Ancestral aneuploidy and stable chromosomal duplication resulting in differential genome structure and gene expression control. The case of Trypanosomatid parasites

Reis-Cunha JL1[*#], Pimenta-Carvalho, SA[2*]; Almeida, LV[2]; Coqueiro-dos-Santos, A[2]; Marques CA[3]; Black, JA[3,4]; Damasceno, J[3]; McCulloch,R[3†]; Bartholomeu, DC[2†]; Jeffares,DC[1†];

1-York Biomedical Research Institute, Department of Biology, University of York, York, United Kingdom; 2-Instituto de Ciências Biológicas, Departamento de Parasitologia, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil; 3-The Wellcome Centre for Integrative Parasitology, School of Infection and Immunity, University of Glasgow, Glasgow, United Kingdom; 4-Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, Brazil

[#]Corresponding Author: João Luís Reis Cunha, Jeffares Group, Department of Biology, University of York, York, YO10 5DD, United Kingdom, Tel +(44) 07495617604, email: joao.cunha@york.ac.uk

*contributed equally

[†]contributed equally

Aneuploidy is widely observed in both unicellular and multicellular eukaryotes, usually associated with adaptation to stress conditions. Chromosomal duplication stability is a tradeoff between the fitness cost of having unbalanced gene copies and the potential fitness gained from increased dosage of specific advantageous genes. Trypanosomatids, a family of protozoans which include species that cause neglected tropical diseases, are a relevant group to study aneuploidies, as their life cycle has several stressors that could select for different patterns of chromosomal duplications and/or losses. Moreover, trypanosomatid biology is unusual, and one reason for aneuploidy-driven gene expression control could be linked to their near universal use of polycistronic transcription, limiting their capacity to alter the transcription of individual genes via promoters, and instead increasing their reliance on mechanisms of gene expansion and contraction, and post-transcriptional control mechanisms. However, it is still unclear when the capacity for aneuploidy arose during trypanosomatid evolution, and its relevance for the parasite long-term evolution. By evaluating the whole genome sequencing data from 866 isolates covering 7 trypanosomatid genera (*Crithidia*, *Endotrypanum*, *Leishmania*, *Leptomonas*, *Paratrypanosoma*, *Porcisia*, *Trypanosoma*), we have revealed three features of aneuploidy in these parasites. First, aneuploidy tolerance is an ancestral characteristic of trypanosomatids, suggesting it is central to their genome functionality. Second, *T. brucei* and related African trypanosomes have more recently evolved to largely dispense with aneuploidy, perhaps reflecting genome reorganisation. Third, we have identified the presence of an ancestral chromosomal duplication, named collectively as Trypanosomatid Ancestral Supernumerary Chromosome “TASC”, which has been maintained throughout Trypanosomatid evolution either as a greater than diploid chromosome or a syntenic duplication in two chromosomes in African trypanosomes. The number of chromosomes with extra copies in a given isolate is usually low, and only TASC was kept for long enough to greatly impact its nucleotide diversity, gene structure, expression control and evolution. TASC has most genes in the same coding strand, is expressed as a disomic chromosome even having four copies and have increased potential for functional variation, but purge highly deleterious mutations more efficiently than other chromosomes. The evidence of stringent control over gene expression in this chromosome suggests that these parasites have adapted to mitigate the fitness cost associated with this ancient chromosomal

duplication. What processes govern aneuploidy in these protozoans and the underlying molecular mechanisms that regulate TASC expression remains unknown. New studies investigating these modifications will be important to address these deficits in our understanding.