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Cancer drug may improve memory in Alzheimer's patients

NEW YORK - A drug now used to treat cancer may also be able to restore memory deficits in patients with Alzheimer's disease, according to a new study conducted by scientists at Columbia University Medical Center, which appeared in the September issue of *The Journal of Alzheimer's Disease*. Volume 18:1.

The loss of short, day-to-day memories is often the first sign of Alzheimer's - a disease that is expected, by the year 2050, to afflict 120 million people worldwide.

"People often joke that they must have Alzheimer's because they can't remember where they put their keys, but for a person with the disease, this type of short-term memory loss is extremely debilitating," says the study's lead author, Ottavio Arancio, Ph.D., associate professor of pathology and cell biology in the Taub Institute for Research on Alzheimer's Disease and the Aging Brain at Columbia University Medical Center.

Dr. Arancio says that the cancer drug targets a previously unknown defect in the brains of mice with Alzheimer's.

The reason why the drug improves memory lies in the way the brain records new memories. To create new memories, the neurons in the brain must manufacture new proteins. The first step is to open up and read the DNA, which contains instructions for making the proteins.

To read the DNA, the neuron attaches a chemical reactive group to the spool around which DNA is tightly wound. "These groups, called acetyls, unwind the DNA to make it more accessible," says co-author Yitshak Francis, Ph.D., a postdoctoral research scientist at Columbia. "It's like unwinding knitting wool from its spool."

This unwrapping step, the researchers found, is impaired in mice with a form of Alzheimer's disease. The mice with Alzheimer's attached about half as many acetyls to DNA as normal mice and had poorer memory.

The researchers then discovered that they could improve memory in the Alzheimer's-afflicted mice with a cancer drug from a family of compounds, called HDAC inhibitors, which increase the DNA's spool acetylation and gene transcription. The drug improved memory performance to the level found in normal mice.

"Because this type of drug has already been approved for some cancer patients," says co-author Mauro Fà, Ph.D., associate research scientist in Columbia's Taub Institute, "we hope that clinical trials for Alzheimer's disease can start in about three to four years."

"For making memories, you need transcription and protein synthesis at the cellular level. If you don't have that, you don't have memory," said Dr. Francis.

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Authors of *The Journal of Alzheimer's Disease* study include: Yitshak I Francis, Mauro Fà, Haider Ashraf, Hong Zhang, Agnieszka Staniszewski, David S. Latchman and Ottavio Arancio.

The Journal of Alzheimer's Disease (<http://www.j-alz.com>) is an international multidisciplinary journal to facilitate progress in understanding the etiology, pathogenesis, epidemiology, genetics, behavior, treatment and psychology of Alzheimer's disease. The journal publishes research reports, reviews, short communications, book reviews, and letters-to-the-editor. Groundbreaking research that has appeared in the journal includes novel therapeutic targets, mechanisms of disease and clinical trial outcomes. *The Journal of Alzheimer's Disease* has an Impact Factor of 5.101 according to Thomson Reuters' 2008 Journal Citation Reports. The Journal is published by IOS Press (<http://www.iospress.nl>).

The Taub Institute for Research on Alzheimer's Disease and the Aging Brain at Columbia University Medical Center is a multidisciplinary group that has forged links between researchers

and clinicians to uncover the causes of Alzheimer's, Parkinson's and other age-related brain diseases and discover ways to prevent and cure these diseases. It has partnered with the Gertrude H. Sergievsky Center at Columbia University Medical Center which was established by an endowment in 1977 to focus on diseases of the nervous system. The Center integrates traditional epidemiology with genetic analysis and clinical investigation to explore all phases of diseases of the nervous system. For more information about these centers visit:

<http://www.cumc.columbia.edu/dept/taub/> <http://www.cumc.columbia.edu/dept/sergievsky/>

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