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Feinberg faculty lead research on Alzheimer's Disease

Three faculty among those leading investigations on causes, treatments

Three faculty members are among Feinberg School of Medicine researchers conducting leading research on the causes and treatment of Alzheimer's disease.

They are Robert J. Vassar, who leads a team working to determine the process of AD in the brain, and D. Martin Watterson and Linda J. Van Eldik, who developed a revolutionary compound they hope will slow the deterioration of brain cells by targeting the inflammation that typically occurs with the onset of Alzheimer's.

There is no treatment yet that addresses the underlying mechanisms of Alzheimer's disease, the leading cause of dementia in the elderly. Current medication offers symptomatic relief to more than 4 million Alzheimer's patients in the United States, but does not treat the underlying progression of the disease. Ultimately nerve cells continue to die, resulting in the agitation, loss of memory and disorientation that is associated with Alzheimer's patients.

Vassar, professor of cell and molecular biology, and researchers in his laboratory are working to determine the process of AD in the brain by identifying the important aspects at the cellular and molecular level that lead to neurodegeneration. Their intent is to be able to design drugs or other interventions that block a particular molecular process.

Vassar identified the enzyme BACE1 in 1999 and determined that it is critically necessary to the production of a peptide, beta-amyloid, that makes up the amyloid plaques, one of the characteristic Alzheimer's brain lesions. He believes that if the production of beta-amyloid could be blocked, Alzheimer's could be slowed down, stopped, or even reversed. He is looking at how BACE1 is regulated in the brain and what role it plays in the disease. His group is also making different genetically engineered mouse models of Alzheimer's — called transgenic and knockout mice — to be used in further study of the Alzheimer's disease process.

Vassar's research is funded by grants from the National Institutes of Health, the National Institute of Aging, the Illinois Department of Public Health, and the Alzheimer's Disease Association, as well as Searle funding through Northwestern.

Watterson, professor of molecular pharmacology and biological chemistry, and Van Eldik, professor of cell and molecular biology, developed a revolutionary compound they hope will slow the deterioration of brain cells by targeting the inflammation that typically occurs with the onset of Alzheimer's.

The co-directors of the Center for Drug Discovery and Chemical Biology, they targeted the brain's inflammatory mechanisms, designing a compound that would limit brain inflammation and thus slow down the progression of the disease. The chief findings of interest with the compound concern the selective nature of the drug and that it appears to specifically block activation of glial cells, considered markers of inflammation in the brain.

Northwestern has licensed this compound, called Minozac, to NMX, a biotechnology company that has

done the FDA-required preclinical toxicology and produced the drug under FDA regulations for planned human trials, which will begin in 2007. The toxicology results so far show that Minozac has no major side effects that might limit its therapeutic use in patients. Recently, Watterson's laboratory received funding from the National Institutes of Health to continue development of drugs in this new class of therapeutics.

> Adapted from an article in the Office for Research Annual Report 2006



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