Volcanic ash activates the NLRP3 inflammasome in macrophages *in vitro*

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Pulmonary exposure to volcanic ash can exacerbate existing conditions, triggering acute diseases such as asthma and bronchitis. However, clinical, epidemiological and toxicological studies have given inconclusive results regarding the capacity of ash to induce chronic disease [1]. Alveolar epithelial cells and macrophages are a first line of defense against inhaled particles and are responsible for coordinating an inflammatory immune response; they are therefore key targets for *in vitro* assessment of the hazard posed by atmospheric particles. Previous work suggests that ash is minimally reactive *in vitro* relative to pure-phase standards, but ash treatment can result in a moderate decrease in the viability of lung epithelial cells and induce sample-dependent cytokine production in macrophages [2].

Inhalation of exogenous crystalline material can induce inflammation by stimulating the NLRP3 inflammasome, a cytosolic receptor complex that plays a critical role in driving inflammatory immune responses. Ingested material results in the assembly of NLRP3 and subsequent secretion of interleukin 1 family cytokines. Here we demonstrate that respirable (<4 μm) volcanic ash from Soufrière Hills volcano, Montserrat, induces the release of mature IL-1β by LPS-stimulated macrophages in a NALP3 inflammasome-dependent manner. Macrophages deficient in components of the NLRP3 inflammasome are incapable of secreting IL-1β in response to volcanic ash exposure. This is a novel mechanism for the stimulation of an inflammatory immune response by volcanic ash and provides a new avenue for screening volcanic ash toxicity.

[1] Horwell & Baxter (2006) *Bull. Volcanol.* **69**, 1-24. [2] Damby (2012) *Doctoral thesis*, 1-359.