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

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Breast cancers cells over express Tumor Associated Carbohydrate Antigens (TACA) but TACA as immunogens is restricted by a limited cooperation between TACA reactive B cell and T cells. To circumvent this draw back we have developed carbohydrate mimetic peptides (CMPs) with overlapping B and T cell epitopes to link TACA reactive humoral responses with anti-tumor cellular responses. Using molecular modeling we have designed a CMP reactive with anti-GD2 and anti-Lewis Y antibodies. CMP immunization 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. Combination with Cyclophosphamide and IL-12 augments survival in murine tumor models. We observe that the limited and targeted attack resembles more the self-limited disease in models of autoimmune inflammation in non-autoimmune prone individuals. Preclinical safety studies indicate that the CMP induces anti-tumor responses in the absence of autoimmunity. These findings encourage us to hypothesize about the possible cascade of immune events initiated by CMP immunization. Apparently, it can reshape cellular responses in vivo facilitating a multifaceted anti-tumor immune response. Such responses targeting TACA parallel those associated with immune surveillance mechanisms required for prevention of recurrence of breast cancer disease and blood borne dissemination of breast cancer cells. In a limited Phase I study CMP immunization is tolerable and induces an anti-CMP response that is cross-reactive with TACA expressing human tumor cells. Immune modulation based on CMPs provides a new intervention for enhancing anti-tumor immunotherapy.

Biography

Thomas Kieber-Emmons, PhD., is known for his work on developing CMPs as vaccines in both the cancer and pathogen areas, and is an acknowledged pioneer in this field. Dr. Kieber-Emmons received a BS in Environmental Engineering Technology from the Florida Institute of Technology and went on for his PhD in Biophysics, focusing on computational chemistry and biology, at the Roswell Park Cancer Institute/State University of New York at Buffalo. Dr. Kieber-Emmons did his post-Doctoral studies in Molecular Immunology at Roswell Park were his research focused on the structural basis for molecular mimicry of antigens. He then moved to Idec Pharmaceuticals (now Biogen-IDEC) where he worked on anti-idiotypic vaccines for lymphoma. He was recruited in 1990 to the Wistar Institute and the University of Pennsylvania. After 12 years in Philadelphia, Dr. Kieber-Emmons was recruited 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 of the Winthrop P. Rockefeller Cancer Institute.

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