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Developing a first in man carbohydrate mimetic peptide vaccine for cancer: A translational story

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Tumor Associated Carbohydrate Antigens (TACAs) are pan-targets on tumor cells because they activate and regulate a network of signaling pathways associated with cell survival. Strategies that target TACAs, therefore, have potential benefit as cell-death therapies. In a dose escalation Phase I clinical trial, we analyzed the safety and immune response to a reverse engineered Carbohydrate Mimetic Peptide (CMP), referred to as P10s, in 6 subjects with advanced breast cancer. P10s was developed as a pan-immunogen to induce responses to multiple TACAs with the intent being to induce antibodies that are proapoptotic. 16 women were consented, with 6 subjects receiving the CMP vaccine. 3 subjects completed the vaccination schedule at 300 µg P10s-PADRE per injection, and 3 completed immunizations at the 500 µg dose. Patients were evaluated for signs of toxicity during and after vaccination. All 6 subjects displayed a persistent IgG response to P10s after vaccination and induced serum and plasma antibodies displayed cross-reactivity to TACA expressing human breast cancer cell lines. Antibody induced by P10s in 5 of the 6 subjects displayed statistically significant apoptotic functionality to several human breast cancer cell lines, including a Trastuzumab-resistant one, and is caspase 3 dependent. Overall survival among the vaccinated subjects had a mean±SE (median) of 908±116 (928) days compared to 583±126 (312) days among the unvaccinated, consented subjects. P10s vaccination was well tolerated, with measurable immune responses and antitumor efficacy was noted. This is the first study to show that CMP vaccination is safe and can induce functional antibodies that potentially have therapeutic benefit in subjects immunized with this CMP-based vaccine.

Biography

Thomas Kieber-Emmons, PhD 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. He is Associate Director for Prevention Research at the Winthrop P. Rockefeller Cancer Institute and holds the Josetta Wilkins Chair in Breast Cancer Research. His group has brought the first structurally designed carbohydrate mimetic peptide into the clinic for breast and other cancer types.

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