Understanding sterile inflammation: pristine graphene evokes NF-KB-dependent cytokine secretion in the absence of cell death

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Abstract

Graphene and related materials display novel and useful chemical, physical/mechanical, electrical, and optical characteristics, making them attractive for a wide range of applications. Their increasing use also necessitates careful evaluation of the safety profile. Graphene oxide (GO) has been extensively investigated in this regard, but there is still a paucity of studies concerning graphene (Fadeel et al., 2025). Here, we report the impact of aqueous dispersions of graphene on proinflammatory cytokine secretion using a human macrophage-differentiated cell line (THP-1), finding minimal cytotoxicity. NF-κB-dependent tumor necrosis factor (TNF)-α and interleukin (IL)-1β secretion was observed, and IL-1β secretion occurred without so-called priming, wherein cells are stimulated with lipopolysaccharide (LPS). IL-1β secretion was independent of lysosomal cathepsin B. Using knockout cell lines, we confirm that the graphene-induced IL-1β secretion is partially NLRP3 inflammasome-dependent. We also find that IL-1β secretion is linked to cellular potassium efflux, an established trigger of inflammasome activation. These findings provide new insights regarding sterile inflammation, demonstrating that graphene evokes proinflammatory cytokine secretion through NF-κB signaling albeit in the absence of cell death.

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Further reading

Fadeel B, Baker J, Ballerini L, Bussy C, Candotto Carniel F, Tretiach M, Pelin M, Buerki-Thurnherr T, Kanerva T, Navas JM, Vázquez E, Rodriguez Unamuno V, Lehtonen P, González M, Rauscher H, Riego Sintes J, Kostarelos K, Bianco A, Prato M. Safety assessment of graphene-based materials. Small. 2025;21(7):e2404570.