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Long-Fibre carbon nanotubes induce Sporadic Pleural Mesothelioma recapitulating Human Disease: A role for epigenetic mechanisms in disease development

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Exposure to asbestos fibres causes pathological changes in the pleural cavity, including malignant mesothelioma. Length-dependent retention of asbestos fibres in the pleural cavity is crucial for disease development. Chronic inflammation induced by biopersistent pathogenic asbestos fibres plays a key role in carcinogenesis. Use of manufacture carbon nanotubes (CNT) is growing which increases occupational exposures of these materials. Manufactured carbon nanotubes (CNT) are similar to asbestos in terms of their high aspect-ratio and thus may pose an asbestos-like inhalation hazard; however, the molecular mechanisms underlying CNT toxicity and carcinogenic potential have not been sufficiently explored. Epigenetics is one area of interest that has been quickly developing to assess disease processes due to its ability to change gene expression and thus the lung environment after exposure. Using a mouse model of direct injection of long asbestos fibres and long-CNT into the pleural cavity, we compared the molecular changes in the mesothelium induced by these fibres over prolonged exposure times following injection.

We show a common molecular signature in the molecular changes induced by long-CNT and long asbestos throughout disease progression leading to the development of sporadic malignant mesothelioma. Our transcriptome analysis shows that gene expression profiles are similarly altered in the presence of long-CNT and long asbestos, compared to control mice at matched exposure times. Epigenetic changes induced by pathogenic fibres (long-CNT and asbestos) occur at the pre-neoplastic stage of disease and may play a key role in progression of pleural inflammatory lesions to malignant mesothelioma. Together, these data demonstrate that exposure to long-CNT induces development of sporadic pleural mesothelioma replicating the pathogenesis of human disease and highlights commonality in the hazard mechanism of long pathogenic fibres at the molecular level. Crucially, our findings reinforce concerns that high aspect-ratio CNT may pose an asbestos-like hazard, leading to malignant mesothelioma.

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