

Introduction

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In this issue, exciting new directions are outlined by fourteen groups of investigators working on critical areas in "Breast Cancer Immunology". In the clinic, patients are responding to Her-2 peptides or GM-CSF transfected tumor cell vaccines. Furthermore, tumors under vaccine induced immune attack can prime the host to additional antigens. Selected chemotherapeutic agents are used to further vaccine efficacy. These promising results highlight the value of breast cancer immunotherapy.

Although the clinical progress is exciting, significant challenges remain. Many tumor-associated antigens are self-antigens and vigorous measures will be required to induce consistent and sustained anti-tumor immunity. Murine models are still the most feasible system for testing new strategies and delineating mechanisms. Before the era of transgenic mice, preneoplastic and neoplastic lesions induced by mammary tumor virus, chemical carcinogens or hormones were used to establish the fundamentals in mammary tumor immunobiology. More recently, transgenic mice expressing human tumor-associated antigens were generated to simulate tolerance to breast cancer associated Her-2 and MUC-1. Lessons learned before the transgenic era and new information derived from transgenic models are summarized and novel vaccination strategies in tol-

erant mice are reviewed. Also, dendritic cell vaccines are evaluated in the context of breast cancer.

There is a pressing need for new immunotherapy targets. In this issue, the better-characterized glycoprotein antigens and novel molecules in angiogenesis are examined as new targets of breast cancer vaccines or immunotherapy. Continued effort in new antigen identification will be critical to cancer control.

Finally, a reality check is warranted. Most breast cancer cells are still elusive to immune intervention. The mechanisms of such evasion are under intense investigation and much progress has been made. Alteration in antigen processing machinery is a major route of tumor evasion. Induction of anti-tumor immunity may be hindered by tumor-associated myeloid or NKT cells. Tumor cells can express chemokines or chemokine receptors to expedite their metastasis. Both tumor cells and inflammatory cells can produce metalloproteinases to modify angiogenesis. New insight to overcome these barriers will come from in-depth analysis of the mechanism. Caution should be exercised when manipulating immune regulatory cells or molecules because autoimmunity may be under the same control. Novel strategies to overcome tumor-tolerance but not self-tolerance are current challenges for breast cancer immunologists.