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Reply to correspondence: Silica-related diseases in the modern world: A role for self-DNA sensing in lung inflammatory

We thank Quesniaux and her colleagues for their commentary¹ regarding our article "Silica-related diseases in the modern world."² We wholeheartedly agree with their sentiment that understanding mechanisms of disease at the cellular and molecular level, rather than at the "macro" level, will lead to more effective therapies. This principle applies just as well to newly emerging diseases such as COVID-19, as it does to ancient conditions such as silicosis. In our review, we provided an overview of current understanding of silicosis epidemiology, risk factors, clinical presentation, radiologic features and pathogenesis and highlighted the central importance of inflammasome activation by macrophages which have phagocytosed reactive-oxygen species producing silica particles.² Quesniaux and her colleagues highlight the increasing interest in the stimulator of interferon genes (STING) pathway and its role in inflammasome activation. The model proposed by Quesniaux, and supported by pre-clinical data, involves silica-provoked cell death, triggering danger-inducing DNA release and activation of the STING pathway rather than direct cytotoxicity and inflammasome activation.³ This pathway is of particularly interest as it has captured the imagination of pharmaceutical companies which are now actively developing both agonists (targeting cancer) and antagonists (targeting autoimmune disease).⁴ It remains to be seen whether direct, or indirect, STING-mediated, inflammasome activation predominates in human silicosis. The most likely scenario is that both will occur, perhaps even to differing degrees in an individual. Deciphering these pathways in human populations, and eventually even in individuals to personalise care and truly deliver "precise" medicine, should be a central objective for researchers. We congratulate Quesniaux and her colleagues for their work and hope that their efforts will eventually lead to better outcomes for workers around the world who are suffering from silicosis.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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