Mitochondrial DNA dynamics in trypanosomatid parasites: a story of loss and gain

Authors and affiliations

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The flagellate protozoa of class Kinetoplastida are characterised by extraordinarily massive and complex mitochondrial DNA, the kinetoplast (kDNA). Members of genus Trypanosoma, important human and animal parasites, have kDNA comprised of two types of interlinked DNA molecules: a few dozen identical maxicircles, which are the equivalent of mitochondrial DNA in other eukaryotes, and thousands of highly heterogeneous minicircles, which encode short “guide RNAs” (gRNAs) that complement genetic information missing from maxicircle-encoded mRNAs. Hence, producing complete open reading frames (ORFs) from maxicircle encoded genes requires post-transcriptional RNA editing directed by gRNAs. Some genes, such as cytochrome oxidase subunit 3 and F1FO-ATP synthase subunit a, are edited extensively and involves dozens of different gRNAs and thus minicircle classes in restoring the ORFs.
Using next-generation sequencing and a bespoken bioinformatics pipeline for kDNA analysis, we demonstrate that different life-history, reproduction and transmission strategies, in closely related trypanosomatids have had profound impacts on their kDNA genome. Subspecies of Trypanosoma brucei that regularly cycle between their mammalian hosts and tsetse fly vectors have highly complex and redundant kDNA genomes, with hundreds of minicircle classes. Imperfect kDNA replication and segregation result in loss of minicircle classes, which is countered by sexual recombination in the tsetse fly vector given the bi-parental inheritance of kDNA. Consequently, kDNA complexity and redundancy (but not size) are streamlined in lab-adapted strains and chronic infections in the field that reproduce strictly clonally, as such strains contain only the minimal set of gRNA genes required to maintain viability. Extensive proliferation in the mammalian stage further reduces the gRNA repertoire, so that the strains have lost the ability to produce ORFs from genes required only for survival in tsetse vectors.