Study shows how mosquitoes handle the heat of a hot blood meal

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Mosquito. Image: UCLA.

Mosquitoes make proteins to help them handle the stressful spike in body temperature that's prompted by their hot blood meals, a new study has found.

The mosquito's eating pattern is inherently risky: Taking a blood meal involves finding warm-blooded hosts, avoiding detection, penetrating tough skin and evading any host immune response, not to mention the slap of a human hand.

Until now, the stress of the hot blood meal itself has been overlooked, researchers say.

Scientists have determined in female mosquitoes that the insects protect

themselves from the stress of the change in body temperature during and after a meal by producing heat shock proteins. These proteins protect the integrity of other proteins and enzymes, in turn helping the mosquitoes digest the blood meal and maintain their ability to produce eggs.

Tests in two other types of mosquitoes and in bed bugs showed that these insects undergo a similar response after a blood meal.

"These heat shock proteins are really important in a lot of stress responses. Our own bodies make these proteins when we have a fever," said David Denlinger, professor of evolution, ecology and organismal biology at Ohio State University and senior author of the study. "It's one of those things that, in retrospect, seems obvious – that blood meals might cause a stress like that. But it hadn't been pursued before."

The research appears this week in the online early edition of the *Proceedings of the National Academy of Sciences*.

Denlinger and colleagues conducted experiments in the *Aedes aegypti* mosquito, which is a carrier of yellow fever.

The researchers placed sensors on female mosquitoes and observed that upon taking in a blood meal on a chicken, the insects' body temperatures increased from 22 to 32 degrees Celsius (71.6 to 89.6 Fahrenheit) within one minute – among the most rapid body temperature increases ever recorded in a cold-blooded animal. After the feeding, their body temperatures decreased to room temperature within a few minutes.

In response to that blood feeding, the mosquitoes' level of Hsp70 – heat shock protein 70 – increased nearly eightfold within one hour and remained at least twice as high as usual for 12 hours. The increase in these proteins was most pronounced in the midgut area.

Denlinger and colleagues tested potential triggers for this protein increase by injecting the mosquitoes with a saline solution at two temperatures: 37 degrees Celsius (98.6 degrees Fahrenheit) and room temperature. Only the warmer saline generated an increase in Hsp70, suggesting that the elevation in temperature associated with the meal, rather than the subsequent increase in body volume, is what causes the generation of those proteins.

Sometimes, mosquitoes feed on cold-blooded amphibians, which should not cause the same amount of stress. To test that theory, the researchers also gave mosquitoes a feeding opportunity on cooler blood, which failed to generate an increase in heat shock proteins.

And what happens if this protein is not produced? The researchers manipulated the mosquitoes' RNA to figure that out.

When the scientists knocked down expression of the gene that encodes the heat shock protein, the amount of Hsp70 production was reduced by 75 percent. Under those circumstances, mosquitoes still ate a normal blood meal. But blood protein levels remained elevated for a longer period of time, suggesting that digestion of those proteins was impaired. In addition, egg production decreased by 25 percent when the heat shock protein was suppressed.

Heat shock proteins help maintain the three-dimensional integrity of enzymes and proteins when temperatures rise suddenly, and can target damaged proteins and enzymes for elimination, Denlinger said. "We think that in this case, they are important to maintaining the integrity of some critical enzymes and proteins involved in digestive processes. When we knock out those proteins, it impairs digestion a bit and as a result the mosquitoes don't lay as many eggs," he said.

The researchers observed similar body temperature increases and

elevations in Hsp70 levels in three other insects: *Culex pipiens* and *Anopheles gambiae*, mosquitoes that are carriers of West Nile virus and malaria, respectively, and *Cimex lectularius*, the bed bug. Though new knowledge about the genetics of these insects, especially the mosquitoes, might someday inform attempts to kill them as a method of disease control, Denlinger said the primary contribution of this research is better understanding of how mosquitoes protect themselves in this novel way.

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