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HEALTHY LIVING: YOUR THURSDAY GUIDE to MEDICINE and HEALTH CARE

Mice provide clues to 1918 killer flu

Scientists attempt to crack virus code

By M.A.J. McKenna/Staff

The quest to unravel the mystery of the 1918 influenza pandemic, which killed 675,000 Americans and an estimated 40 million people worldwide in less than a year, has taken a significant step.

Scientists who are reassembling the genetic sequence of the flu virus, recovered in tiny fragments from the preserved and frozen bodies of victims who died more than 80 years ago, report in a paper published today that they

have infected laboratory mice with another virus containing a segment of the 1918 strain.

The work, published in the Proceedings of the National Academy of Sciences by Peter Palese of Mount Sinai School of Medicine in New York and Jeffery K. Taubenberger of the Armed Forces Institute of Pathology in Washington, brings researchers closer to understanding the unique virulence of the 1918 outbreak, which swept the

globe in months, then vanished. It also proves that complete reassembly of the long-lost virus in potentially infectious form may someday be possible.

In their paper, Palese and Taubenberger report that they reassembled a gene that is believed to direct flu's counterattack once the immune system notices and responds to the virus. That gene was then inserted into a version

of flu commonly used for research, which was given to lab mice --- under very high levels of biological security ---

at the Southeast Poultry Research Laboratory, a U.S. Department of Agriculture facility in Athens.

The researchers expected the mice to die quickly; the lab version of the virus into which the gene was inserted has been engineered to be fatal to mice, which don't normally develop flu. But in fact the gene made the virus less

virulent. All of the mice infected with the usual lab virus died; none of those infected with the 1918-bearing virus did.

The failure of the mice to develop fatal flu, once the segment targeting their immune systems was removed to allow the addition of the 1918 segment, suggests that influenza's ability to overcome the body's defenses is specific

to different species, Taubenberger said.

Further research might be conducted in ferrets or pigs, species that are known to be vulnerable to the same influenza viruses as humans, he said.

Taubenberger heads a team of molecular pathologists who have been working since 1995 to sequence the 1918 virus, using tissue from autopsies done on two soldiers who died of the flu and from a frozen body found in a mass grave in Alaska.

So far, the group has recovered most of the genetic sequence for five of the virus's eight genes; today's paper is the third they have published on individual genes. (A parallel effort, which searched for the virus in graves in the Norwegian Arctic, has not yet reported detailed results.)

None of the analyses done so far has solved the central mystery of the 1918 epidemic: how the virus was able to kill so quickly, usually in days, and why it was most lethal in healthy young people who are usually in the least danger from flu. That knowledge is vital, not just to solve a longstanding medical mystery, but because health authorities fear that the world is overdue for the appearance of a similarly virulent strain. Understanding the 1918 epidemic, among the worst known to history, could provide the molecular equivalent of an early-warning system for detecting the next one.