Reviewer 3

1. It would be clearer if the author chose several key figures or tables as displayed items in this figure.

We have added a brief summary of all of the studies cited in the manuscript in newly added Tables 1,2,3,4,5. We have also divided the manuscript into 8 sections with summary paragraphs added to section 2-7. Finally, we added a brief summary of the toxicological signaling pathways to the manuscript as Figure 2.

2. The conclusion of the carcinogenic trend of CNTs is clear given the comprehensive literature review that the authors collect. However, I am curious about detailed molecular mechanism of the carcinogenic and inflammation properties in lung. If the current research does not include the issue above, I suggest the authors include more perspective about it in the discussion.

We have added a brief summary of the toxicological signaling pathways in the lung and pleural and peritoneal cavities to the manuscript as Figure 2. Basically, as determined by Nagai et al. (2011) and Yang et al. (2010), in the pleural and peritoneal cavities rigid MWCNTs can pierce and damage mesothelial cells, leading to release of HMGB1 and promote an inflammatory response. In contrast, tangled MWCNTs do not damage mesothelial cells and are either removed from the pleural cavity or sequestered in granulation tissue, and therefore do not induce an inflammatory response or the development of mesothelioma. In contrast, in the lung it is the interaction with alveolar macrophages that induces an inflammatory response. Therefore, in the lung direct epithelial cell damage is not needed for the induction of an inflammatory response and lung carcinogenicity.

We have also cited Hojo et al., 2023 (Reference 69), which describes Time-Course of Transcriptomic Change in the Lungs of F344 Rats Repeatedly Exposed to a Multiwalled Carbon Nanotube in a 2-Year Test.

"Hojo et al. (2023) have determined that the lung carcinogenicity of MWCNT-7 is associated with persistent inflammation and ROS generation [69]."