Tsetse transmitted trypanosomes: from the skin to a systemic infection

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The African trypanosome species responsible for human sleeping sickness (*Trypanosoma brucei rhodesiense* and *T. b. gambiense*) are transmitted by tsetse flies (*Glossina* sp.). Due to major control efforts, the annual number of reported human cases has declined to about 800, with a roadmap to reach elimination of the gambiense form by 2030. However, the major challenges that remain are the lack of protective vaccines and the occurrence of asymptomatic individuals that sustain the transmission cycle. Moreover, knowledge on the exact immunological basis for the highly efficient trypanosome transmission and asymptomatic infection remains scarce.

Following an infectious bite, inoculated metacyclic parasites rapidly adapt to the skin environment to establish a local infection and to continue a journey to systemic colonization. Making use of the tsetse fly vector, parasite reporter lines for fluorescent detection and *in vivo* bioluminescent imaging, immune-deficient mouse models and immunological profiling of parasite/saliva-exposed cells, we explored the role of innate immune responses in infection establishment and systemic colonization. This led to the discovery of an interesting role for the neutrophil in parasite control and dissemination from the skin microenvironment. Higher parasite loads were observed in the presence of neutrophils and neutrophil antiparasitic functions did not seem to hamper parasite expansion. Despite the armory of recruited anti-pathogen effector functions, parasites escape immune elimination and prominently distribute to tissues such as adipose, spleen and lungs. Parasites adapt to the specific tissue niches, creating specialized microenvironments that contribute to the infection.

The discovery of asymptomatic colonization of the skin and lungs as tissue reservoirs pinpoints future challenges for disease control, but also offers opportunities for the development of novel non-invasive diagnostic tests.

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