Powerful class of antioxidants may be potent Parkinson's treatment

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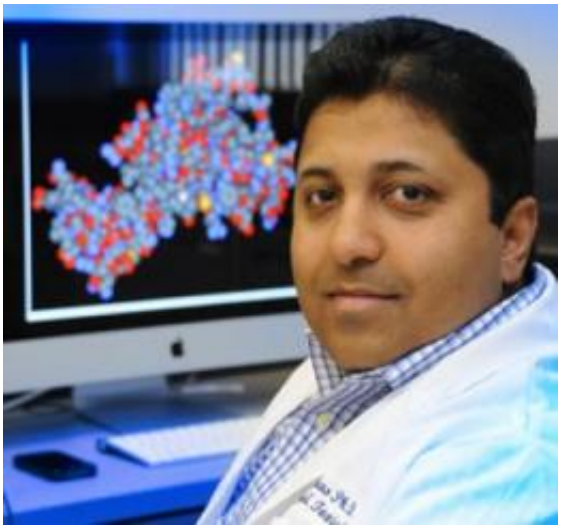

A new and powerful class of antioxidants could one day be a potent treatment for Parkinson's disease, according to research by Dr. Bobby Thomas, neuroscientist at the Medical College of Georgia at Georgia Health Sciences University. Credit: Phil Jones, photographer, Georgia Health Sciences University/Georgia Health Sciences Medical Center

A new and powerful class of antioxidants could one day be a potent treatment for Parkinson's disease, researchers report.

A class of antioxidants called synthetic triterpenoids blocked development of Parkinson's in an animal model that develops the disease in a handful of days, said Dr. Bobby Thomas, neuroscientist at the

Medical College of Georgia at Georgia Health Sciences University and corresponding author of the study in the journal *Antioxidants & Redox Signaling*.

Thomas and his colleagues were able to block the death of dopamine-producing brain cells that occurs in Parkinson's by using the drugs to bolster Nrf2, a natural antioxidant and inflammation fighter.

Stressors from head trauma to insecticide exposure to simple aging increase oxidative stress and the body responds with inflammation, part of its natural repair process. "This creates an environment in your brain that is not conducive for normal function," Thomas said. "You can see the signs of oxidative damage in the brain long before the neurons actually degenerate in Parkinson's."

Nrf2, the master regulator of oxidative stress and inflammation, is – inexplicably – significantly decreased early in Parkinson's. In fact, Nrf2 activity declines normally with age.

"In Parkinson's patients you can clearly see a significant overload of oxidative stress, which is why we chose this target," Thomas said. "We used drugs to selectively activate Nrf2."

They parsed a number of antioxidants already under study for a wide range of diseases from kidney failure to heart disease and diabetes, and found triterpenoids the most effective on Nrf2. Co-author Dr. Michael Sporn, Professor of Pharmacology, Toxicology and Medicine at Dartmouth Medical School, chemically modified the agents so they could permeate the protective blood-brain barrier.

Both in human neuroblastoma and mouse brain cells they were able to document an increase in Nrf2 in response to the synthetic triterpenoids. Human dopaminergic cells are not available for research so the scientists

used the human neuroblastoma cells, which are actually cancer cells that have some properties similar to neurons.

Their preliminary evidence indicates the synthetic triterpenoids also increase Nrf2 activity in astrocytes, a brain cell type which nourishes neurons and hauls off some of their garbage. The drugs didn't protect brain cells in an animal where the Nrf2 gene was deleted, more proof that that Nrf2 is the drugs' target.

The researchers used the powerful neurotoxin MPTP to mimic Parkinson's-like brain cell damage in a matter of days. They are now looking at the impact of synthetic triterpenoids in an animal model genetically programmed to acquire the disease more slowly, as humans do. Collaborators at Johns Hopkins School of Medicine also will be providing induced pluripotent stem cells, adult stem cells that can be coaxed into forming dopaminergic neurons, for additional drug testing.

Provided by Georgia Health Sciences University

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