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STUDY IN MICE IDENTIFIES MOLECULAR TARGET FOR TREATMENT OF WEST NILE ENCEPHALITIS

Critical mechanism enables blood-borne immune cells to sense West Nile virus and to neutralize and clear infection in the brain

LOS ANGELES (Feb. 5, 2009) – In animal studies, researchers at Cedars-Sinai Medical Center and Yale University have identified molecular interactions that govern the immune system's ability to defend the brain against West Nile virus, offering the possibility that drug therapies could be developed to improve success in treating West Nile and other viral forms of encephalitis, a brain inflammation illness that strikes healthy adults and the elderly and immunocompromised.

In a series of laboratory experiments and studies in mice, the research team found that a specific molecule and "signaling pathway" are critical in detecting West Nile virus and recruiting specialized immune cells that home to and clear infected cells. In mice genetically engineered to lack this molecular pathway, immune cells were detected at a distance but they did not home to brain cells infected by the virus, according to an article published online Feb. 5 in the Cell Press journal *Immunity*.

The key molecule in this process is Toll-like receptor 7, part of the innate immune system that recognizes pathogens entering the body and activates immune cell responses. Effective signaling is dependent on interleukin 23, a protein that stimulates an inflammatory response against infection. In West Nile encephalitis, according to these studies, Toll-like receptor 7 enables macrophages – immune system cells circulating in the blood – to sense the brain-penetrating virus. These macrophages then respond to interleukin 23 produced in the brain. This brain signal in turn promotes their infiltration and homing from the blood into the brain, where they neutralize and clear the virus.

Transmitted to humans by mosquitoes, West Nile virus is the most common cause of epidemic viral encephalitis in North America and has become a worldwide public health concern. While most healthy people who contract the virus have few if any symptoms, an infection can result in life-threatening brain disease – particularly in the elderly and those with compromised immune systems.

"There is no approved therapy for West Nile encephalitis in humans, in part because the mechanisms of the immune response to the virus are not completely understood. Our results suggest that drug therapy aimed at promoting this signaling pathway may enhance the immune response and thereby promote clearance of this potentially deadly virus," said Terrence Town, Ph.D., one of the article's lead authors and

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a research scientist at Cedars-Sinai's Maxine Dunitz Neurosurgical Institute. Town is an associate professor in the Department of Neurosurgery and the Department of Biomedical Sciences at Cedars-Sinai Medical Center. He holds the Ben Winters Endowed Chair in Regenerative Medicine at Cedars-Sinai.

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