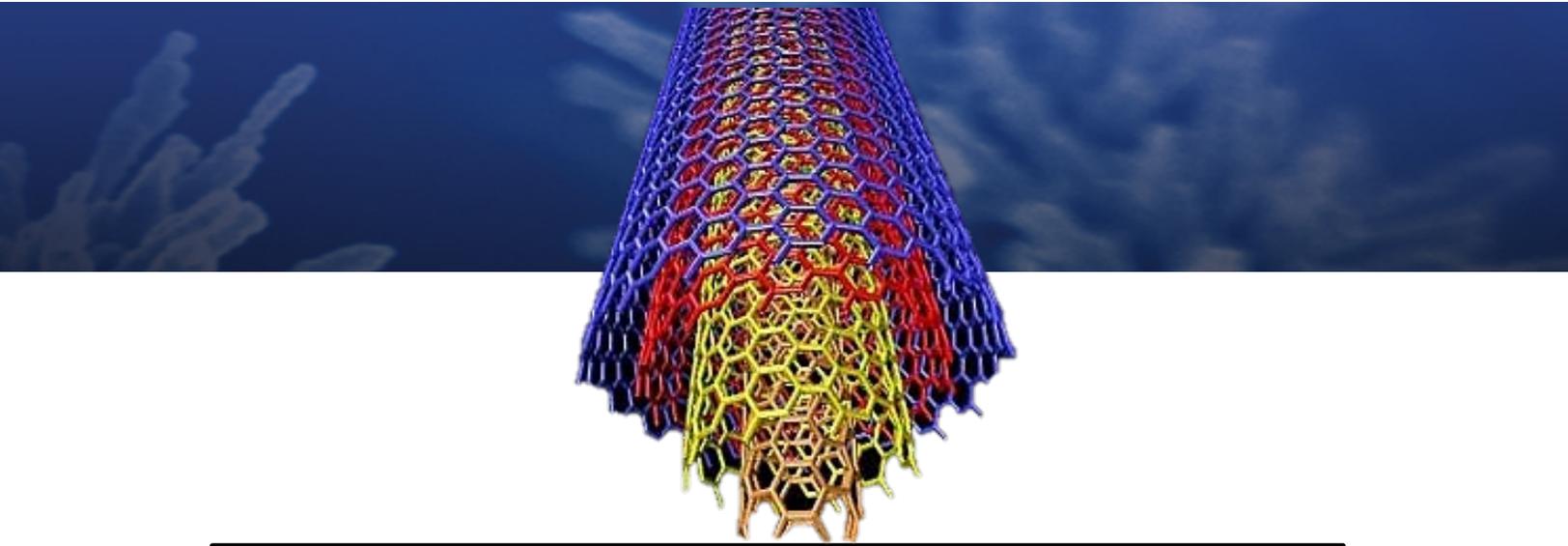


223. Mechanistic Evaluation of Oxidant Generation and the Development of Inflammation after Pulmonary Exposure to Metal-Rich Welding Nanoparticles

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Welding generates incidental nanoparticles composed of cytotoxic metals (e.g., Cr, Mn, Ni, Fe). The goal was to use both in vivo and in vitro methodologies to determine the mechanisms by which welding nanoparticles may damage the lungs. To assess lung injury/inflammation, Sprague-Dawley rats were treated by intratracheal instillation (ITI) with 2.0 mg/rat of gas metal arc-mild steel (GMA-MS) or manual metal arc-stainless steel (MMA-SS) welding particles. At 1, 3, and 10 d, bronchoalveolar lavage was performed. To determine the cytotoxicity of the welding nanoparticles, RAW264.7 macrophages were exposed to MMA-SS or GMA-MS particles for 24 hr (0-50 mg/mL), and ROS generation and activation of inflammatory markers were assessed. Particle metal composition and size distribution were characterized by ICP-AES and MOUDI, respectively. MMA-SS (41% Fe, 29% Cr, 17% Mn, 3% Ni) and GMA-MS (85% Fe, 14% Mn) were arranged as chain-like agglomerates (MMAD: 240 nm) of primary nanoparticles (~20-50 nm). Lung injury (LDH) and inflammation (neutrophil influx) were increased with ITI MMA-SS treatment compared to saline control and GMA-MS. RAW264.7 cells treated with MMA-SS caused increases in ROS, lipid aldehyde (4-hydroxynonenal) production, and COX-2 protein/gene expression. MMA-SS exposure also increased in vitro and in vivo protein expression of Nrf2 and HO-1 and in vitro gene expression of Hmox1. Welding generates nanoparticles with different metal profiles depending on the process. Welders exposed to SS particles are at a greater risk due to the presence of specific metals (e.g., Cr, Ni), increased cytotoxicity, and enhanced oxidative stress. Funding provided by NIOSH927ZLEG.

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