

TFEB

Atmospheric particulate matter (PM) exacerbates the risk factor for Alzheimer's and **Parkinson's diseases** (PD) by promoting the **alpha-synuclein** (α -syn) pathology in the brain. However, the molecular mechanisms of astrocytes involvement in α -syn pathology underlying the process remain unclear.

Li et al. in a study investigated PM with particle size <200 nm (PM_{0.2}) exposure-induced α -syn pathology in ICR mice and primary astrocytes, then assessed the effects of mammalian target of rapamycin inhibitor (PP242) in vitro studies. We observed the α -syn pathology in the brains of exposed mice. Meanwhile, PM_{0.2}-exposed mice also exhibited the activation of glial cell and the inhibition of autophagy. In vitro study, PM_{0.2} (3, 10 and 30 μ g/mL) induced inflammatory response and the disorders of α -syn degradation in primary astrocytes, and lysosomal-associated membrane protein 2 (LAMP2)-mediated autophagy underlies α -syn pathology. The abnormal function of autophagy-lysosome was specifically manifested as the expression of microtubule-associated protein light chain 3 (LC3II), cathepsin B (CTSB) and lysosomal abundance increased first and then decreased, which might both be a compensatory mechanism to toxic α -syn accumulation induced by PM_{0.2}. Moreover, with the transcription factor EB (TFEB) subcellular localization and the increase in LC3II, LAMP2, CTSB, and cathepsin D proteins were identified, leading to the restoration of the degradation of α -syn after the intervention of PP242. Our results identified that PM_{0.2} exposure could promote the α -syn pathological dysregulation in **astrocytes**, providing mechanistic insights into how PM_{0.2} increases the risk of developing PD and highlighting TFEB/**LAMP2** as a promising therapeutic target for antagonizing PM_{0.2} toxicity ¹⁾.

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Li B, Liu T, Shen Y, Qin J, Chang X, Wu M, Guo J, Liu L, Wei C, Lyu Y, Tian F, Yin J, Wang T, Zhang W, Qiu Y. **TFEB/LAMP2** contributes to PM_{0.2}-induced autophagy-lysosome dysfunction and alpha-synuclein dysregulation in astrocytes. *J Environ Sci (China)*. 2024 Nov;145:117-127. doi: 10.1016/j.jes.2023.09.036. Epub 2023 Oct 5. PMID: 38844312.

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