Searching for brain's defenses to ward off infections, prevent memory loss

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Researchers at the Case Western Reserve University School of Dental Medicine and School of Medicine will look for evidence within the brain for human beta defensin peptide function -- proteins important to the peripheral body's natural defense system against infection from the outside environment.

They will examine brain tissues to explore the possibility that the beta defensins contribute to degenerative brain diseases and in particular Alzheimer's disease (AD).

"Chronic inflammation within the aging human brain and in the brains of individuals suffering from a variety of neurodegenerative diseases, including Alzheimer's disease, is now recognized as a major contributor to neuronal cell death and subsequent decline in cognitive function," said Wesley M. Williams, a neurobiologist and researcher in the Department of Biological Science at the dental school.

Williams and Mark A. Smith, a professor from the Department of Pathology at the medical school, are co-investigators for the University Center on Aging and Health-funded pilot study, "Beta defensin antimicrobial peptides—compromised immunomodulators of inflammation within the aging and Alzheimer's brain." Sandy Richardson and Sandi Siedlak, both research assistants, are also engaged on the project.

Williams became interested in beta defensins through studies with

gingival epithelial cells in the mouth and his work on diabetes, a risk factor for AD.

Preliminary findings by the researchers suggest that beta defensins may be adversely affected by AD, thus contributing to chronic inflammation that can lead to neuronal cell death.

While the blood-brain barrier generally blocks harmful pathogens from reaching brain tissue, Williams said not all parts of the brain have this protection.

Those pathogens reaching the brain can produce an inflammatory response, which is known to have a role in brain cell death.

Beyond AD, neuronal cell death is a part of the degenerative process in Parkinson's disease, multiple sclerosis, and in normal aging and contributes to cognitive memory loss among combat veterans and accident victims who have suffered traumatic brain injuries.

The big question is what role, if any, do beta defensins play in the development of chronic inflammatory response in the brain, Williams said.

"We don't know what we will find. This study is thinking outside the box for something that has not been studied previously," said Williams.

The researchers received a $20,000 launch grant to pilot a study to gather evidence that they hope leads to further research projects. They will investigate if beta defensins influence the immune response by the brains resident immune cells, the astrocytes and microglia. This project focuses on the most commonly found defensins, HBD1 and HBD2, both prevalent in the mouth and skin, and whether they are found in two types of brain cells.

Beta defensins are found in the skin and in lung, kidney, intestines, mouth, stomach, and vagina. Whenever a wound occurs in these areas, the beta defensins kick in to fight off infection.

Some 20-beta defensins are known to exist in humans, other mammals and plants.

The researchers will work with brain tissue generously donated by individuals with and without AD.

This study is among a number of funded projects by the University Center on Aging and Health supported by the President's Strategic Initiatives Fund and McGregor Foundation, located in the Frances Payne Bolton School of Nursing and under the direction of Diana Morris, that encourage interdisciplinary research projects among campus researchers.

Provided by Case Western Reserve University