Trypanosomes and renal insufficiency

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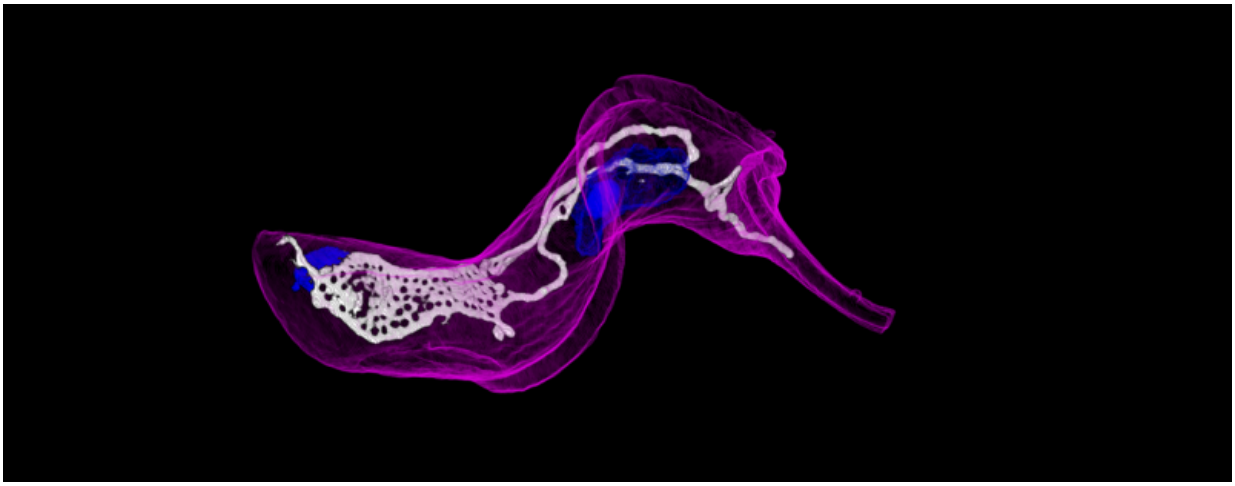

Trypa

The African trypanosome Trypanosoma brucei is a blood parasite capable of infecting many mammals. Humans are provided with natural immunity against infection through the activity of the protein apolipoprotein L1 (APOL1): captured via endocytosis, APOL1 forms pores in the lysosomal membrane, leading to the death of the trypanosome.

In a publication in the scientific journal *Nature Communications*, Prof Etienne Pays and his team from the ULB's Laboratory of Molecular Parasitology (Faculty of Science) sheds further light on the way human APOL1 kills the parasite. APOL1 does not just induce lysosomal

membrane permeabilization. Once it has accomplished this, it is transported to the mitochondrion where it again induces membrane permeabilization. The subsequent release of a mitochondrial endonuclease into the nucleus leads to trypanolysis.

However, this defence mechanism is not infallible: two trypanosomes, Trypanosoma brucei gambiense and Trypanosoma brucei rhodesiense manage to evade APOL1, and can infect humans with sleeping sickness. Two distinct mutations of APOL1 enable a number of West African populations to be immune to one of these trypanosomes. However, in 2010, Etienne Pays' laboratory proved that this evolutionary advantage went hand in hand with an increased risk of renal insufficiency.

While the mechanism allowing these mutations of APOL1 to trigger renal pathology remains completely unknown, our new observations on the biology of APOL1 allow us to imagine how the disease could occur in human kidney cells and to develop new research hypotheses.

More information: "Coupling of lysosomal and mitochondrial membrane permeabilization in trypanolysis by APOL1." *Nature Communications* 6, Article number: 8078 DOI: 10.1038/ncomms9078

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