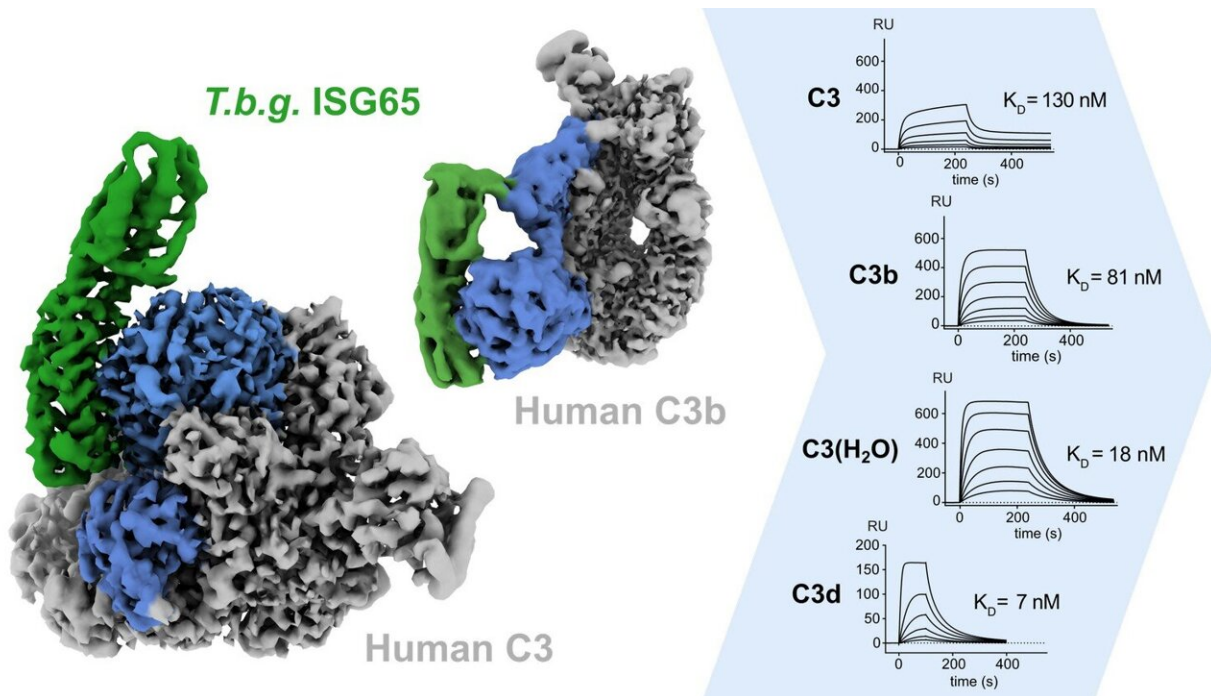


Cryo-EM structures show how Trypanosomes escape the human innate immune response

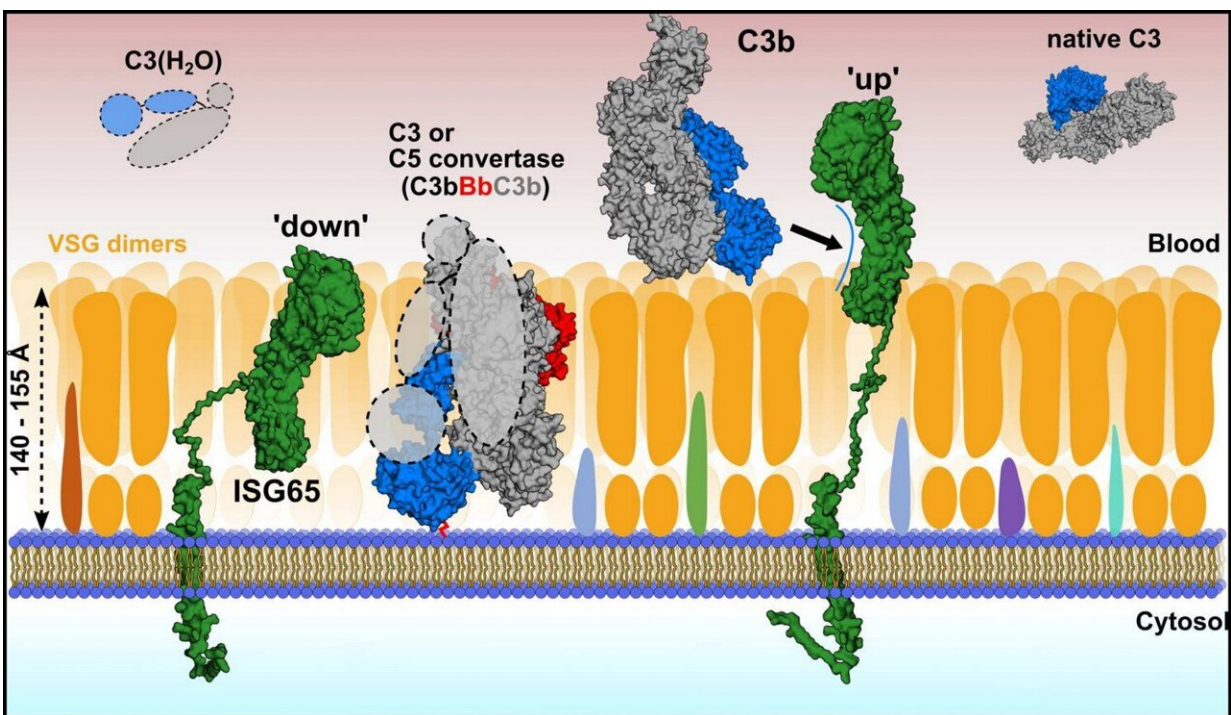
April 27 2023



Credit: Hagen Sülzen

Researchers from Sebastian Zoll's group at IOCB Prague determined the first cryo-EM structures of a surface receptor of the human-infective parasite *Trypanosoma brucei gambiense* in complex with human complement factor C3 in different conformations. This provides the structural basis to understand how the parasite escapes the immune response at an early stage of infection.

While most pathogens have found ways to avoid the deleterious effects of the immune system by escaping neutralizing [antibodies](#) and other effector proteins inside cells or less accessible tissues, African trypanosomes are hiding in [plain sight](#) and proliferate within the human blood stream. The [parasites](#) are exposed to the full pressure of both branches of the immune system and must employ a plethora of countermeasures to avoid clearance from the cardio-vascular system.



Credit: Hagen Sülzen

The mechanisms of this "molecular warfare" have been identified and, particularly with regard to the adaptive [immune response](#), described in detail. However, our understanding of innate immune defense mechanisms had remained incomplete until now.

Under the leadership of Sebastian Zoll, a team of researchers, with Hagen Sülzen as the first author of the study, and including Petr Pompach and Martin Zoltner from BIOCEV, employed an integrative structural biology approach and demonstrated that the interaction between ISG65 and C3, the central hub of the human complement system, is inhibitory and remarkably specific. Inhibiting only a single pathway within the complement system allows the [pathogens](#) to maintain a tailored and efficient immune defense.

The study was published in *Nature Communications* and shows the first 2 cryo-EM structures from IOCB Prague alongside one of the first cryo-EM—Alphafold hybrid models that was deposited to the PDBdev.

More information: Hagen Sülzen et al, Cryo-EM structures of *Trypanosoma brucei gambiense* ISG65 with human complement C3 and C3b and their roles in alternative pathway restriction, *Nature Communications* (2023). [DOI: 10.1038/s41467-023-37988-7](https://doi.org/10.1038/s41467-023-37988-7)

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