



**Title of Research:**

21-2-01 Development of evaluation method of inflammatory particles based on alveolar macrophage function.

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**Summary of Research:**

The number of patients with allergic diseases have increased in developed countries. Many factors are thought to be involved in this issue, and multiple studies have demonstrated that particulate pollution such as PM2.5 might be one of factors of exacerbation of allergic inflammation. These particulates function as adjuvant and induce allergic immune responses. However, the mode of action of particulate and the mechanisms by which they induce allergic responses remain to be elucidated. In general, inhaled particles are engulfed by alveolar macrophages as sentinel cells of the lung immune systems, and then excreted. Recently we found that inflammatory particulate alum induced cell death in alveolar macrophages after phagocytosis and then IL-1  $\alpha$  was released as dead cell factor, and also that released IL-1  $\alpha$  was involved in allergen-specific IgE production in vivo. These results suggest that responses of alveolar macrophages against particulates are a useful tool for detecting particulates that cause inflammation.

In this term, we performed four types of experiments, those are 1) study of in-vitro-differentiated alveolar macrophages and of establishment of alveolar macrophage cell line, 2) search for new factor(s) specifically induced in response to inflammatory particulates, 3) establishment of in vivo experiment systems to evaluate in vitro study, and 4) study of live cell imaging as a new method for monitoring alveolar macrophages in response to particulates. In these experiments, we found new factor for evaluating inflammatory particulates by comprehensive analysis of lipid mediator release from alveolar macrophages. This lipid mediator was released both in vitro and in vivo. We are currently investigating its efficacy for in vivo evaluation method, along with IL-1  $\alpha$ . For live cell imaging analysis, we observed that IL-1  $\alpha$  was released from alveolar macrophage death by alum. We will perform same experiments using other particulates such as Al<sub>2</sub>O<sub>3</sub>, ZnO, silica, TiO<sub>2</sub>, sand dust and so on to understand detailed mechanisms of alveolar macrophage function in response to particulates.

**Timeline:**

March 1, 2021—February 28, 2022

**Topics:**

Research meeting of LRI by JCIA, oral, "Development of evaluation method of inflammatory particles based on alveolar macrophage function", online, August 31, 2021.

**Publications:**

Kuroda Etsushi "Lung immune responses and allergic inflammation induced by fine particles", The 62<sup>nd</sup> Annual Meeting of Japan Society for Atmospheric Environment, special meeting, online, September 16, 2021.