

Media Contact: Rachel Skei Donihoo
214-648-3404
rachel.donihoo@utsouthwestern.edu

UT Southwestern's public forum on Alzheimer's disease will focus on brain-cell preservation efforts

DALLAS – March 9, 2011 – In their search for a drug that could keep brain cells from dying, a team of UT Southwestern Medical Center researchers faced more than just a needle-in-a-haystack search. They first had to assemble the haystack.

But the resulting three-year investigational journey has led to a compound that preserves the viability of newly created brain cells and boosts learning and memory in an animal study.

Dr. Steven McKnight, chairman of biochemistry, and Dr. Andrew Pieper, assistant professor of psychiatry and biochemistry, will describe their work in a March 23 talk at a Spring Public Forum presented by the Friends of the Alzheimer's Disease Center.

The forum, titled "Early-Stage Efforts to Discover Drugs That Preserve Brain Cells," will be held at 7 p.m. in the Simmons/Hamon Biomedical Research Buildings on the North Campus, 6000 Harry Hines Blvd. Complimentary valet parking is available.

The event is free to the public, but because seating is limited, attendance should be confirmed by calling the Office of Development at 214-648-2344.

The research team led by Drs. McKnight and Pieper screened 1,000 individual molecules to see which ones might enhance the production of neurons in the adult mouse hippocampus, a region of the brain critical to learning and memory. The scientists found that one of the compounds, called P7C3, achieved this by protecting newborn neurons from dying.

"We don't know yet whether P7C3 can block the death of mature nerve cells, which is what occurs in humans suffering from Alzheimer's disease and other neurodegenerative diseases," Dr. McKnight said.

A test using elderly rats, which characteristically show a decline in the birth and formation of hippocampal neurons, has shown that P7C3 increased both the birth and survival of new neurons, as well as the memory and learning capability of the aged rodents.

The researchers currently are studying the mechanism by which P7C3 protects cells from

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dying and whether it might have any protective effect in other models of neurodegenerative disease.

Because the study involved live animals rather than cultured cells, it took much longer to test each compound, limiting the number that the researchers could test. In starting the study, they went to UT Southwestern's small-molecule library, a collection of more than 200,000 substances usually used in high-speed robotic tests. From that collection, they selected 1,000 chemically diverse compounds.

P7C3, the 73rd compound tested, was the first to show a marked neuroprotective effect. As the study continued, the researchers found seven more candidates but none with as strong an effect.

The researchers, in collaboration with Dr. Joseph Ready, associate professor of biochemistry and a synthetic chemist, are continuing to work on P7C3, modifying it in an attempt to improve its actions. They also plan to test the substance in animal models of other neurodegenerative diseases, including Huntington's disease and amyotrophic lateral sclerosis (Lou Gehrig's disease).

The Friends of the Alzheimer's Disease Center was established in 1996 to provide financial support for Alzheimer's research at UT Southwestern. All the group's contributions go directly to support Alzheimer's research at the medical center.

Since its founding, the group has raised more than \$1 million for grants to researchers. For information on joining the group, call the development office.

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