarian cancer.

The antibody domains that are used to create CARs are often developed in mice and therefore contain mouse regions. When these CAR T cells are injected into the human body, the immune system recognizes the mouse portions as foreign material, and reacts against the CAR T cells, a phenomenon called transgene immunogenicity. This immune reaction can potentially lead to rejection or inhibition of the activity of the transferred anti-cancer CAR T cells, and represents a potential limitation to the CAR approach.

Evripidis Lanitis, BS and colleagues from the Powell lab at the University of Pennsylvania, constructed and evaluated a fully-human anti-mesothelin CAR that contained an antibody domain of human origin, called P4 which can redirect T cells to attack and destroy tumor cells that express mesothelin. Due to its full human composition, the new CAR reduces the likelihood of inducing transgene immunogenicity, thereby allowing CAR T cells to exert their full anti-tumor function. Human T cells expressing the P4 CAR release an array of anti-cancer molecules when they encounter mesothelin-expressing tumor cells. They also mediate the direct killing of mesothelin-positive cancer cells, as well as surrounding cancer cells that do not express mesothelin. The mesothelin protein is also secreted from tumor cells and presents in a soluble form in the serum of patients. However, this soluble form of mesothelin cannot prevent the new P4 CAR T cells from binding to mesothelin expressed on tumor cells and subsequently eliminating these cancers.

Researchers evaluated the effects of the P4 anti-mesothelin CAR T cells in a preclinical model of human ovarian cancer, where infusion of CAR T cells resulted in robust anti-tumor activity and regression of large, established human tumors in mice, even in the presence of high serum mesothelin levels.

The results of this study describe for the first time the generation and preclinical evaluation of primary human T cells engineered to express a CAR that is fully-human and that reacts against the cancer antigen, mesothelin, which is over expressed on a number of human cancers, including mesothelioma, pancreas cancer, and ovarian cancer.

Founded in 1984, the Society for Immunotherapy of Cancer (formerly the International Society for Biological Therapy of Cancer; iSBTc) is a non-profit organization of clinicians, researchers, students, post-doctoral fellows, and allied health professionals dedicated to improving cancer patient outcomes by advancing the development and application of cancer immunotherapy through interaction, innovation and leadership. For more information about SITC, please visit the Society website at www.sitcancer.org.

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