"The 90th of Stem Cell Biology and Regenerative Medicine Forum"

Date：Apr 14th (Thu) 2016
Time : 18:00 ～ 19:30
Place：8th floor Hospital Building

（Internal Speaker）

18:00-18:30 Ai Kawana-Tachikawa (AIDS Research Center, National Institute of Infectious Diseases Department of AIDS Vaccine Development, IMSUT hospital)
Disruption of T cell immunity during chronic HIV-1 infection

（External Speaker）

18:30-19:30 Norimitsu Kadowaki (Department of Internal Medicine Division of Hematology, Rheumatology and Respiratory Medicine Faculty of Medicine, Kagawa University)
Combination of targeted therapy and immunotherapy for cancer

Hosted by Center for Stem Cell Biology and Regenerative Medicine

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* Please register attendance at the reception desk.
* Next forum will be held on Oct. I will contact you after the schedule is decided.
* Please contact tatsu-m@ims.u-tokyo.ac.jp, for Forum speaker recommendations

Disruption of T cell immunity during chronic HIV-1 infection

Ai Kawana-Tachikawa (AIDS Research Center, National Institute of Infectious Diseases Department of AIDS Vaccine Development, IMSUT hospital)

During chronic HIV-1 infection, T cells undergo cell intrinsic phenotypic and functional impairments that are coupled to increased pathogenesis. Phenotypic changes of T cells during chronic HIV-1 infections have been characterized by skewed maturation and/or elevated levels of activation and exhaustion markers. We and other researchers have previously showed reduction of specific cytokines expression of T cells in HIV-1 non-controllers, which is associated with activation/exhaustion status in memory T cells. However, molecular mechanisms underlying the gene-specific reduction have not been revealed.

Epigenetic modification is a critical mechanism for stable gene expression, especially DNA methylation mediated gene silencing. We observed that CpG sites in the *IL2* promoter of $CD4^+$ T cells were highly methylated in HIV-1 non-controllers. Furthermore, the hyper-methylation status in the *IL2* promoter was associated with CD57 expression, a marker of replicative senescence on T cells and a characteristic feature of T cells in HIV-1 infected individuals. These data suggest that DNA methylation at the *IL2* locus in $CD4^+$ T cells is coupled to immunosenescence and plays a critical role in the broad dysfunction that occurs in polyclonal T cells during HIV-1 infection.

Combination of targeted therapy and immunotherapy for cancer

Norimitsu Kadowaki (Department of Internal Medicine Division of Hematology, Rheumatology and Respiratory Medicine Faculty of Medicine, Kagawa University)

Targeted therapies and immunotherapies attack tumor cells through different mechanisms. In addition, these therapies exhibit quick and delayed effects, respectively. Thus, combining both therapies complement each other. Furthermore, as targeted therapies may enhance functions of immune cells, both therapies are expected to have synergistic effects.

A BCR-ABL tyrosine kinase inhibitor for chronic myeloid leukemia, dasatinib, is capable of inhibiting a broad array of kinases in addition to ABL. Thus, dasatinib may suppress activity of various immune cells. In fact, it has been reported that the drug suppresses activation of T cells, NK cells *in vitro*. In addition, we previously reported that dasatinib strongly suppresses IFN-□ production by plasmacytoid dendritic cells. Unexpectedly, however, dasatinib activates cytotoxic lymphocytes in a substantial proportion of leukemia patients *in vivo*.

Here we tried to solve this conundrum, and found out an unexpected encounter of targeted therapy and immunotherapy for cancer.