The key is hidden in the brain's immune system.

It holds the secret that will unlock the mysteries behind some of the biggest medical challenges of this new century.

Diseases, such as Alzheimer's, Parkinson's, multiple sclerosis and AIDS, play havoc with the internal workings of the cerebrum. The common denominator of all these diseases can be found in the mechanism behind the brain's response to attack.

Putting the brakes on BRAIN DAMAGE

by Elizabeth Kumru

Inflammation.

It is inflammation that leads to the breakdown of the brain's communication system and the eventual death of neurons. It disables a person mentally and physically. It causes degeneration of the brain.

"Inflammation is a key to understanding how neurodegenerative disorders occur and how they may someday be effectively treated or even eliminated," said Howard Gendelman, M.D., Purtilo professor of pathology and microbiology and director of the Center for Neurovirology and Neurodegenerative Disorders (CNND).

"Several years ago, we theorized that the immune cells significantly responsible for Alzheimer's disease and AIDS-dementia can be used to regenerate the nervous system as well."

It was a revolutionary thought — one that evoked snickers at the time. Dr. Gendelman's colleagues snicker no more.

Today, a 40-year-old teacher is living proof that his theory is correct. Nearly three years ago, the woman was lost in a walking coma induced by AIDS-dementia and was near death.

Under Dr. Gendelman's care, she was given a combination of anti-inflammatory and HIV drugs that halted the disease process within weeks. This was accomplished by deactivating the brain's immune system. Now, she's fully functioning and back to teaching.

"This was the first time virus-induced neurodestructive events were reversed. The idea that significant damage to neurons could not be repaired was changed. It is now firmly established in the medical community that inflammation in the brain is a cause of neurodegeneration."

Dr. Gendelman and his team of CNND investigators opened the door to an entirely new path of exploration by linking inflammation as a common pathway for neuronal destruction in Alzheimer's and AIDS-dementia. This revelation secured their place among the world's leaders in neuroscience research.

UNMC came under criticism in late November from anti-abortion groups because part of CNND's research uses tissue from elective abortions. Although opponents claim that using the tissue is morally unethical, they have never proven that the research affects the woman's decision.

The University of Nebraska Board of Regents, administration, faculty and countless citizens across the state have rallied in support of the research.

"When you stand back and look at the research objectively, it quickly becomes clear that our work is about saving lives." Dr. Gendelman said. "The research and abortion are not linked. There are no products being developed, no effect

on the procedure, no influence on a woman's decision, no exchange of money, and no involvement with the procedure. If any of these were true, we all know that the research would not continue," Dr. Gendelman said.

"Our research is about saving lives here in Nebraska and throughout the world. The continued development and growth of this important research will positively affect our medical center and state for generations to come," he said.

Already, millions of people have been saved from the crippling and often deadly polio virus because a vaccine was discovered in 1954. Human fetal cells were instrumental in the development of the polio vaccine.

Animals do not get polio, Alzheimer's disease or AIDS. They are unique human disorders. Although some animal models are used for testing, only human cells provide a human response.

"Human fetal cells are critical.

They provide a unique environment to test disease mechanisms and potential cures. Monkey and rat brains don't function as humans do," Dr. Gendelman said.

There is no substitute, said Eugene Major, Ph.D., chief of the Laboratory of Molecular Medicine and Neuroscience of the National Institute of Neurologic Disorders and Stroke, a division of the National Institutes of Health (NIH).

"We could potentially use brain tissue from adults, as opposed to fetal tissue, but adult tissue does not have the ability to remain in culture for a long period of time as is needed to ask experimental questions. That is a critical point. It doesn't have the ability to remain viable," Dr. Major said.

"Inflammation is a key to understanding how neurodegenerative disorders occur and how they may be effectively treated or even eliminated."

"The research under way in Nebraska is ground-breaking work. These are complicated, multi-factorial diseases that have many different levels of biologic and pathogenic processes."

The basis of research at the CNND is to understand the immune function of the cells and how to switch the process from a degenerative to a regenerative process within the brain, Dr. Gendelman explained.

Dr. Howard Gendelman

Human fetal cells are used for only a small — 5 to 10 percent — but crucial part of the research at the CNND. Five of the center's 32 scientists are involved in research projects using the tissue. Consent for elective abortion is given to the physician before consent is given for use of the cadaveric tissue for medical research. The cells are received from elective abortions carried out at 10- to 19-weeks at a clinic not connected to UNMC.

Dr. Gendelman's research has been continuously funded by federal grants, including the NIH, for nearly 20 years. Fetal cell research at the CNND is supported by NIH grants. The NIH, which funds 288 research projects using fetal cells at more than 45 research institutions in the country. Although federal regulations do not require review of fetal cell research that does not involve patients, CNND scientists from the onset requested a review, which was carried out by the executive committee of UNMC's Institutional Review Board (IRB). In addition, the research was reviewed and approved by UNMC's Biosafety Committee and the Institutional Animal Care and Use Committee. All three review groups include community members. Recently, UNMC Chancellor, Harold M. Maurer, M.D., announced that all research proposals involving fetal cell use will receive full IRB review.

UNMC is diligently exploring the use of living human adult neural cells and stem cells obtained from rapid brain autopsies performed within two hours of death. The stem cells will be used to grow specific brain cells — neurons, microglia and astrocytes — that are special to this research, Dr. Gendelman said.

In addition, sources of neural cells are being developed from ectopic pregnancies and miscarriages.

The general theory of CNND scientists is that the immune cells in people with dementia secrete above normal toxic substances, which then damage neurons, the brain's thinking cells, and also microglia and astrocytes, the brain's immune regulatory cells.

"The only way we can determine if this hypothesis is right is by using human neuron cultures. Once we confirm our theory, we can establish how neurons are injured and figure out ways to stop dementia," he said.

Additional information about fetal tissue research can be found at UNMC's website: www.unmc.edu. d