

Genetic code of the deadly tsetse fly unraveled

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Side view of a pregnant tsetse fly. Credit: Geoffrey M. Attardo

Mining the genome of the disease-transmitting tsetse fly, researchers have revealed the genetic adaptations that allow it to have such unique biology and transmit disease to both humans and animals.

The tsetse fly spreads the parasitic diseases human African trypanosomiasis, known as sleeping sickness, and Nagana that infect humans and animals respectively.

Throughout sub-Saharan Africa, 70 million people are currently at risk of deadly infection. Human African trypanosomiasis is on the World Health Organization's (WHO) list of neglected tropical diseases and since 2013 has become a target for eradication. Understanding the tsetse fly and interfering with its ability to transmit the disease is an essential arm of the campaign.

This disease-spreading fly has developed unique and unusual biological methods to source and infect its prey. Its advanced sensory system allows different tsetse fly species to track down potential hosts either through smell or by sight. This study lays out a list of parts responsible for the key processes and opens new doors to design prevention strategies to reduce the number of deaths and illness associated with human African trypanosomiasis and other diseases spread by the tsetse fly.

"Tsetse flies carry a potentially deadly disease and impose an enormous economic burden on countries that can least afford it by forcing farmers to rear less productive but more trypanosome-resistant cattle." says Dr Matthew Berriman, co-senior author from the Wellcome Trust Sanger Institute. "Our study will accelerate research aimed at exploiting the unusual biology of the tsetse fly. The more we understand, the better able we are to identify weaknesses, and use them to control the tsetse fly in regions where human African trypanosomiasis is endemic."

The team, composed of 146 scientists from 78 research institutes across 18 countries, analysed the genome of the tsetse fly and its 12,000 genes that control protein activity. The project, which has taken 10 years to complete, will provide the tsetse research community with a free-to-access resource that will accelerate the development of improved tsetse-control strategies in this neglected area of research.

The tsetse fly is related to the fruit fly – a favoured subject of biologists for more than 100 years – but its genome is twice as large. Within the

genome are genes responsible for its unusual biology. The reproductive biology of the tsetse fly is particularly unconventional: unlike most insects that lay eggs, it gives birth to live young that have developed to a large size by feeding on specialised glands in the mother.

Researchers found a set of visual and odour proteins that seem to drive the fly's key behavioural responses such as searching for hosts or for mates. They also uncovered the photoreceptor gene *rh5*, the missing link that explains the tsetse fly's attraction to blue/black colours. This behaviour has already been widely exploited for the development of traps to reduce the spread of disease.



The tsetse fly is quite unique in the insect world: it feeds exclusively on the blood of humans and animals, gives birth to live young and provides nutrition to its young by lactation. But in the invertebrate world, it's a killer: its bite can transfer the parasite that causes sleeping sickness. If left untreated, the disease is

fatal. Credit: Geoffrey M. Attardo, Research Scientist, Yale School of Public Health

"Though human African trypanosomiasis affects thousands of people in sub-Saharan Africa, the absence of a genome-wide map of tsetse biology was a major hindrance for identifying vulnerabilities, says Dr Serap Aksoy, co-senior author from the University of Yale. "This community of researchers across Africa, Europe, North America and Asia has created a valuable research tool for tackling the devastating spread of sleeping sickness."

Tsetse flies have an armament of salivary molecules that are essential for feeding on blood. The team found one family of genes, the *tsal* genes, that are particularly active in the salivary glands of the tsetse fly. This allows the tsetse fly to counteract the responses from the host to stop bloodfeeding. This finding and several others are explored in more detail in eight research papers that accompany the publication of the tsetse fly genome in *Science*.

"This information will be very useful to help develop new tools that could reduce or even eradicate tsetse flies," says Dr John Reeder, Director of the Special Programme for Research Training in Tropical Diseases, at WHO. "African sleeping sickness is understudied, and we were very pleased to help bring together so many research groups to work collaboratively with the one shared goal in sight – the elimination of this deadly disease."

More information: "Genome Sequence of the Tsetse Fly (*Glossina morsitans*): Vector of African Trypanosomiasis," *Science*, 2014.
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