Crystalline silica impairs the efferocytosis ability of human and mouse macrophages : a pathogenic link between autoimmunity and silica exposure.

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Background: Inhalation of crystalline silica (SiO2) can lead to pulmonary diseases and systemic autoimmune disorders, such as systemic sclerosis (SSc). A failure of apoptotic cell clearance, also called efferocytosis, is reported in autoimmune diseases and notably occur in macrophages from SSc patients. However, the precise relationship between crystalline silica exposure and efferocytosis impairment remains to be determined. To explore this question further, this study characterizes the effects of crystalline silica on efferocytosis abilities of human and mouse macrophages.

Methods: Human monocyte-derived macrophages (MDM) or C57BL/6J mice were exposed to crystalline silica and then to CFSE-positive apoptotic Jurkat cells and engulfment efficiency was measured by flow cytometry.

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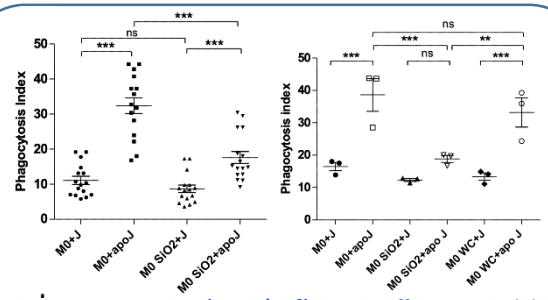

In vitro exposure to SiO2 (25 µg/cm²) impairs efferocytosis ability of human monocyte-derived-macrophages

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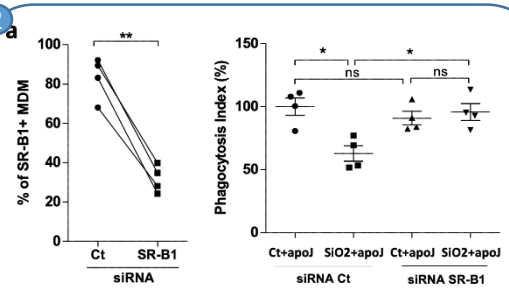

This effect of SiO2 exposure is SRB1 dependent

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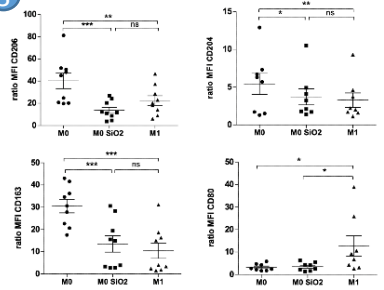

Exposure to SiO2 induces a pro-inflammatory M1-like phenotype

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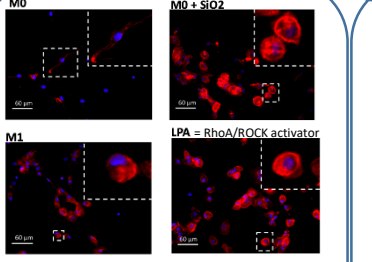

Exposure to SiO2 induces stress fiber formation similarly to M1 -Mϕ and RhoA activation by LPA

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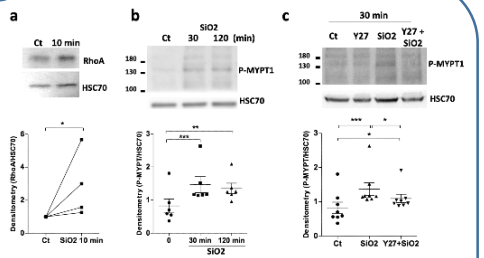

Exposure to SiO2 activates the RhoA/ROCK pathway and this activation is partly reduced by the ROCK inhibitor Y-27632

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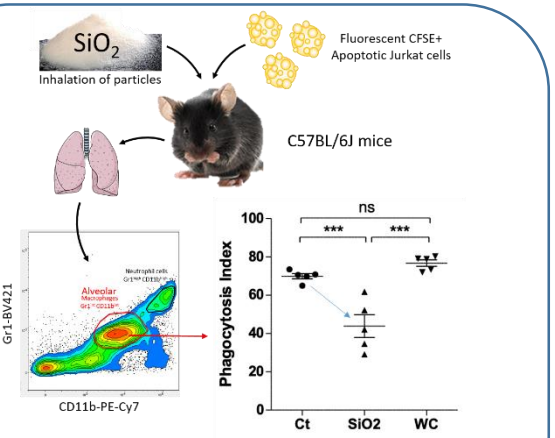
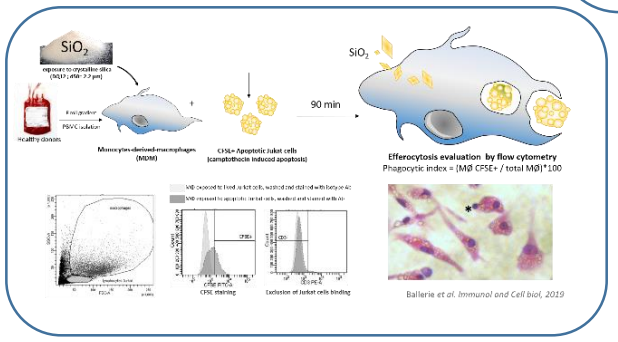


These effects of SiO2 in vitro are also observed in vivo in C57BL/6J : inhalation of SiO2 particles impaires efferocytosis ability of mouse alveolar macrophages

Conclusion: Crystalline silica impairs efferocytosis capacities of human and mouse MΦ, and this impairment provides new insights in the possible mechanisms linking silica exposure and the emergence of silica-induced autoimmune diseases characterized by the production of antibodies targeting apoptotic cell-associated antigens

Efferocytosis assay on MDM



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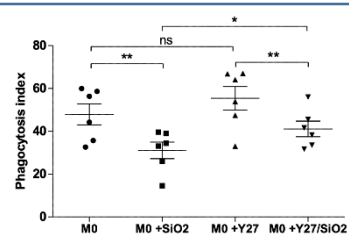

Rock inhibition by Y-27632 partly restores impaired efferocytosis ability of human MDM after silica exposure

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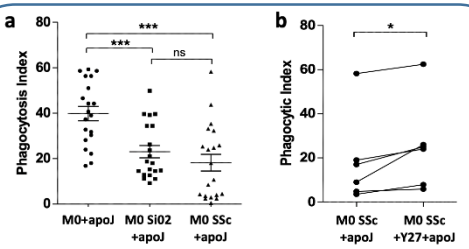

Rock inhibition by Y-27632 partly restores impaired efferocytosis ability of human MDM from SSc patients