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Crystalline silica impairs the efferocytosis ability of human and mouse macrophages
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Background: Apoptotic cell clearance or efferocytosis, a major function of macrophages, is decreased in autoimmune diseases such as systemic sclerosis (SSc) and systemic lupus erythematosus (SLE). One etiology of these autoimmune diseases is the inhalation of crystalline silica which can also lead to pulmonary diseases. However, the precise relationship between crystalline silica exposure and efferocytosis impairment remains to be determined. To explore this question, this study characterizes the effects of crystalline silica on efferocytosis abilities of human and mouse macrophages.
Results: Human monocyte-derived macrophages (MDM) or C57BL/6J mice were exposed to crystalline silica and then to CFSE-positive apoptotic Jurkat cells. Flow cytometry evaluation revealed that crystalline silica significantly decreased efferocytosis capacities of both human MDM in vitro and mouse alveolar macrophages in vivo. Such effects were specific to crystalline silica particles since tungsten carbide particles had no effect on efferocytosis. In human MDM, silica-reduced efferocytosis was dose-dependent and, required the expression of SR-B1. Crystalline silica increased F-actin staining, RhoA activation and phosphorylation of myosin phosphatase subunit 1 (MYPT1), a known Rho kinase (ROCK) target. Y27632, a ROCK inhibitor, reversed the increased F-actin staining, the phosphorylation of MYPT1 and, at least partly, the silica-induced impairment of efferocytosis. Moreover, efferocytosis abilities of MDM from SSc patients were similar to those of silica-exposed MDM. Treatment of SSc-MDM by Y27632 significantly increased their efferocytosis capacities, suggesting a likewise activation of the RhoA/ROCK pathway in SSc MDM.
Conclusion: Exposure to crystalline silica impairs in vivo efferocytosis in mouse alveolar macrophages. In vitro exposure of human MDM also reduces efferocytosis, likely via an activation of the RhoA/ROCK pathway. Silica exposure may consequently contribute to the impaired efferocytosis capacities of macrophages from patients suffering from silica-associated autoimmune disorders such as SSc.

Keywords : Efferocytosis, macrophage, Rho Kinase, crystalline silica, autoimmunity
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