Abstract

Although PD-1 discovered by Dr. Honjo at Kyoto University was initially found to play an important role in peripheral self-tolerance serving as a checkpoint for autoimmunity, our subsequent studies revealed that PD-1 expressed on effector T cells could significantly affect a potential immunity of host against cancer.

We found that cancer cells expressing PD-1 ligands could mimic normal self cells and avoid a potential immune attack, and that the inhibition of PD-1/PD-L interaction could lead to a remarkable augmentation of potential host tumor immunity and significant therapeutic effects in animal models.

A decade later, the idea, currently called PD-1 checkpoint blockade therapy, was substantiated by successful clinical trials in human cancer patients with humanized anti-PD-1 or anti-PD-L1 antibody, and current efforts are directed to the improvement of the therapeutic efficacy as well as the search for predictive biomarkers of the therapy. The clinical success of immune checkpoint blockade therapy confirmed a potential importance of host immunity in controlling cancers.

Incidentally, accumulating evidence in large-scale clinical studies also indicates that the accessibility of immune effectors to cancer cells in tissue microenvironment, on which efficacy of immune checkpoint blockade and other immunotherapies may count, shows a significant correlation with a better prognosis of cancer patients. Nonetheless, the mechanism assuring the immune accessibility to cancer in tissue involves apparently complex cellular processes and may be hampered by various conditions and factors.

In this talk, I will briefly summarize the history of PD-1 checkpoint and then introduce a unique animal model of chronic myelogenous leukemia (CML), in which the effective access of memory T cells to tumor cells in tissue is remarkably promoted via coordinated interplay with mesenchymal stroma cells and is capable of eradiating CML-initiating cells that otherwise cause lethal CML development.