



## **Autophagy plays a protective role in the development of Alzheimer-like pathogenic changes promoted by ultrafine black carbon in SH-SY5Y cells**

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Epidemiological studies have revealed that ambient black carbon (BC) might be involved in the development of Alzheimer's disease (AD). BC is normally enriched in the ultrafine fraction of PM<sub>2.5</sub>, and can potentially cross blood brain barrier. Till now, very little is known about the effects they may have on central nervous system. This study aimed to investigate the potential roles of autophagy in p-Tau accumulation and other Alzheimer-like pathogenic markers promoted by uBC. A manufactured nano-sized carbon black, widely used in toxicological studies, was selected as a surrogate particle for ambient BC in this study. Firstly, we found uBC could induce extensive toxic effects in SH-SY5Y cells, including cell proliferation inhibition, LDH release, apoptosis, DNA damage and pro-inflammatory cytokine expressions. Oxidative stress and reactive oxygen species (ROS) were also observed in SH-SY5Y cells after treated with uBC. Then we found uBC could promote autophagy process possibly through the regulation of PI3K/Akt pathway. Moreover, uBC induced phosphorylated tau (p-Tau) protein accumulation and up- or down-regulated several gene markers related to AD. RNA interference and autophagy inhibitor were applied to block autophagy process at different stages. We further found that autophagy dysfunction at the initial membrane expansion stage could further aggravate p-Tau accumulation and other Alzheimer-like changes (including cytokine expressions) in SH-SY5Y cells. Meanwhile, autophagy inhibition at the final stage could alleviate p-Tau accumulation and other AD related marks caused by uBC. This suggested that the inhibition of autophagosome and lysosome infusion could possibly activate ubiquitination degradation pathway to maintain the p-Tau equilibrium in SH-SY5Y cells. Our findings further raise the concerns about the adverse effects of uBC on the risk of AD and also indicate the important roles of autophagy on early Alzheimer-like pathogenic changes caused by ambient BC particles.