A tsetse fly's bite can be fatal: New research takes a step toward ending that

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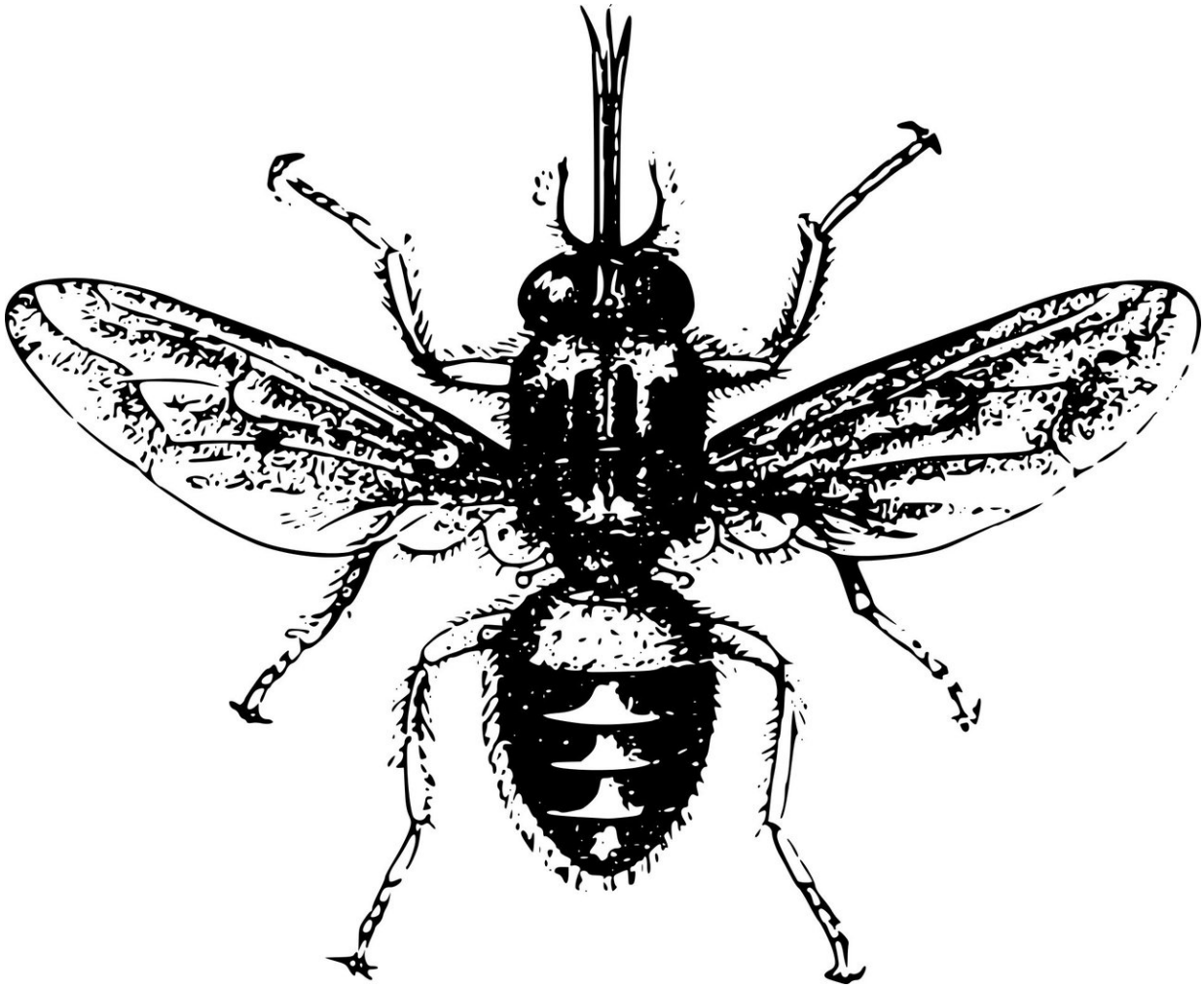

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When an infected tsetse fly bites humans or other mammals to feed on their blood, microscopic parasites (African trypanosomes) in the fly's saliva are transferred. The unfortunate recipient of the bite, once infected, often faces severe health consequences, even death.

Unfortunately, current public health approaches to control African sleeping sickness are limited. Diagnosis and treatment are especially difficult in remote areas of sub-Saharan Africa where the disease is pronounced. To complicate matters further, the trypanosomes have evolved so that they can evade their victim's immune response and sustain an infection.

But a promising disease control strategy being developed by researchers at the Yale School of Public Health might overcome these challenges. It involves blocking the transmission of parasites at the point of entry: the bite site.

Until recently, examining molecular and biochemical metacyclic cells (the infectious form of the parasite that is deposited at the bite site) has been hampered by the relatively small number of parasites present in saliva and by the presence of various non-infectious parasite developmental forms in the fly's salivary glands.

In a new study published in the journal *PNAS*, a team of researchers led by Yale School of Public Health Professor Serap Aksoy describe how they performed single-cell RNA sequencing of individual parasite cells (*T. brucei brucei*) from infected tsetse salivary glands. The cells were sorted into distinct developmental forms, the data from which provides unique and high-resolution insights into the molecular processes that give rise to infective metacyclic parasites transmitted at the host bite site. The study also identified a new family of surface proteins (known as Fam10), which are uniquely associated with the infectious metacyclic parasites. Vaccination of mice with one member of this family

(SGM1.7) significantly reduced parasitemia early during the infection process. This indicates that Fam10 proteins are promising vaccine candidates for blocking transmission of the parasite at the bite site.

This has never been done before and it marks an important step toward curbing the severe threat posed by the tsetse fly and its parasites.

"The ability of African trypanosomiases parasites to bypass the mammalian immune responses by changing their surface coat proteins has hampered development of vaccines. Our discovery has opened up a new chapter into these investigations," said Aksoy, a member of the Yale School of Public Health's Department of Epidemiology (Microbial Diseases).

Future studies will test the efficacy of multivalent protein vaccines that target the trypanosome Fam10 protein family to enhance transmission blocking. The Fam10 proteins are also found on the surface of other disease-causing African trypanosomes, indicating their potential use for combatting a plethora of devastating tsetse-transmitted infections.

According to the Centers for Disease Control and Prevention, West African trypanosomiasis, which is more widespread than a second form of the disease known as East African trypanosomiasis, results in 7,000 to10,000 new human cases each year, though many cases are not recognized or reported and the actual number of cases is likely far higher.

The disease's toll on domesticated animals, meanwhile, is rampant throughout sub-Saharan Africa.

More information: Aurélien Vigneron et al, Single-cell RNA sequencing of Trypanosoma brucei from tsetse salivary glands unveils metacyclogenesis and identifies potential transmission blocking antigens,

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