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Cancer immunotherapy: Special issue of BMB Reports in 2021

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Basically, cancer is a disease initiated by mutations in the genome. However, cancer is regarded not only as a genetical disease but also an immunological disease because cancer cells can be targeted by the immune system. The immune system recognizes mutated proteins as non-self, foreign antigens, so-called neoantigens, and exerts diverse effector functions to eliminate tumor cells. Anti-tumor immune responses resemble immune responses against viruses. In anti-tumor immune responses, $CD8^+$ and $CD4^+$ T cells are the main effector cells. In addition, dendritic cells (DCs) play a crucial role in the priming of $CD8^+$ and $CD4^+$ T cells, and natural killer (NK) cells also contribute to the anti-tumor immune responses.

Recently, immune checkpoint inhibitors (ICIs), including antibodies against cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), programmed cell death 1 (PD-1), and programmed cell death ligand 1 (PD-L1), became available for the treatment of various types of cancer. Moreover, chimeric antigenic receptor (CAR)-T cells have been successfully used to treat hematologic malignancies. However, current cancer immunotherapy has some limitations. ICIs fail to control tumors in a considerable proportion of cancer patients and CAR-T cell therapy does not effectively control solid tumors. To overcome these limitations, further research and development are required.

In the current issue of *BMB Reports*, seven review articles in the field of cancer immunotherapy were published. First, Drs. Hyung-seung Jin and Yoon Park reviewed a complex immune checkpoint system consisting of T-cell immunoglobulin and ITIM domain (TIGIT), CD226, CD96, and CD112R. They described the biology of these molecules in relation to the function of T and NK cells and discussed their possible application for cancer immunotherapy.

Dr. Inhak Choi and colleagues reviewed the cancer-intrinsic roles of PD-L1, which have recently become known as the non-immunological functions of PD-L1. Particularly, they described the protumoral functions of PD-L1, including mesenchymal transition, metabolism, stemness, and autophagy.

Dr. Seung-Woo Lee and colleagues discussed T-cell targeting cytokines. Recombinant cytokines have been used to boost the proliferation and activation of T cells since the early era of cancer immunotherapy. In the current review, the authors focused on IL-2 and IL-7 and described the biology of IL-2 and IL-7 in T cell responses. In addition, they also described recent clinical trials using IL-2 and IL-7 for cancer immunotherapy.

To elicit anti-tumor immune responses, $CD8^+$ and $CD4^+$ T cells should be primed by DCs presenting tumor antigens. Therefore, DCs have been targeted in cancer immunotherapy. Dr. Heung Kyu Lee and colleagues reviewed the roles of various DC subsets, including conventional, plasmacytoid, and monocyte-derived DCs in anti-tumor immune responses and described cancer immunotherapies employing DCs.

NK cells are innate effector cells that exert anti-tumor responses by direct cytotoxicity and cytokine production. Dr. Hun Sik Kim and colleagues reviewed NK cell-based cancer immunotherapy. The authors described the expression and functions of various immune checkpoint receptors on NK cells. They also described the potential advantage of CAR-NK cells over CAR-T cells and the current status of CAR-NK cell development.

Dr. Chan Hyuk Kim and colleagues reviewed genome editing technology in cancer immunotherapy. They introduced CRISPR/Cas9 technology and described CRISPR/Cas9-based genome editing for the therapeutic engineering of T cells and other immune cells.

Recently, data from early phase clinical trials of cancer immunotherapeutics provided insight for future directions of new drug development. Dr. Dae Ho Lee reviewed the current status of early phase clinical trials in cancer immunotherapy, including novel therapeutic targets and promising combinational regimens. He described not only novel ICIs but also co-stimulatory agonists and other modulators.

An exact understanding of the anti-tumor immune response and its regulation mechanisms will pave the way to developing effective immuno-oncologic agents, combination regimens, and clinically useful biomarkers, leading to conquering cancer.