

**Title: Mechanisms of life-cycle simplification in field-derived and laboratory-selected African trypanosomes**

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**Abstract:** African trypanosomes undergo development to transmissible stumpy forms in their mammalian host to favour uptake by their tsetse fly vector. However, *Trypanosoma brucei evansi* and *Trypanosoma brucei equiperdum* have simplified their lifecycle by escaping dependence on tsetse allowing an expanded geographical range, with direct transmission achieved via biting flies or through sexual transmission between animals. Concomitantly, stumpy formation is lost, and the isolates are described as monomorphic. Through genomic analysis of distinct field isolates we identified and functionally confirmed molecular changes that reduce stumpy formation. Further, by laboratory selection for reduced stumpy formation, we identified reversible steps in the initial development to monomorphism. This identifies a trajectory of events that simplify the trypanosome life cycle with impact on disease spread, geographical range and virulence.