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## **Vitamin B3 reduces Alzheimer's symptoms, lesions**

### ***UC Irvine starts clinical trial on nicotinamide effect in Alzheimer's patients***

Irvine, Calif. — An over-the-counter vitamin in high doses prevented memory loss in mice with Alzheimer's disease, and UC Irvine scientists now are conducting a clinical trial to determine its effect in humans.

Nicotinamide, a form of vitamin B3, lowered levels of a protein called phosphorylated tau that leads to the development of tangles, one of two brain lesions associated with Alzheimer's disease. The vitamin also strengthened scaffolding along which information travels in brain cells, helping to keep neurons alive and further preventing symptoms in mice genetically wired to develop Alzheimer's.

"Nicotinamide has a very robust effect on neurons," said Kim Green, UCI scientist and lead author of the study. "Nicotinamide prevents loss of cognition in mice with Alzheimer's disease, and the beauty of it is we already are moving forward with a clinical trial."

The study appears online Nov. 5 in the *Journal of Neuroscience*.

Nicotinamide is a water-soluble vitamin sold in health food stores. It generally is safe but can be toxic in very high doses. Clinical trials have shown it benefits people with diabetes complications and has anti-inflammatory properties that may help people with skin conditions.

Nicotinamide belongs to a class of compounds called HDAC inhibitors, which have been shown to protect the central nervous system in rodent models of Parkinson's and Huntington's diseases and amyotrophic lateral sclerosis. Clinical trials are underway to learn whether HDAC inhibitors help ALS and Huntington's patients.

In the nicotinamide study, Green and his colleague, Frank LaFerla, added the vitamin to drinking water fed to mice. They tested the rodents' short-term and long-term memory over

time using water-maze and object-recognition tasks and found that treated Alzheimer's mice performed at the same level as normal mice, while untreated Alzheimer's mice experienced memory loss.

The nicotinamide, in fact, slightly enhanced cognitive abilities in normal mice. "This suggests that not only is it good for Alzheimer's disease, but if normal people take it, some aspects of their memory might improve," said LaFerla, UCI neurobiology and behavior professor.

Scientists also found that the nicotinamide-treated animals had dramatically lower levels of the tau protein that leads to the Alzheimer's tangle lesion. The vitamin did not affect levels of the protein beta amyloid, which clumps in the brain to form plaques, the second type of Alzheimer's lesion.

Nicotinamide, they found, led to an increase in proteins that strengthen microtubules, the scaffolding within brain cells along which information travels. When this scaffolding breaks down, the brain cells can die. Neuronal death leads to dementia experienced by Alzheimer's patients.

"Microtubules are like highways inside cells. What we're doing with nicotinamide is making a wider, more stable highway," Green said. "In Alzheimer's disease, this highway breaks down. We are preventing that from happening."

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LaFerla and Green are affiliated with the Institute for Brain Aging and Dementia, which is conducting the clinical trial with funding from the Alzheimer's Association.

The institute seeks volunteers who have been diagnosed with Alzheimer's, are 50 or older, and have a friend or relative who can accompany them to clinic visits and answer questions. Study participants will take the vitamin supplement or a placebo twice daily for 24 weeks, with seven visits to the UCI clinic.

For more information on the clinical trial, contact Beatriz Yanez at 949-824-5733.

UCI scientists Joan Steffan, Hilda Martinez-Coria, Xuemin Sun, Steven Schreiber and Leslie Thompson also worked on the study, which was supported in part by the Alzheimer's Drug Discovery Foundation and the National Institutes of Health.



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