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Moving forward with an immunotherapy for the prevention of breast cancer recurrence

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Changes in cell surface glycosylation are a hallmark of the transition from normal to inflamed and neoplastic tissue. High levels of some Tumor Associated Carbohydrate Antigens (TACAs) correlate with metastasis and worse prognosis. We have developed carbohydrate mimetic peptides (CMPs) that induce broad-spectrum humoral and cellular responses to TACA that inhibit tumor growth in preclinical studies. We have moved one of these CMPs (referred to as P10s) into a Phase I clinical trial in stage IV breast cancer subjects to assess P10s-vaccine safety and tolerability. P10s was designed, using reverse engineering concepts, to induce responses to several TACAs including the neolactoseries antigen Lewis Y (LeY) and the ganglioside GD2. P10s is reactive with human TACA reactive antibody that blocks the migration of breast cancer cells. It is possible that these human antibodies modulate the expression of TACA on tumor cells in as yet undefined way. In preclinical studies immunization with P10s and its variants leads to an inhibition of tumor cell growth in animal models, which proved dependent on cellular cytotoxicity in the context of Th1 responses induced by CMP vaccination and activation of NK cells. In our Phase I trial, the most important outcome of the immunization regimen is the observation that immunized subjects are observed to mount an anti-P10s response, and the serum and plasma antibodies of post-immunized subjects mediate cytotoxicity against human breast cancer cell lines, including a cell line with *de novo* resistance to Trastuzumab, by as-yet unknown mechanism(s).

Biography

Thomas Kieber-Emmons, Ph.D., is known for his work on developing peptide mimetics of carbohydrate antigens as vaccines in both the cancer and pathogen areas, and is an acknowledged pioneer in this field. Dr. Kieber-Emmons was recruited from the University of Pennsylvania in 2002 to the University of Arkansas for Medical Sciences where he holds the Josetta Wilkins Chair in Breast Cancer Research, and is Deputy Director at the Winthrop P. Rockefeller Cancer Institute. His group is moving forward with bringing the first structurally designed carbohydrate mimetic peptide into the clinic to prevent breast cancer recurrence in high-risk women.