

## Increase in ferric and ferrous iron in the mouse lung after asbestos exposure

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Pulmonary toxicity induced by asbestos is thought to be mediated through redox-cycling of fiber-bound and bioavailable iron (Fe). This impacts an oxidative stress which potentially mediates a cascade of events culminating in inflammation, fibrosis and cancer (Ghio et al, 2008 and 2009).

The present study aimed to elucidate in a murine model of asbestos exposure the distribution of ferric and ferrous iron and its relation with the development of fibrosis.

C57/Bl/6 mice were exposed to saline or crocidolite asbestos in saline (55 and 110  $\mu\text{g}$  intra-tracheally) and examined at 1 and 6 months for lung pathology. The left lung was embedded in paraffin, sectioned and stained with hematoxylin and eosin (H&E) and Masson's trichrome. A modified Perl's or Turnbull's blue histochemical stain was used to demonstrate Fe<sup>3+</sup> and Fe<sup>2+</sup> respectively (Wang et al, 2002).

One month following exposure, mice instilled with crocidolite displayed a significant inflammatory injury on staining with H&E (relative to animal exposed to saline). Crocidolite fibers could be observed most frequently in the region of distal bronchioles. The retention of these fibers was associated with an accumulation of inflammatory cells, predominantly macrophages. This response persisted 6 months following asbestos instillation. Increased collagen was observed at one and 6 months after asbestos exposure. One important observation made in 1-month H&E-stained slides of asbestos-exposed mice was the presence of focal atypical hyperplastic lesions. These lesions did not progress in severity from 1 to 6 months. Histological lung sections from saline exposed mice did not stain for both ferric and ferrous Fe. However, one month following crocidolite instillation, a number of Fe<sup>3+</sup>-positive (but no Fe<sup>2+</sup>-positive) cells (predominantly macrophages) were present, in the lower respiratory tract. At 6 months postinjection, an increase number of Fe<sup>3+</sup>-positive cells was observed and also some Fe<sup>2+</sup> positive cells were present.

The observation of some Fe<sup>2+</sup> positive cells in the lung of asbestos exposed mice at 6 months postinjection suggests a shift in the oxidation state of the accumulated iron, with more cells becoming Fe<sup>2+</sup>-positive at a late stage. These growing amounts of Fe<sup>2+</sup> could support a continued generation of oxidative stress resulting in clinical manifestations, which culminate in inflammatory, fibrotic and hyperplastic lesions.

### References

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### Key words

Ferric and ferrous iron, asbestos, mouse lung.