The enduring challenge of crystalline silica toxicity in the exposome era: insights from a decade of research

Crystalline silica remains one of the most studied yet mechanistically elusive environmental and occupational toxicants. While its capacity to induce pulmonary diseases such as fibrosis and cancer is well established, accumulating evidence points to broader systemic effects, including autoimmune conditions, even at low exposure levels. These effects are increasingly examined through the lens of the exposome, which emphasizes the lifelong interplay of diverse environmental exposures and biological responses.

Recent interdisciplinary efforts have significantly advanced understanding of silica's toxicity, revealing that biological reactivity cannot be fully explained by traditional metrics such as size, shape, or composition. A key finding from this body of work is the identification of *nearly free silanols (NFS)* - specific surface structures capable of disrupting cellular membranes and triggering proinflammatory and profibrotic signaling cascades. These insights emerged from the integration of surface chemistry, in vitro mechanistic studies, and in vivo models, bridging molecular-scale interactions with inflammatory and pathophysiological outcomes.

Emerging hypotheses suggest that systemic manifestations may stem from particle translocation beyond the lungs and subsequent biodistribution, raising critical questions about current exposure limits and risk assessment models. Placing crystalline silica within the exposomic framework allows for a more nuanced evaluation of long-term health risks and underscores the need for refined strategies in toxicological assessment and prevention.

Selected bibliography:

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