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MWCNTs induced epithelial-mesenchymal transition of BEAS-2B cells

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BACKGROUND & OBJECTIVES

The use of multi-walled carbon nanotubes (MWCNTs) is growing. Pulmonary exposure during production, use, and handling rises concern about their potential adverse health effects.

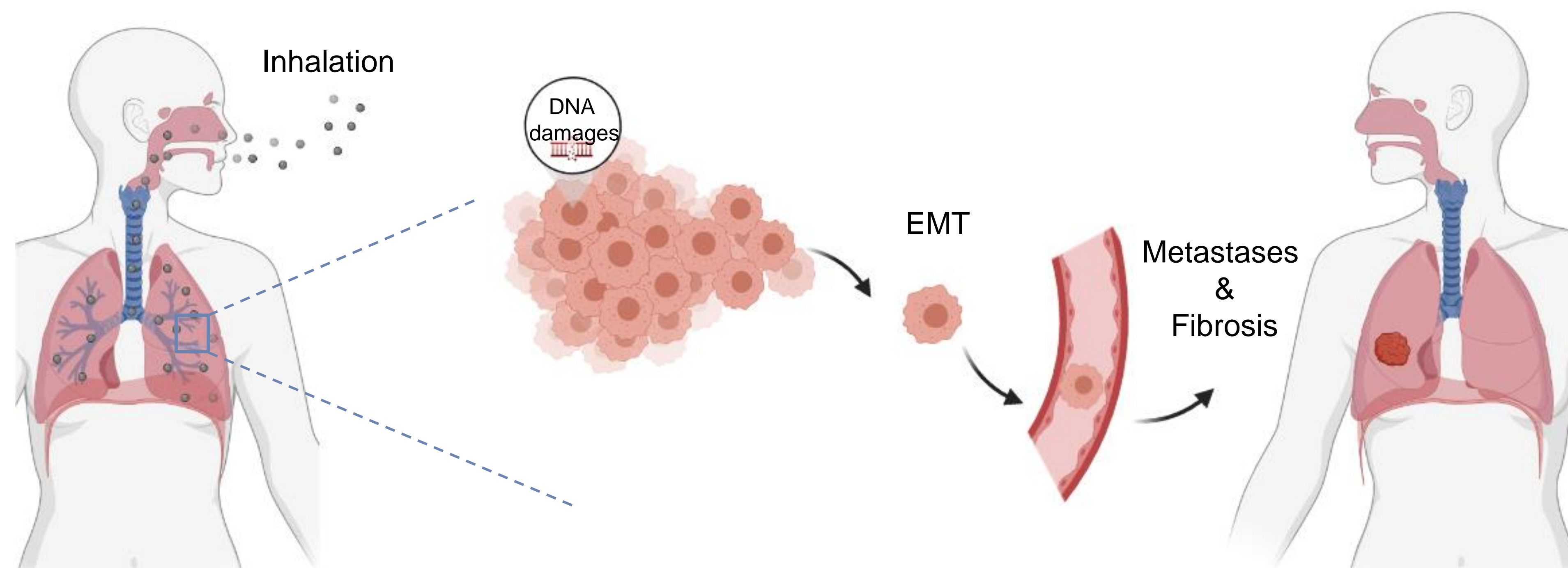
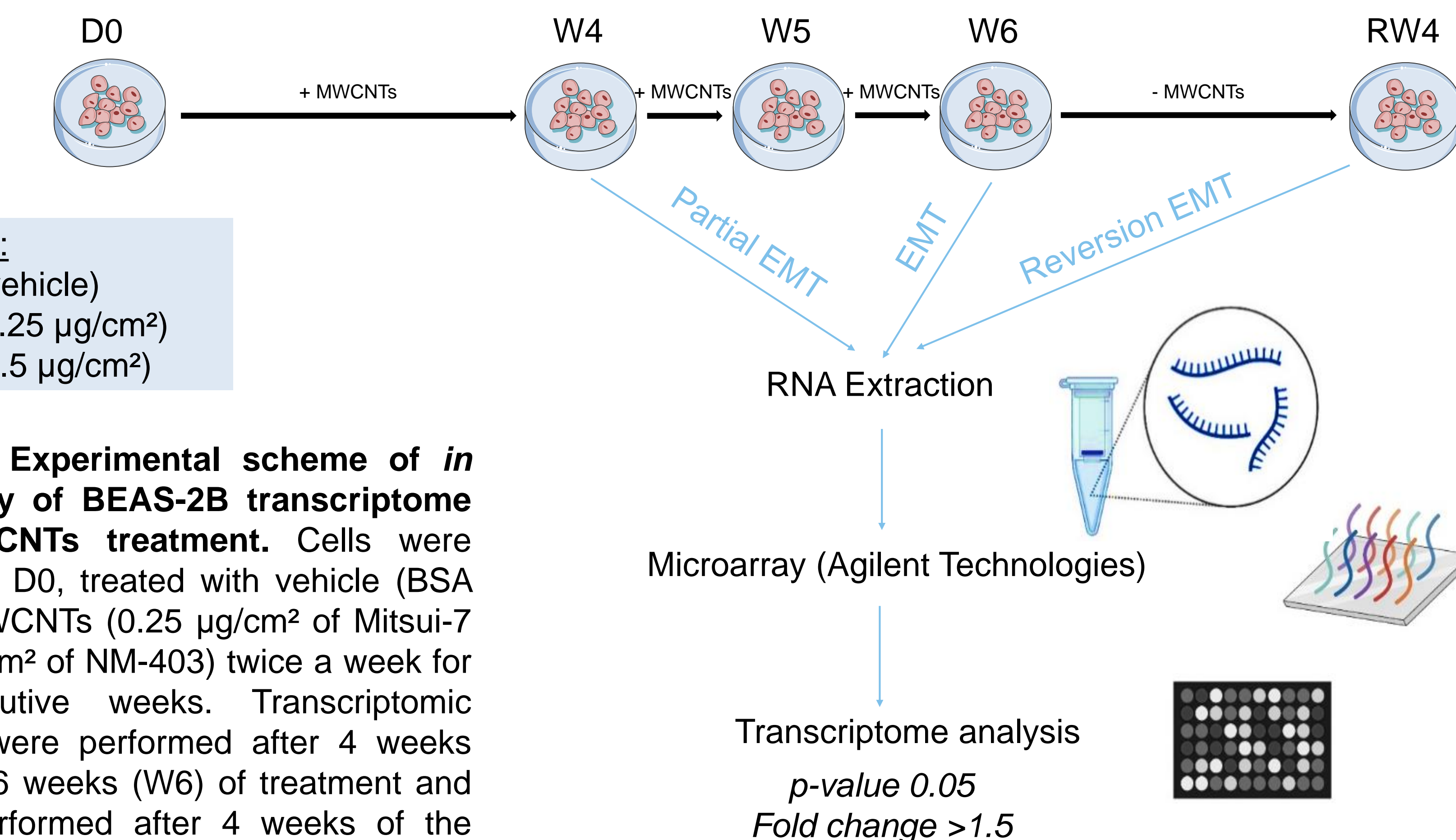


Figure 1: Multi-walled carbon nanotubes & pulmonary toxicity. Due to their small size, MWCNTs can be inhaled and deposit in the deep regions of the lung. Such exposure may induce genotoxicity and promote the establishment of an epithelial-mesenchymal transition (EMT), process that is related to the development of adverse outcomes such as fibrosis and metastases.

We have demonstrated the genotoxic potential of MWCNTs (**abnormal mitoses and micronucleus formation**). Furthermore, the treatment of BEAS-2B cells with low concentrations of MWCNTs induced a progressive **epithelial-mesenchymal transition**, which could be involved in the development of metastasis or pulmonary fibrosis (Barthel *et al.*, 2021). At least partial reversion of the effects occurs after 4 weeks of recovery.

Although the cells revert to an epithelial phenotype, this reversion may not be complete in terms of gene expression. Therefore, we aimed to study the transcriptome after 4 weeks of treatment (mix epithelial – needle shape cells), 6 weeks of treatment (mainly needle shape cells). The transcriptomic status after 4 weeks of recovery (mainly reversion to epithelial cells) is under analysis.

METHODS



Conditions:
BSA 1% (vehicle)
Mitsui-7 (0.25 µg/cm²)
NM-403 (0.5 µg/cm²)

Figure 2: Experimental scheme of *in vitro* study of BEAS-2B transcriptome after MWCNTs treatment. Cells were seeded on D0, treated with vehicle (BSA 1%) or MWCNTs (0.25 µg/cm² of Mitsui-7 or 0.5 µg/cm² of NM-403) twice a week for 6 consecutive weeks. Transcriptomic analyses were performed after 4 weeks (W4) and 6 weeks (W6) of treatment and will be performed after 4 weeks of the recovery period (RW4).

RESULTS

Differentially expressed genes (W4 & W6):

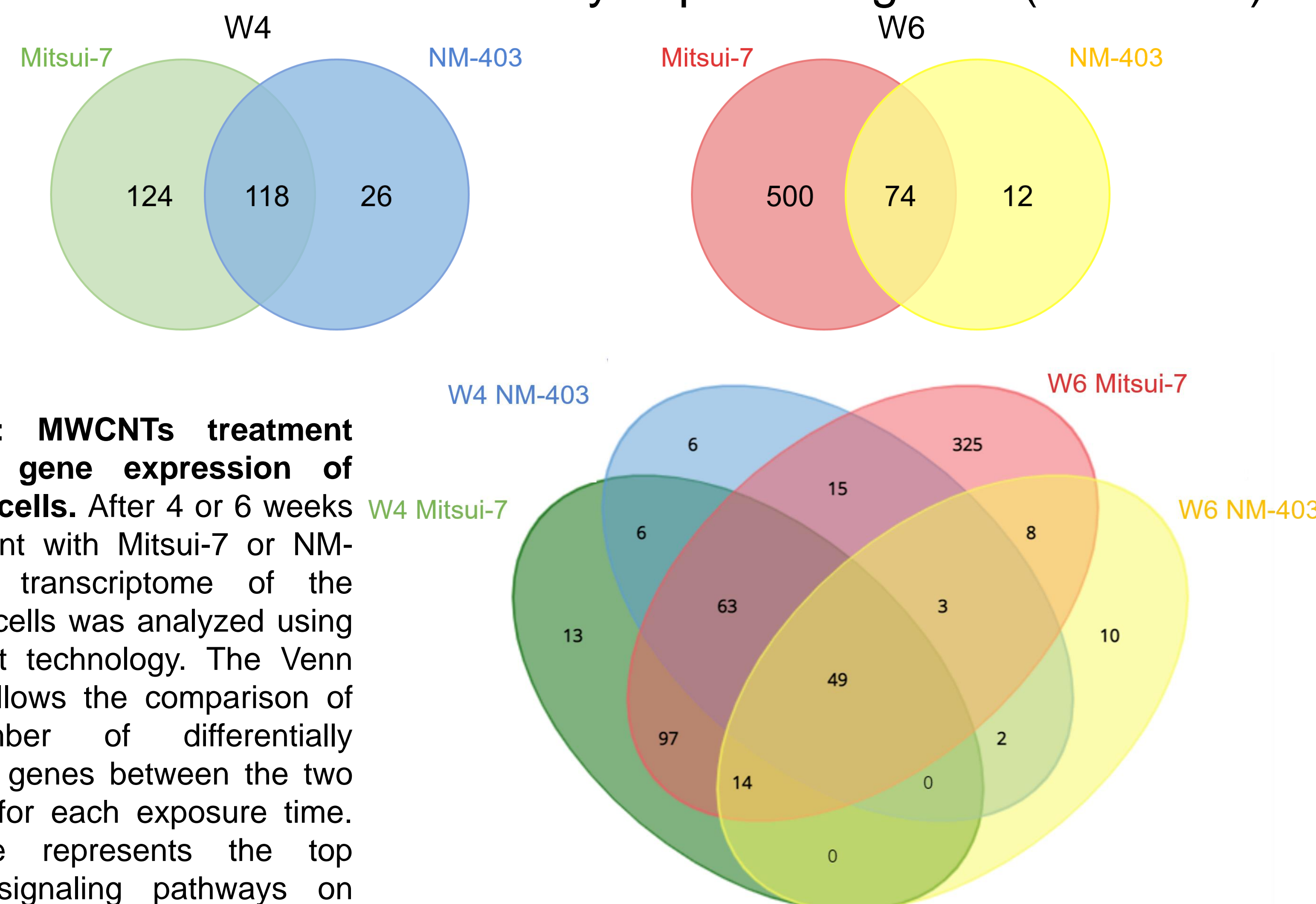


Figure 3: MWCNTs treatment modulate gene expression of BEAS-2B cells. After 4 or 6 weeks of treatment with Mitsui-7 or NM-403, the transcriptome of the BEAS-2B cells was analyzed using the Agilent technology. The Venn diagram allows the comparison of the number of differentially expressed genes between the two MWCNTs for each exposure time. The table represents the top modified signaling pathways on W6. W: week.

Top modified signaling pathways on W6
(Elsevier Pathway collection)

Mitsui-7 (long & thick):

- 1- Proteins with altered expression in cancer metastases
- 2- Epithelial to Mesenchymal transition in Cancer: Overview
- 3- TGFB family in Epithelial to Mesenchymal Transition in cancer
- 4- WNT in Epithelial to Mesenchymal Transition in Cancer
- 5- IL13/STAT6/ZEB1 Signalling Promotes Cancer Metastatic Progression

NM-403 (short & thin):

- 1- Epithelial to Mesenchymal transition in Cancer: Overview
- 2- IL13/STAT6/ZEB1 Signalling Promotes Cancer Metastatic Progression

DISCUSSION

- Mitsui-7 have a stronger and faster effect than NM-403
- EMT is the main biological process induced by MWCNTs
- MWCNT exposure may lead to metastasis development or fibrosis
- Are the cells completely reverted to an epithelial phenotype after 4 weeks of recovery ?

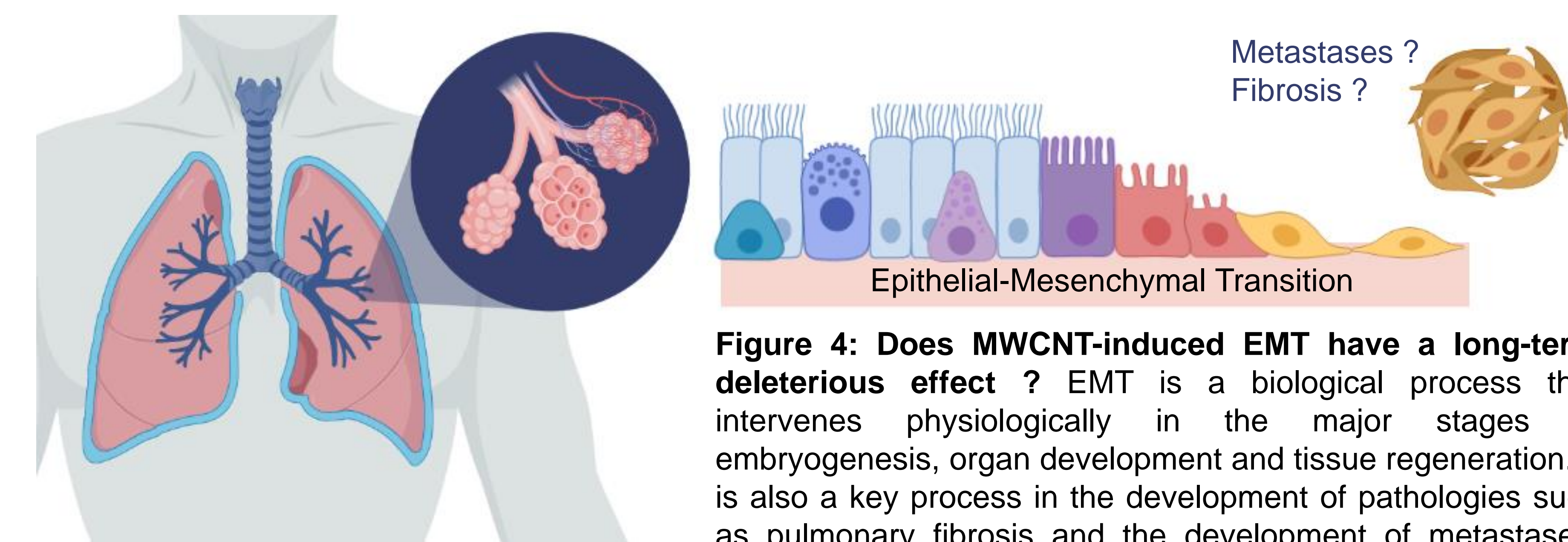


Figure 4: Does MWCNT-induced EMT have a long-term deleterious effect ? EMT is a biological process that intervenes physiologically in the major stages of embryogenesis, organ development and tissue regeneration. It is also a key process in the development of pathologies such as pulmonary fibrosis and the development of metastases. Question arises whether the reversion of the effects is complete at the phenotypical and molecular levels after 4 weeks of recovery.