SOUTHWESTERN NEWS

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UT SOUTHWESTERN RESEARCHERS UNCOVER KEY TO SURVIVAL ABILITY OF BACTERIUM THAT CAUSES LYME DISEASE

DALLAS – Feb. 23, 2004 – A specific outer-surface protein found in the bacterium that causes tick-borne Lyme disease is essential to survival of the bacterium in its natural life cycle and colonization in the insect, researchers at UT Southwestern Medical Center at Dallas have found.

A study published online today in *The Journal of Experimental Medicine* provides the first proof of a long-held theory that outer surface lipoprotein A (OspA) must be present for *Borrelia burgdorferi* (*Bb*) – the bacterium that causes Lyme disease – to colonize in ticks.

"This OspA molecule has been intensively studied for the last 20 years, but nobody really knew what it did," said Dr. Michael Norgard, chairman of microbiology at UT Southwestern and the paper's senior author. "Now we know that it's needed for the organism to colonize and replicate in the midgut of the tick. If the bacterium doesn't have this molecule, it can't sustain itself there."

Lyme disease, discovered in 1977, is the most prevalent tick-borne infection in the United States. The bacterium that causes the disease is transmitted to humans by the bite of infected deer ticks. In 2002 more than 23,000 cases of Lyme disease were reported to the Centers for Disease Control and Prevention, with 95 percent of the cases located in the northern and northeastern portions of the country. Symptoms include fever, malaise, fatigue, headache, muscle and joint aches, and a characteristic "bull's-eye" rash that surrounds the site of infection.

Dr. Xiaofeng Yang, assistant professor of microbiology at UT Southwestern and lead author of the journal article, created a mutant of an infectious human strain of the *Bb* bacterium by inactivating, or "knocking out," a DNA fragment encoding OspA. He then injected the mutant strain into ticks and mice and found that, while it was not required for infection of mice, it was crucial for colonization of the ticks.

After observing the difference between the bacterium containing OspA and the mutant,

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Dr. Yang introduced a wild-type *OspA* gene back into the mutant strain, and colonization of the bacterium was restored.

The first agent of Lyme disease was discovered in ticks 23 years ago, but the molecular basis of how the bacterium thrives in nature through a complex life cycle involving ticks and mammals has not been understood. This research is an important step toward unraveling that mystery, Dr. Norgard said.

"The medical implications are not yet clear, but it adds an important piece to the puzzle," said Dr. Norgard, who holds the B.B. Owen Distinguished Chair in Molecular Research. "One of the real technical advances here is in genetics, because so many other investigators have tried to inactivate this gene unsuccessfully."

Dr. Thomas Templeton of the Department of Microbiology and Immunology at Weill Medical College of Cornell University, commented on the significance of the findings in an editorial that will be published with the paper in the March 1 print edition of the journal.

"These results greatly solidify a body of experimentation implicating OspA and OspB as midgut stage antigens ... but more importantly set the stage for dissection of OspA/OspB function," Dr. Templeton wrote.

Sophie Alani, a research assistant in microbiology at UT Southwestern, and researchers from Yale University School of Medicine, also collaborated on the study.

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