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IWU Receives Grant from Central Illinois Neuroscience Foundation To Support Pioneering Research in New Stroke Treatment

BLOOMINGTON, Ill.--Illinois Wesleyan University has purchased a Laser Doppler blood flow meter under a \$12,300 grant from the Central Illinois Neuroscience Foundation (CINF) for pioneering research into new ways to treat stroke, the nation's No. 3 killer.

The instrument will help IWU researchers develop an animal model of a type of stroke characterized by blood clots that block arteries, cutting off blood flow and oxygen to the brain. Blood-clot-related strokes account for 85 percent of all strokes.

Research aimed at better treatment of strokes--now dubbed "brain attacks" by physicians and other researchers--is moving along two tracks: development of drugs designed to break up blood clots and pharmaceuticals designed to shield the brain from the damaging effects of strokes.

IWU Stroke Research

The blood flow meter will be used by IWU faculty, students, and other researchers associated with CINF in sophisticated experiments designed to trigger strokes in specific types of laboratory rats to test the safety and effectiveness of new drugs designed to protect the brain from the harmful affects of strokes.

Wayne Doman, IWU associate professor of psychology, who received the CINF grant, said: "I'm very pleased that the Central Illinois Neuroscience Foundation has awarded IWU a grant that permitted us to purchase the Laser Doppler blood flow meter, an instrument that will play an important role in our studies of a neuroprotective drug. Once we conclude whether the drug has potential to protect the brain from the affects of strokes, as a result of our animal studies, then the next step--after proper medical reviews--will be to test the drug on patients."

Ann Stroink, a Bloomington neurosurgeon and a CINF founder, said: "Studies done in the last 10 years have made us more optimistic in our attitude toward treating strokes. Strokes are no longer met with complacency. Consequently, the stroke research using the Laser Doppler instrument is a good investment."

Stroink, a 1976 IWU biology graduate added: "Researchers are now seeing possible relationships between strokes and Alzheimer's Disease in the sense that oxygen deprivation in deep portions of the brain may trigger Alzheimer's. This needs more full investigation."

Doman founded IWU's Alzheimer's research project in 1992. Since then, the project has given research opportunities to about 30 psychology, chemistry, biology, and other IWU

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undergraduates. Over the last five years, IWU faculty-student researchers have presented papers about their Alzheimer's research at about 10 international scientific conferences, including annual meetings of the Society for Neuroscience.

Research Game Plan

Doman's research using the Laser Doppler instrument will assess drugs as potential candidates for clinical trials. These drugs are designed to protect the brain after a stroke by stopping brain cells from dying.

Doman will gauge the drugs' effectiveness by inducing strokes in a key artery in older laboratory rats.

"Previous trials showed the potential of neuroprotective drugs," Doman explained, "but there were nasty side effects. One reason for those side effects was that only healthy, young, male rats were used. We're going to use aged rats in our experiments--rats who are two-to-three years old--which is equivalent to humans, age 65-70, so they won't be in perfect health due to their age."

A target of Doman's research is the brain's penumbra, the area believed responsible for stroke recovery.

"If we could get that area salvaged by giving neuroprotective agents," Doman explained, "then we might have a significant impact on how people recover from strokes."

When a stroke takes place, the region of the brain under attack loses blood supply, triggering a lack of oxygen and glucose (sugar), and setting off a cascade of events--none of them good, according to Doman.

A neurotransmitter, glutamate, reaches toxic concentrations in the brain by stimulating a receptor called NMDA.

"So, one strategy," Doman explained, "is to protect the brain against this cascade by trying to block the stimulation of the receptor. Several years ago, a couple of neuroprotective agents were in clinical trials and they blocked NMDA. However, their side effects caused hallucinations and enthusiasm for these types of drugs waned.

"But, recently," Doman added, "another way has been discovered to block the activity of receptors by using another type of drug."

Surgical Training

Doman received training in the surgical technique required for his experiments at Detroit's Henry Ford Hospital in March and expects to return there for additional instruction. He also has trained with Kundan Gupta, an interventional neuroradiologist at Bloomington's BroMenn Regional

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Medical Center (BMRC) and a member of the hospital's stroke team, sharpening his skills in delicate catheter manipulations. Catheters are slender, flexible tubes typically inserted into veins and other bodily channels.

During a teaching leave in the fall, Doman plans on teaching the required surgical techniques to an IWU student, who will work closely with him. They will be joined by an interventional neuroradiologist from Canada's leading research hospital and a Russian doctor who will be a CINF research fellow. The team should be assembled by July 1.

The IWU, CINF, and BroMenn research relationship is unique, according to Doman.

"Usually the type of research we're doing," he said, "takes place at huge institutions with medical schools--not at an undergraduate university."

Student Involvement

Four IWU students have expressed interest in working with Doman on his stroke-related experiments.

However, in February about 20 IWU students participated in a wide-ranging telephone survey of about 1,300 randomly selected Bloomington-Normal residents, probing the warning signs and risk factors associated with strokes.

While 91 percent of the people sampled said they knew what a stroke was, 43 percent of those people did not know a single warning sign of strokes, and only 19 percent could name at least one warning sign.

Looking at the survey results, Stroink said: "The student survey revealed a problem. We need to educate the community on issues related to strokes."

Survey results, according to Doman, probably will be presented next February in Orlando at the 23rd International Joint Conference on Stroke and Cerebral Circulation, sponsored by the American Heart Association and the National Stroke Association.

"This conference is for doctors," Doman said, "and it will be the first time in the history of the conference that undergraduates and non-physicians will be making presentations."

Follow-up surveys are planned to gauge the effectiveness of public education programs about strokes.

Successful Stroke Treatment

Successful treatment of strokes depends on two factors, according to Stroink: rapid diagnosis and immediate treatment. Consequently, treatment is impaired if the warning signs of stroke are not quickly recognized.

There is only a six hour window of time after stroke symptoms begin to get a patient

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treatment and avoid devastating, permanent brain damage, Stroink said.

"Among the warning signs of stroke," she said, "are numbness, weakness, sudden onset of difficulty in speaking, double or blurred vision, dizziness or the sudden onset of a severe headache. When the warning signs occur, people should immediately call 911 and get to a hospital."

Stroink points out that there are three types of strokes. The most common are dry strokes, when blood supply to a portion of the brain is restricted by a blockage and brain cells can die in minutes or hours. Wet strokes, the second most common variety, occur when the brain hemorrhages from a ruptured blood vessel. The third type of stroke involves blood spilling along the surface of the brain, a condition related to an aneurysm.

Stroke is the third leading cause of death in the United States after heart disease and cancer. It is the leading cause of severe disability. Annually, there are about 1.5 million new cases of stroke in the United States and Europe. In the United States, there are about 600,000 new strokes every year, which kill about 200,000 and forever change the lives of the 400,000 survivors. About four million stroke survivors are alive. Strokes affect people of all ages, however, their incidence doubles with each decade over age 45.

PROACT Study

IWU researchers also are part of a landmark North American study--involving CINF, BRMC, and Abbott Laboratories--designed to test a clot-busting drug, prourokinase, which could form the basis of a revolutionary new treatment of strokes that attack the brain's middle cerebral artery.

The PROACT study, launched in January, 1996, involves 60 health care, academic and private institutions in the United States and Canada.

Abbott Laboratories, the pharmaceutical company, selected BroMenn and its seven-member stroke team as one of only three sites in Illinois to participate in the study. Doman is a stroke team member and serves as CINF's pre-clinical director of neuroscience research. Other BRMC stroke team members are: Stroink, Gupta, Herman Dick, M.D.; Curtis Hayden, M.D.; Keith Kattner, neurosurgeon; and Edward Pegg, neurologist. CINF played a key role in forming the stroke team.

"This is by far the most comprehensive and complex clinical trial ever undertaken in North America for stroke treatment," Doman said, referring to the PROACT study.

"If results of this trial are positive," Doman added, "it would represent a revolutionary new approach for the treatment of stroke."

The PROACT study and Doman's experiments with neuroprotective drugs require researchers

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to have the skill to deliver medication to the scene of a stroke deep within the brain.

"We now know that treatments using clot-dissolving drugs are effective," Stroink said, "but certain areas of the brain are not currently as responsive to the medicines. Because of that, we want to deliver medicine right to the specific target area in the brain.

"We feel there's a strong likelihood," Stroink added, "that if you can bring clot-dissolving agents to the clot, and break it up, we can improve the outcome of a stroke. Furthermore, the addition of neuroprotective agents to be delivered to the patient by an ambulance crew can allow for protection of vulnerable brain tissue prior to the arrival of the patient at the hospital. Time is absolutely critical."

Once the PROACT study is completed, an independent group will review its findings and Abbott will present the results to the U.S. Food and Drug Administration for final approval.

About IWU

IWU, founded in 1850, enrolls about 1,900 students in a College of Liberal Arts, and its Schools of Music, Theatre Arts, Art, and Nursing. A \$15 million athletics and recreation center opened in the fall of 1994; and a \$25 million science building opened in the fall of 1995. The \$4.6 million Center for Liberal Arts--a facility housing 60 faculty offices, six classrooms, and other facilities for social science, humanities, business and economics, and interdisciplinary studies' faculty--is slated to open next fall, as well as a \$6.5 million residence hall, accommodating about 118 students. The Carnegie Commission for the Advancement of Teaching ranks Illinois Wesleyan a "Baccalaureate I" institution, a classification that places it among the 161 highly selective National Liberal Arts Colleges.