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Harnessing benefit from targeting tumor associated carbohydrate antigens

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Integrating additive or synergistic antitumor effects that focus on distinct elements of tumor biology are the most rational of strategies for cancer treatment. The real challenge is to define what elements of tumor biology make the most sense to be targeted? Signal transduction (pathways) can define therapeutic strategies and approaches that might be tailored to harness benefit from sustained immunity much like that observed from natural antibodies involved in immune surveillance mechanisms. Tumor associated carbohydrate antigens (TACAs) are pan-targets on tumor cells because they play roles in initiation and metastases of cancer, and considered as common targets shared by many tumor types, and regulating a network of signaling pathways associated with cell survival. Strategies that target TACAs therefore have potential benefit as cell death therapies. We have been developing an active immunization strategy targeting TACAs using carbohydrate mimetic peptides (CMP) designed as pan-immunogens. One CMP called P10s was computer designed to induce anti-GD2 and anti-LeY antibodies with the intent of inducing multiple sets of antibodies reactive with multiple TACAs when immunizing with a single agent. We have completed a Phase I clinical trial in breast cancer with a CMP, showing that this designed CMP can induce proapoptotic antibodies in humans that can sensitize tumor cells to chemotherapeutics. We have progressed to a Phase II trial in the neoadjuvant setting where we observe tumor shrinkage in combination therapy.

Biography

Thomas Kieber-Emmons is a Professor of Pathology, Co-Leader of the Therapeutic Sciences Program at the Winthrop P Rockefeller Cancer Institute and holds the Josetta Wilkins Endowed Chair in Breast Cancer Research. He has obtained his PhD in Biophysics and Molecular Immunology at the Roswell Park Cancer Institute applying structural immunology design principles to develop antibody based immunogens. He is known for his work on developing carbohydrate mimetic peptides (CMPs) as vaccines in both the cancer and pathogen areas and is an acknowledged pioneer in this field. His work reflects one of the very true bench-to-bedside initiatives as a CMP immunogen is in several Phase 2 clinical trials.

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