**Commensal Microbiota Promote Lung Cancer Development via γδ T Cells**

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**Presenter**: Yi-Nuo, Tsai  **Date/Time:** 2020/03/12, 16:10-17:00

**Commentator**: Jhen-Wei Ruan **Location**: Room 601, Med College Building

**Background**:

Lung cancer is a malignancy with high morbidity and mortality worldwide. The lung is an organ constantly exposed to the environment and has unique homeostasis to maintain specific microbiome. More evidences indicated that microbiome plays an important role in the carcinogenesis and progression of lung cancer by inflammation and immune response. Indeed, lung cancer is closely associated with chronic inflammation characterized by infiltration of inflammatory cells and accumulation of pro-inflammatory factors including cytokines, chemokines that stimulate cell proliferation, tissue remodeling. It is now clear that the lung has a distinct microbiome and that this may influence the development of lung cancer. However, the underlying mechanisms responsible for the tumor-associated inflammation in lung cancer have not been clearly defined.

**Results:**

The author using genetically engineered mouse model of human lung adenocarcinoma induced by expression of *Kras*G12D and deletion of *p53* in lung epithelial cells. The author compared tumor initiation and progression in germ-free (GF) and specific pathogen-free (SPF) control conditions. This revealed that both tumor growth was decreased in GF mice compare to SPF mice. Accompanying the elevated bacterial abundance in tumor-bearing lungs of SPF mice was an increase in expression of genes encoding the pro-inflammatory cytokines interleukin-1β and IL-23, known to be produced by myeloid cells in response to microbial exposure, as well as an expansion of lung-resident γδ T cells. Otherwise, these phenotypes were absent from tumor-bearing GF lungs. Moreover, the majority of these γδ T cells were defined as Vγ6+Vδ1+ γδ T17 cells as they secreted the pro-inflammatory cytokine IL-17A. Accompany with the expanded population of γδ T cells was increased infiltration of neutrophils into lung tumors compared with healthy lungs of SPF mice. Using monoclonal antibodies to inhibit γδ T cell depleted IL-17A levels, neutrophil accumulation and tumor cell proliferation, indicating how microbiota-induced γδ T cells could modulate lung cancer development.

**Conclusion:**

The author discovered a new mechanism that lung tumors promote their own survival: tumors alter bacterial populations within the lung, provoking the immune system to create an inflammatory environment that in turn helps the tumor cells growth.

**References:**1. A defined commensal consortium elicits CD8 T cells and anti-cancer immunity.

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