Researchers uncover West Nile's targets

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Screening the entire human genome, a team headed by Yale University scientists have identified several hundred genes that impact West Nile virus infection. The findings reported Wednesday online in the journal *Nature* may give scientists valuable new clues about ways to intervene in a host of deadly viral infections.

"Diseases like West Nile affect millions of people," said Erol Fikrig, professor of medicine and microbial pathogenesis at Yale, an investigator with the Howard Hughes Medical Institute, and senior author of the paper. "We have found a dictionary of genes critical to a viral infection. Using these techniques, this can be done with any virus."

West Nile is transmitted by mosquitoes and has become a significant health threat in many parts of the United States since being introduced into North America in 1999. Symptoms range from mild flu-like symptoms to potentially fatal inflammation of the brain and central nervous system. West Nile is part of the flavivirus family, which includes dengue, yellow fever and tick- borne encephalitis viruses, among others, and causes thousands of deaths annually.

West Nile virus consists of only 10 proteins so it must hijack dozens of cellular processes of the host in order to infect individuals and replicate. To find out exactly which of those processes were involved in an infection, the team from Yale and three other research instituitions used a technique called global RNA interference targeting strategy.

Using tiny snippets of small interfering RNA, scientists are now able to

disable individual genes and thereby assess their function. Testing the entire human genome, the team was able to identify 305 individual proteins that can alter viral infection. Many of those proteins appear crucial to the ability of the virus to infect people and reproduce. About 30 percent of the genes involved in West Nile infection also appear to play a role in Dengue fever, the researchers report.

Theoretically, if scientists can find a way to interfere in the virus' ability to use those proteins it might be possible to treat or prevent a variety of different infections. "It might be possible to find a 'pan flavivirus' target," Fikrig said.

Source: Yale University