Editorial

New Insights into the Genomes of Kinetoplastid Parasites

The parasites belonging to the order Kinetoplastidae are an early eukaryotic branch of unicellular flagellated cells that have evolved from free-living monoxenous organisms to a parasitic lifestyle. The diseases caused by these parasites (Chagas, Leishmaniasis or African trypanosomiasis) have an outstanding clinical importance in terms of mortality and morbidity, being catalogued among the most important 16 Neglected Tropical Diseases (NTDs) by the WHO. This group of parasites represents a beautiful example of evolution in motion, where these cells have been adapted to a wide variety of different environments and stressful conditions in either the insect vector or the mammalian host. Indeed, stressful conditions are triggers for developmental regulation, which dictates drastic changes in parasite's morphology and biochemistry. Since the different life cycle stages of *Trypanosoma cruzi*, *Leishmania* spp. and *Trypanosoma brucei* could be easily cultured *in vitro* and their pathology reproduced *in vivo* in different animal models, it is possible to study the biology of these genomes in different situations providing many clues on how these parasites establish chronic infections in their hosts and how they tackle immune responses, enzymatic attacks or environmental differences in temperature or pH. The release in 2005 of the first kinetoplastid genome drafts unveiled and confirmed the uniqueness and apparent simplicity of these genomes, with the absence of canonical transcriptional promoters where clusters of dozens or hundreds of genes were arranged in polycistronic transcriptional units along with the presence of a kinetoplast, being an apparent mitochondrial DNA structure composed by maxi and minicircles of kinetoplastid DNA (kDNA). The study of these genomes is essential for providing insights into not only in fundamental biology and/or evolution but also new avenues for vaccine and/or drug discovery. The selected reviews in this special issue will address aspects such as coordination, structure, regulation or evolution of the kinetoplastid genomes, providing a big picture for the reader and paving the way for future research on this hot topic within kinetoplastid parasites.

In the first place, Marques & McCulloch will discuss about the highly divergent nuclear replication and the Origin of Replication Complex (ORC) machinery of *Leishmania* spp. and *T. brucei*, which needs to coordinate DNA replication in the context of highly replicative cells (~7-9h per cell cycle). One striking feature of genomes of *Leishmania* and *T. cruzi* is the sustained presence of chromosomal aneuploidies and Copy Number Variations (CNVs). This will be the focus of the review by Reis-Cunha *et al.*, which points out that big genome variations will create different gene dosages within populations of parasites thus increasing the fitness and possibilities for surviving to sudden stressful conditions.

In the absence of transcriptional regulation of protein-coding genes, epigenetic and post-transcriptional regulation is essential for the control of Kinetoplastid cells. Four reviews will show different angles on the regulation of this very unusual genome: i) Martínez-Calvillo and collaborators will show the latest research in epigenetic control of transcription by the three RNA polymerases in Kinetoplastid parasites, ii) Cestari & Stuart will discuss how *T. brucei* accounts for antigenic variation of its Variant Surface Glycoprotein through regulation of Telomeric expression and how inositol phosphate pathway has a novel role in the regulation of these antigenic variants iii) Dr. Esteban Erben will highlight the progress of using high-throughput approaches for identifying key players for the function of messenger ribonucleoprotein particles (mRNPs) which control the fate of mature mRNAs in the different forms of the Kinetoplastid parasites; iv) Francisco Macías-Huete and co-workers will focus on the biology of *T. cruzi* retrotransposons with special regard to L1Tc non-LTR retrotransposon and its truncated version NARTc, which co-exist in these parasites alluding to the possible impact of mobile elements in gene expression and genome regulation.

Comparative genomics has provided insights on how these parasites have adapted and diversified in a wide variety of different environments. In this regard, Butenko and collaborators will show a very interesting picture of the characteristics that have evolved from monoxenous to dixenous parasitic life styles by analyzing evolution of the proteins involved in proper lipophosphoglycan assembly, cell attachment and establishment in *Leptomonas pyrrhocoris*, *L. seymouri*, and *Leishmania* spp. Finally, Nicolás Tomassini reviews on the kDNA transference and inheritance in the context of sexual reproduction in *T. cruzi*.

Luis Miguel De Pablos

Guest Editor

Department of Parasitology
University of Granada
Granada, Spain
E-mail: lpablos@ugr.es