“The role of myeloid cells to lung cancer development and treatment”

Esra A. Akbay

(Assistant Professor, Department of Pathology,

University of Texas Southwestern Medical Center)

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Time **10:00 am - 11:00 am**

Venue **Biken Hall, RIMD Main Building 1F**

Brief summary

Tumor orchestrated changes in the immune cell composition in the microenvironment limits generation of sufficient anti-tumor immune responses. One of the most prominent features of Kras mutant lung tumors is their rich myeloid cell content. To study this systematically, we generated bi-transgenic mice expressing a conditional *IL-17A* allele along with conditional $Kras^{G12D}$ and performed immune phenotyping and survival analysis. Tumors in IL-17:$Kras^{G12D}$ mice grew more rapidly, resulting in a significantly shorter survival as compared to $Kras^{G12D}$. IL-6, G-CSF, MFG-E8, and CXCL1 were increased in the lungs of IL17:Kras mice. Time course analysis revealed that tumor-associated neutrophils (TANs) were significantly elevated, and lymphocyte recruitment was significantly reduced in IL17:$Kras^{G12D}$ mice as compared to $Kras^{G12D}$. In therapeutic studies, PD-1 blockade was not effective in treating IL-17:$Kras^{G12D}$ tumors. In contrast, blocking IL-6 or depleting neutrophils with an anti-Ly-6G antibody in the IL17:$Kras^{G12D}$ tumors resulted in a clinical response associated with T cell activation. Through RNA sequencing of sorted neutrophils, we identified arginase 1 as one of the highly induced genes in the tumor as compared to the normal lungs. Inhibition of arginase activity resulted in a similar therapeutic effect highlighting the importance of myeloid cell derived arginase as a biomarker of resistance to immune checkpoint blockade and a viable therapeutic target.

Host Shohei Koyama (Department of Immunopathology, IFReC/ Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University)