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**Title:** Airway region-specific effects of carbon black nanoparticles (CBNP)

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**Body:** CBNP are present in industrially produced soot used for reinforcement of elastomers (e.g. in tyres) but also for paints, toner and batteries. CBNP may have lung cytotoxic and pro-inflammatory effects. The commercially available CBNP Printex 90 (P90) and the quartz DQ12 were shown to possess cytotoxic and pro-inflammatory properties in mice and human epithelial cell lines. We sought to investigate whether these particles exert similar effects in distal versus proximal airway explants of mice. The impact of CBNP on different airway regions was assessed by microdissection of proximal and distal airways from mouse lungs and ex vivo stimulation. Cytotoxicity was measured by LDH release and cytokine mRNA expression by qRT-PCR. In contrast to previous findings in mice and epithelial cell lines our study could not show pro-inflammatory effects of P90 or DQ12 on microdissected airways. IL-1 $\beta$, KC and TNF $\alpha$ mRNA expression was unchanged. There was only a trend towards slightly upregulated IL-6 expression in proximal airways incubated with P90. Incubation with DQ12 did not result in increased cytotoxicity in distal and proximal airways which is also different from findings in cell culture. A slight increase in cytotoxicity was indicated with increasing P90 concentrations. Although our results do not show significant cytotoxic or pro-inflammatory effects of P90 and DQ12 on proximal and distal airways, this does not exclude that oxidative stress, apoptosis or proliferation of airway cells are affected by P90 or DQ12. In the future, chemically modified CBNP will be analysed to reveal the impact of functional surface groups on the particle's toxicological properties. Supported by the BMBF: joint project Carbon Black (03X0093A).