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Antitumor immunity and advances in cancer immunotherapy

Tomoharu Sugie[1] · **Masakazu Toi**[2]

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Breast cancer is a common disease in women worldwide. Although the conventional treatments such as surgery, radiotherapy, chemotherapy and endocrine therapy are effective strategies for patients with locally advanced or metastatic breast cancer, they have limitations in patients who subsequently develop an acquired resistance. Immunotherapy was expected to eradicate this resistance with higher specificity and lower toxicity. However, the clinical efficacy of immunotherapies was unsatisfactory for routine clinical practice. Understanding the dynamic interaction between tumors and the immune system is a key issue in the development of a new cancer immunotherapy.

Tumor infiltrating lymphocytes (TILs) are mononuclear immune cells in the tumor microenvironment. A high level infiltration of TILs is correlated with a good prognosis and a good response to chemotherapy in triple negative and HER2-positive breast cancer [1]. TILs represent the pre-existing antitumor immunity in the tumor microenvironment. In the clinical manifestation of the tumor, immune checkpoint and regulatory cells exhaust T cells so that they cannot kill tumor cells (peripheral tolerance). A cancer vaccine was developed targeting the shared antigens, most of which are non-mutated self-antigens. As these antigens are shared in the patients with a malignant disease, they are good candidates for immunotherapy logistically. However, cancer vaccines and adoptive T cell transfer targeting the shared antigens could not provide satisfactory clinical benefits. As T cells with high affinity receptors for self-antigens are eliminated during maturation in the thymus (central tolerance), there are few intrinsic effector cells targeting the shared antigens.

Releasing the brake used by CTLA-4 and PD-1/PDL-1 is a promising approach to reactivate pre-existing intrinsic effector T cells. Recently, next generation sequencing identified neoantigens, which are individually mutated antigens generated during the proliferation and metastasis of tumors. Neoantigens are thought to be good targets for immune cells to activate antitumor immunity [2]. In melanoma and colon cancer, checkpoint inhibitors are more effective in tumors with a high frequency of mutation load on the genome, which might be a surrogate for the frequency of neoantigens. Personalized cancer vaccines targeting these neoantigens have already been developed by some biotech companies. Combination therapy using these methods involving neoantigens and checkpoint inhibitors may enable the achievement of an effective method to cure breast cancer in the near future.

In the review following this editorial, Burugu et al. [3] describe the clinical relevance of TILs in breast cancer based on previous studies. The authors explain the function of each immune subset participating in innate and acquired immunity. Moreover, the authors discuss the outcome of immune checkpoint blocking of CTLA-4 and PD-1 and potential targets for a new checkpoint inhibitor. In the review, Kakimi et al. [4] describe the current strategy for the development of a personalized immunotherapy based on the explained notion of the cancer immunity cycle [5]. Future immunotherapies will need to be personalized in terms of both the identification of patient-specific immunosuppressive mechanisms and the targeting of

✉ Tomoharu Sugie
sugiet@hirakata.kmu.ac.jp

Masakazu Toi
toi@kuhp.kyoto-u.ac.jp

[1] Department of Surgery, Kansai Medical School, Hirakata, Japan

[2] Department of Breast Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan

neoantigens. Moreover, another review focusing on PD-1 by Terawaki [6] is included in this special feature of Breast Cancer. These reviews never fail to contribute to the reader's understanding of the current status and future perspectives of immunology and immunotherapy for the treatment of breast cancer.

Compliance with ethical standards

Conflict of interest All authors declare that there are no conflicts of interest.

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