

## Editorial



# Coalition Forces of Immunologists and Oncologists for Defeating Cancer

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There has been a long journey in the effort to harness the immune system for the treatment of cancer since Coley's toxin was first used to treat cancer 120 years ago. However, almost all efforts failed to improve patient outcomes. Meanwhile, the concept of cancer immunosurveillance and immunoediting has been established (1), and T cells have been considered major players in the immune responses to cancer. Moreover, immunologists have found that tumor antigen-specific T cells are largely 'exhausted' in both murine and human tumors (2).

During immune responses, Ag-specific T cells are regulated by various mechanisms, including inhibitory receptors, to avoid excessive and persistent immune responses (3). These immune checkpoints suppress T-cell responses, particularly in cancer patients, leading to T-cell exhaustion. CTLA-4 and PD-1 are the most well-known immune checkpoint inhibitory receptors and have been targeted for drug development. As a result, anti-CTLA-4 and anti-PD-1/PD-L1 blocking antibodies are now successfully used for cancer treatment and known as immune checkpoint inhibitors (ICIs) (4).

The current ICIs have some limitations. First, ICIs fail to control tumors in a significant proportion of cancer patients. Moreover, tumor growth becomes accelerated after ICI treatment in some patients. This is known as hyperprogressive disease (HPD) (5,6). In addition, certain patients suffer from immune-related adverse events (irAEs) following ICI treatment (7). However, we do not yet know the mechanisms underlying a non-response, HPD, and irAEs following ICI treatment, hampering mechanism-driven development of new immuno-oncological agents and rationale-based patient management.

The recent explosive growth of 'immuno-oncology' has been enabled by successful translational research from bench-side basic immunology to bedside clinics. Now, it is time to raise questions from the bedside and answer them with basic immunology. These findings will then be translated to the clinic, creating a virtuous cycle to boost the growth of immuno-oncology. Coalition forces of immunologists and oncologists are necessary to defeat cancer.

In the current issue of *Immune Network*, we publish 10 review articles in the field of tumor immunology and immuno-oncology. First, T-cell exhaustion and inhibitory receptors (8) and co-stimulatory receptors (9) are discussed. The roles of regulatory T cells (10),  $\gamma\delta$  T cells (11), IL-17-producing cells (12), and NANOG signaling (13) in tumor immunity are also described. From the translational and clinical aspect, peripheral blood biomarkers (14) and irAE-related

issues (15) are comprehensively reviewed. The recent progress in immunotherapy for non-small cell lung cancer (16) and hepatocellular carcinoma (17) are discussed.

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