URI cancer researcher now aiming sights on Lyme disease

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As part of her research into breast cancer, University of Rhode Island scientist Roberta King has for years been studying the role of an enzyme in regulating estrogen activity.

King is specifically interested a type of enzyme, called sulfotransferases, which contribute to balancing and regulating numerous biologically active compounds such as estrogen and dopamine.

Now the associate professor of biomedical sciences in the College of Pharmacy is targeting dopamine sulfotransferase and its potential role in the transmission of the bacteria that causes Lyme disease. In a partnership with Thomas Mather, professor of entomology and director of the URI Center for Vector-Borne Diseases, King and her research team are looking at how tick dopamine sulfotransferase affects tick salivation and ultimately the feeding process that leads to Lyme disease and other tick-borne diseases.

“In the lab, we have shown that the tick sulfotransferase controls dopamine activity. Because others have shown that dopamine controls tick salivation, we expect that manipulating the sulfotransferase may turn off salivation, which in turn would prevent ticks from feeding,” King said. “If we can prevent ticks from feeding, then we can stop them from transmitting diseases.”

King said the research findings of her team will be printed in an upcoming edition of the American Chemical Society journal, *ACS*

Chemical Biology.

King said she and Mather have been working together since 2006 when he approached her about targeting molecular pathways and mechanisms that lead to Lyme disease and other illnesses caused by ticks. Mather has been researching vaccines against Lyme disease for more than a decade.

“Tom’s team, which has included Sivakamasundari Pichu, a former post-doctoral fellow, and Dr. Jose Ribeiro from the National Institutes of Health in Rockville, Md., identified tick genes that looked like sulfotransferase and that the gene expression level changed from before a tick fed to after a tick fed,” King said. “He keyed in on that action because it should be important biologically. Organisms don’t waste energy changing things unless they benefit from the change. We wanted to discover the purpose of the gene and to see if the protein it produced could be targeted for a vaccine or drug.”

“As the research progressed, I was convinced that the sulfotransferase was controlling something important in the tick, just as estrogen sulfotransferase controls something important in breast cancer development. After three years of research, we’ve got a good understanding of what the enzyme does for ticks and why the gene levels change before and after feeding.”

She said deer ticks need to blood feed for longer than 24 hours to transmit disease.

“We don’t have to stop the initial bite, as much as we need to shorten the feeding process,” King said. “With these long-feeding ticks (they typically feed for 3 or more days), if we shorten the attachment time by interrupting salivation, then we may have an effective way to stop transmission of Lyme disease. We found that tick sulfotransferase turns off dopamine, which should turn off salivation, and in turn prevent

feeding. The tick then would drop off the person and/or die."

Since King and her team have found that tick sulfotransferase is potentially a key to regulating salivation in lab tests with tick tissue, they are now proceeding with tests on live ticks in Mather's lab.

King said they were initially looking at two options for attacking Lyme disease--a vaccine, which would target the sulfotransferase in the tick saliva, or a drug, which would be absorbed into the tick. Mather's research focus is on anti-tick vaccine development, "but it also may be possible to target the tick sulfotransferase using a topical drug," King said.

King said a cream or lotion could be developed that people could apply to prevent ticks from feeding.

"This is a very exciting collaboration," she said. "And while I have done much of my work studying human metabolic changes in relation to cancer to prevent illness, through this collaboration I am looking at similar metabolic changes in ticks to also prevent human illness."

Provided by University of Rhode Island