

Drug protects against air pollution-related Alzheimer's signs in mice

August 12 2024



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A study led by the USC Leonard Davis School of Gerontology shows how feeding mice a drug called GSM-15606 provides protection against air pollution-related increases in proteins linked to Alzheimer's disease.

Senior author Caleb Finch, USC University Professor and holder of the ARCO/William F. Kieschnick Chair in the Neurobiology of Aging at the USC Leonard Davis School, has studied air pollution's effects on the



brain for several years, especially the consequences of <u>exposure to fine</u> <u>particulates</u> found in pollution from automobiles, factories and more. Many studies have shown that <u>air quality</u> has a sizeable impact on risk of Alzheimer and accelerates cognitive decline, he said.

Air pollution is correlated with systemic inflammation and promotes the formation of amyloid plaques, the clumps of aggregated peptide A β 42 that form between the brain's nerve cells in Alzheimer's.

The latest work from Finch's lab, published August 12 in *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, highlights the potential protection offered by a type of <u>drug</u> called a gamma-secretase modulator. The team tested a specific drug called GSM-15606, which was developed by study co-authors Rudolph E. Tanzi of Harvard and Kevin D. Rynearson of the University of California, San Diego.

GSM-15606 was fed to <u>mice</u> over eight weeks; during that time, the animals were regularly exposed to air pollution in the form of either ambient nanoparticulate matter (nPM) or diesel exhaust particles (DEP). Following air pollution exposure, mice fed GSM-15606 had much lower levels of A β 42 in the brain than mice exposed to pollution but not the drug.

The results indicate that GSM-15606 may one day have a role as a <u>preventive measure</u> against Alzheimer's in people living with air pollution, Finch said.

"Because gamma secretase is needed for normal functions body-wide, this drug was designed to modulate, but not inhibit, production of $A\beta42$," he said.

"This is the first example of a new drug developed to slow Alzheimer's that may also protect aging individuals from the environmental risk



factor of air pollution."

More information: Air pollution amyloidogenesis is attenuated by the gamma-secretase modulator GSM-15606, *Alzheimer s & Dementia* (2024). DOI: 10.1002/alz.14086

Provided by University of Southern California

Citation: Drug protects against air pollution-related Alzheimer's signs in mice (2024, August 12) retrieved 12 August 2024 from https://medicalxpress.com/news/2024-08-drug-air-pollution-alzheimer-mice.html

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