News Release

Title

Intraperitoneal administration of tangled multiwalled carbon nanotubes of 15 nm in diameter does not induce mesothelial carcinogenesis in rats

Key Points

- A tangled form of multiwalled carbon nanotubes (MWCNTs) lacks mesothelial carcinogenic potential, as tested in a long-term carcinogenesis experiment.
- Even a type of iron-rich MWCNTs lacks carcinogenic potential due to its structural characteristics.

Summary

Shinya Toyokuni (Professor, Department of Pathology and Biological Responses), Hirotaka Nagai (Visiting scholar) and his team in Nagoya University Graduate School of Medicine (Dean: Masahide Takahashi, MD, PhD) found that, based on a long-term observation up to three years, a tangled form of multiwalled carbon nanotubes lacks mesothelial carcinogenic potential despite its abundant contaminant iron. This work was published online in Pathology International on October 8th, 2013.

Research Background

Multiwalled carbon nanotubes (MWCNTs) are newly-developed nanomaterials made of carbon. They have attracted public attention for their potential applications in engineering and materials science. However, due to the morphological similarity between MWCNTs and asbestos fibers, there have been social concerns that MWCNTs may provoke similar environmental hazards as asbestos fibers did. Asbestos fibers are well-known carcinogens, causing malignant mesothelioma and lung cancer. The mechanism of the asbestos-induced carcinogenesis is still elusive, though carcinogenesis with extremely long incubation period (30-40 years) is thought to be mediated by high durability and needle-like structure. MWCNTs and asbestos fibers share these characteristics, and the determinant factors for MWCNT-induced mesothelial carcinogenesis have been elusive until recently.

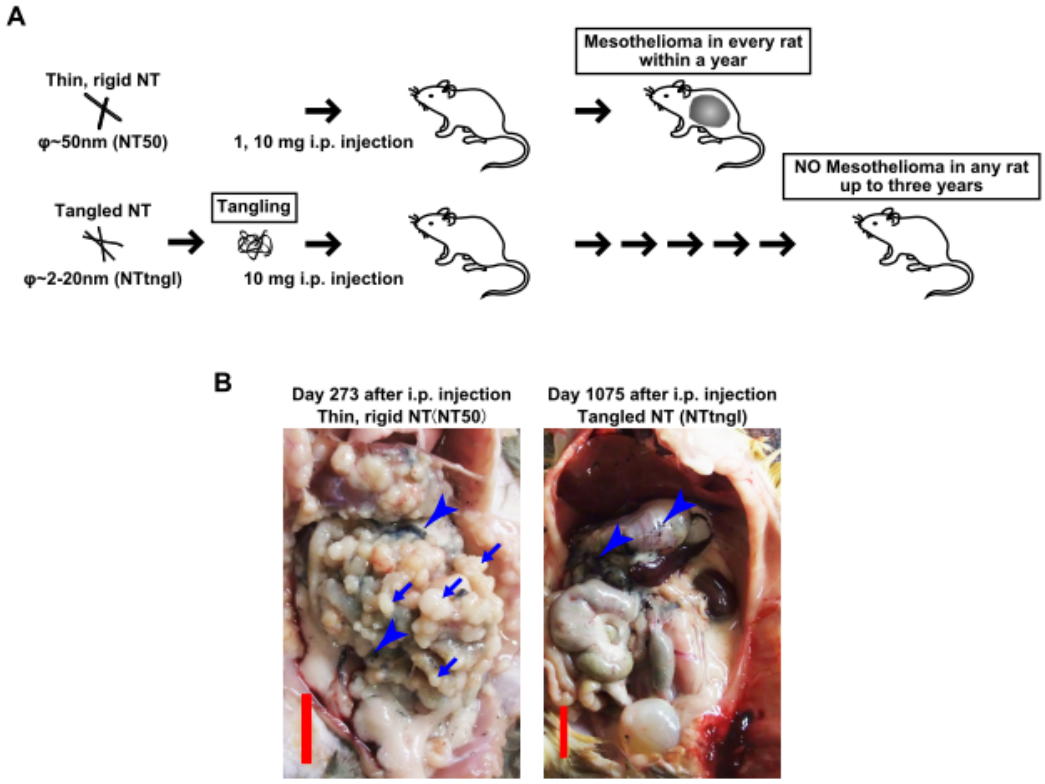
In 2011, we reported that, in addition to the two characteristics mentioned

above, diameter and rigidity of MWCNTs are critical factors for mesothelial injury and carcinogenesis. In the previous experiment, we observed the rats for one year following administration of MWCNTs. However, it has been unknown whether tangled MWCNTs, which did not induce malignant mesothelioma after intraperitoneal injection for one year, would not induce malignant mesothelioma after a longer incubation period. Here, in order to exclude the possibility that the tangled MWCNTs induce mesothelioma after a long incubation, we injected a large amount (10 mg) of tangled MWCNTs into the intraperitoneal cavity of rats and observed them for up to 3 years.

Research Results

Following 10 mg of tangled MWCNT administration, we found that 9 out of 21 male rats acutely died for unknown reasons. This acute death is not specific to the nanotubes we currently used, because we found previously that other types of MWCNTs also induced similar acute deaths after 10 mg of injection.

We continuously observed the condition of remaining rats. The 6 out of 12 remaining rats were sacrificed one year after the injection, as reported previously (Nagai H *et al.* Proc. Natl. Acad. Sci USA 108: E1330-8, 2011). The remaining 6 animals were evaluated in the present study. They were euthanized after they showed severe health problems such as development of tumors or weight loss. We found that none of the 6 rats developed malignant mesothelioma despite the long observation period (~3 years). We found instead that some of them obtained other tumors that may be observed in the control animals of old age.



Research Summary and Future Perspective

In summary, our study provided first evidence that tangled MWCNTs do not induce malignant mesothelioma following intraperitoneal injection in rats. Our work suggests that modulation of structure of MWCNTs may increase safety of nanomaterials and relieve social concerns.

Title: Intraperitoneal administration of tangled multiwalled carbon nanotubes of 15 nm in diameter does not induce mesothelial carcinogenesis in rats. **Pathology International 63: 457-62, 2013** (October 8, 2013).