Title: Chronic low-grade systemic inflammation causes DNA damage in the lungs of mice

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Background: Whether systemic inflammation compromises the pulmonary system is largely unknown. We tested the hypothesis that chronic low-grade systemic inflammation damages alveolar wall cells.

Methods: A chronic low-grade systemic inflammatory state was induced in 8-week-old male C57/BL6J mice by administration of lipopolysaccharide (LPS, 44.4 µg/day) for a 90-day period by subcutaneous implantation of a delayed-release pellet system. Acute systemic inflammation was induced in another group of mice by a single intraperitoneal injection of LPS (125 µg/body). The lungs of mice were examined for histologic changes and genetic damage to alveolar wall cells. Results: Chronic LPS exposure for a 30-day period or a 90-day period did not cause any obvious architectural changes in the lungs except for a mild level of alveolar macrophage infiltration. Despite the lack of architectural changes in the lung, immunofluorescence staining for γH2AX and phosphorylated 53BP1 showed that chronic LPS exposure resulted in an almost doubling of the number of DNA double-strand breaks (DSBs) in type 1 and type 2 alveolar epithelial cells and in alveolar endothelial cells. Acute LPS exposure also resulted in a doubling of the number of DSBs in type 1 and type 2 alveolar epithelial cells and in alveolar endothelial cells at 24 h, but the increased number of DSBs returned to the baseline level by 48 h. Conclusions: These results suggest that chronic systemic low-grade inflammation induces persistent DNA damage in alveolar epithelial and endothelial cells before architectural changes in the lung become evident.