HER2/neu-based peptide vaccination-pulsed with B-cell epitope induced efficient prophylactic and therapeutic antitumor activities in TUBO breast cancer mice model

ABSTRACT

Breast cancer is the most common invasive cancer diagnosed among women. A cancer vaccine has been recognized as a form of immunotherapy with a prominent position in the prevention and treatment of breast cancer. The majority of current breast cancer vaccination strategies aim to stimulate antitumor T-cell responses of the HER2/neu oncogene, which is abnormally expressed in breast cancer cells. However, the role of the B-cell humoral response is often underappreciated in the cancer vaccine design. We have advanced this idea by elucidating the role of B-cells in cancer vaccination by designing a chimeric antigenic peptide possessing both cytotoxic T lymphocytes (GP2) and B-cell (P4) peptide epitopes derived from HER2/neu. The chimeric peptide (GP2–P4) was further conjugated to a carrier protein (KLH), forming a KLH–GP2–P4 conjugate. The immunogenicity of KLH–GP2–P4 was compared with KLH–GP2 (lacking the B-cell epitope) in BALB/c mice. Mice immunized with KLH–GP2–P4 elicited more potent antigen-specific neutralizing antibodies against syngeneic TUBO cells (cancer cell line overexpressing HER2/neu) that was governed by a balanced Th1/Th2 polarization in comparison to KLH–GP2. Subsequently, these immune responses led to greater inhibition of tumor growth and longer survival in TUBO tumor-bearing mice in both prophylactic and therapeutic challenge experiments. Overall, our data demonstrated that the B-cell epitope has a profound effect in orchestrating an efficacious antitumor immunity. Thus, a multi-epitope peptide vaccine encompassing cytotoxic T-lymphocytes, T-helper and B-cell epitopes represents a promising strategy in developing cancer vaccines with a preventive and therapeutic modality for the effective management of breast cancer.

Keyword: Multi-epitope; Peptide vaccines; Antitumor; HER2/neu; B-cell epitope; Breast cancer