Inhaled carbon nanotube-induced gene expression profile in rat lung

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BACKGROUND & OBJECTIVES

Due to their physical and chemical properties, carbon nanotubes are among the most promising nanomaterials for industrial and medical applications. Since the main route of occupational exposure is inhalation and regarding the increasing number of workers potentially exposed to carbon nanotubes, inhalation experiments performed on laboratory rodents remain the most suitable and reliable approaches to assess their toxicity. In addition to conventional toxicological assays, the identification of lung molecular signatures induced by carbon nanotube exposure could help to better understand their mechanism of toxicity and identify molecular initiating events or toxicological pathways in order to predict adverse outcome.

The aim of this work is to study the gene expression profile induced by inhaled carbon nanotubes and interpret it in the light of physiopathological effects of such exposures.

METHODS

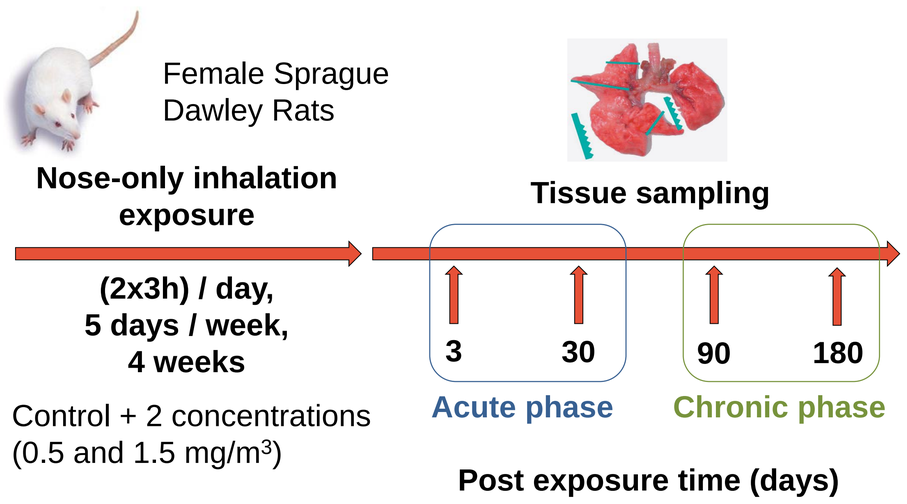

Fig 1. Experimental protocol.
Sprague Dawley rats were exposed to carbon nanotube (NM-401) aerosol in nose-only inhalation chambers, 6 h per day, 5 days per week for four weeks. Tissues were collected 3, 30, 90 and 180 days after the end exposure.

RESULTS

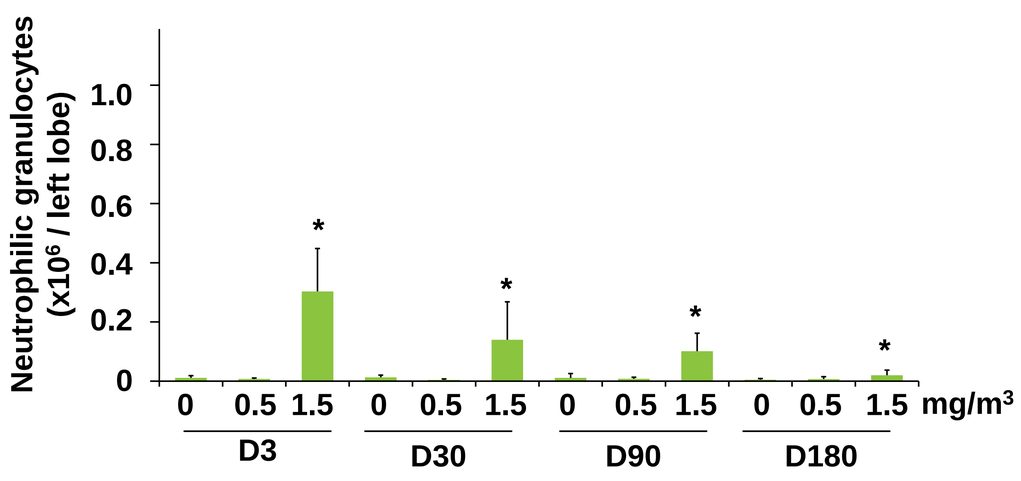

Fig 2. Neutrophil cell count in the broncho-alveolar lavage fluid of control and NM-401 exposed animals.
Analysis revealed an alveolar influx of neutrophilic granulocytes in animals exposed to the highest dose which decreased over time.

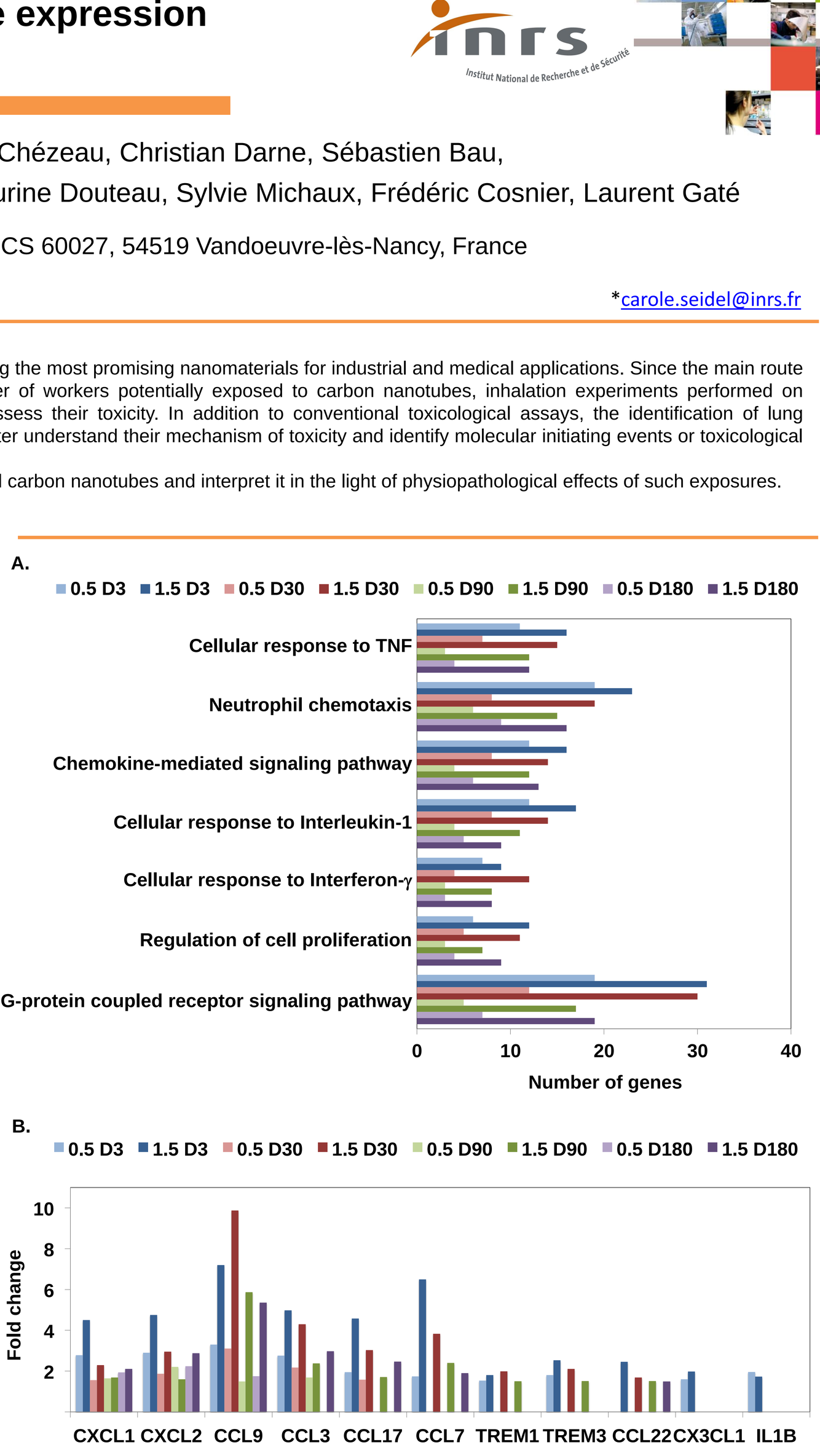

Fig 3. Gene expression profile in NM-401 exposed rat lung.
A. Gene Ontology Biological Pathway annotations in 3, 30, 90 and 180 days after the end of exposure to 0.5 or 1.5 mg/m³ of NM-401. **B.** Differential expression of selected genes involved in GO BP “Neutrophil chemotaxis”.

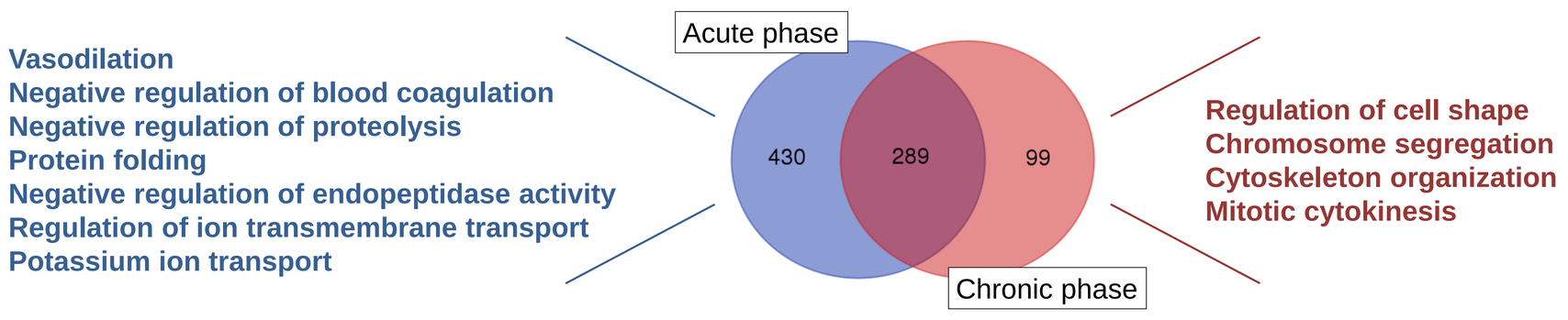

Fig 4. Gene expression profile in acute and chronic phases.
Gene Ontology Biological Pathways significantly enriched in either acute (blue) or chronic phase (red). Number of genes differentially expressed either in acute or chronic phase as well as in both of them are indicated for animals exposed to 1.5 mg/m³ of NM-401.

CONCLUSION

NM-401 inhalation modulated the gene expression in different pathways involved in the inflammatory response from post-exposure day 3 and up to 180 days. Up- and down-regulation of these genes were even observed at the lower dose of NM-401 that did not induce any inflammatory response in the conventional approach (i.e. alveolar influx of neutrophilic granulocytes). Genes involved in these pathways were however differentially regulated depending on concentration and time.
In the acute phase (3 and 30 post-exposure days), genes involved in vasodilation, blood coagulation and ion transport are specifically regulated; whereas during the chronic phase (90 and 180 post-exposure days), specific regulation of genes involved in cytoskeleton organization and cell cycle progression was observed.
Differentially expressed genes in the chronic phase should be further investigated in order to assess their potential role in pathology development.

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