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Review

Diversity of mitochondrial genome structure in the phylum Apicomplexa

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ABSTRACT

Mitochondria are ubiquitous organelles in all eukaryotes that are essential for a range of cellular processes and cellular signaling. Nearly all mitochondria have their own DNA or mitochondrial (mt) genome, which varies considerably in size, structure and organization. The phylum Apicomplexa includes a variety of unicellular eukaryotes, some of which are parasites of clinical or economic importance. Recent studies have demonstrated that apicomplexan mt genomes, which include the smallest 6 kb genome of the malaria parasites, exhibit remarkably diverse structures. Apicomplexan parasites are interesting model organisms in order to understand the evolution of mt genomes. This review summarizes the structure of apicomplexan mt genomes and highlights the unique features and the evolution of the mt genome.

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1. Introduction

Mitochondria are organelles with essential roles in a number of cellular processes as well as in cellular signaling and they possess their own genome, termed the mitochondrial (mt) genome. Anderson et al. reported the complete sequence of the 16.5 kb human mt genome in 1981[1]. Since that time, complete mt-genome sequences from more than 2000 eukaryotic species have been determined and are available in public databases such as those of the National Center for Biotechnology Information (NCBI; http://www.ncbi.nlm.nih.gov/genome/). The NCBI database shows that mt genomes from diverse phylogenetic groups vary considerably in size, structure, and organization. With few exceptions, all vertebrate mt genomes are 15–20 kb circular molecules, and contain the same 37 genes: two genes for large subunit and small subunit rRNAs, 13 protein-coding genes and 22 genes for tRNAs [2] (Fig. 1). While vertebrate mitochondrial genome organization is

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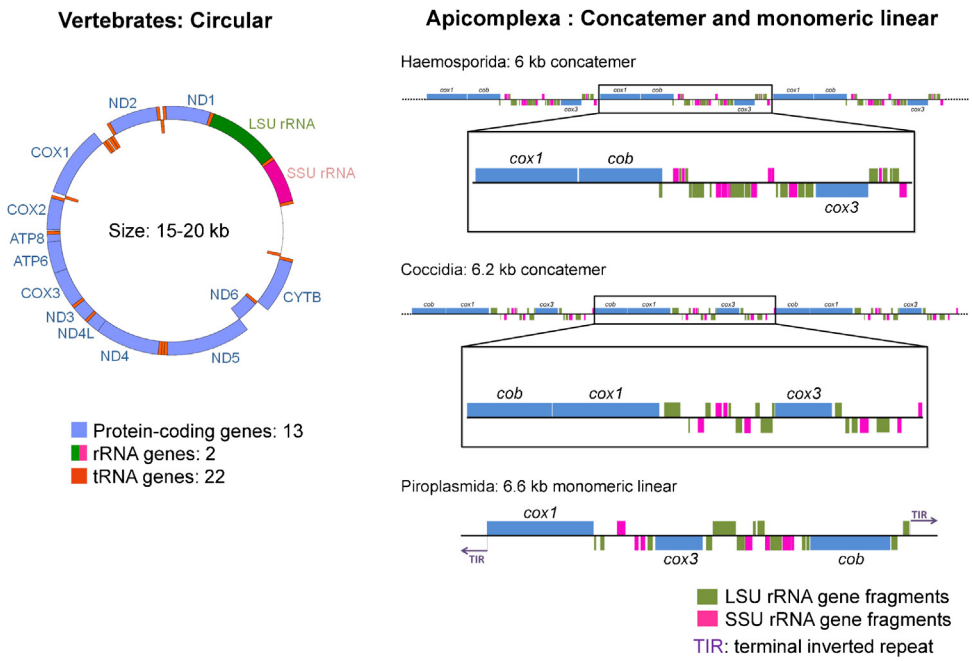

Fig. 1. Three types of mitochondrial genome structure. The circular form is represented by a vertebrate mt DNA. The concatemer and monomeric linear forms are represented by haemosporidian and coccidian mtDNAs, and piroplasm mt DNA in the phylum Apicomplexa, respectively.

highly conserved, the mitochondrial genomes of protists are highly diverse, as might be expected given the wide evolutionary distance spanned by the various protist groups. Protist mt genomes are either circular or linear, and range in size from 6 kb to 69 kb with the number of genes ranging from 4 to 100 [3]. The smallest mt genome of 6 kb is found in haemosporidian parasites (*Plasmodium* and relatives) [4–6], which belong to the phylum Apicomplexa.

The phylum Apicomplexa is a large group of protists, related to dinoflagellates and ciliates [7]. The Apicomplexa includes more than 5000 species and some members of this phylum are clinically and/or economically important pathogens [8]. Members of Apicomplexa include *Plasmodium*, which is the etiological agent of human malaria; *Babesia*, which causes babesiosis in ruminants, dogs and humans; *Theileria*, which are the causal agents of tropical theileriosis and East Coast fever in cattle; *Eimeria*, which are responsible for the intestinal coccidiosis diseases in intensively-reared livestock; *Toxoplasma*, which is the etiological agent of toxoplasmosis in immune-compromised patients and congenitally infested fetuses; and *Cryptosporidium*, which are the pathogens that cause cryptosporidiosis in humans and animals. The apicomplexan parasites have complex life cycles, which involve the development of various morphologically distinct stages.

The genomes of apicomplexan mitochondria have only three protein-coding genes (cytochrome *c* oxidase subunits I and III: *cox1*and *cox3* and cytochrome *b*: *cob*) and highly fragmented rRNA genes have been identified (Fig. 1). This review highlights that the mt genome structure is remarkably diverse among apicomplexan parasites and explores the relationship between structures in mt, plastid and nuclear genomes among apicomplexans.

2. Mitochondrial genome organization

In the phylum Apicomplexa, mt genomes have either concatemeric or monomeric linear form as represented by malaria parasites and *Eimeria*, and piroplasms, respectively (Fig. 1). The structural features of the mt-genome of each apicomplexan are discussed in detail in the following subsections.

2.1. *Plasmodium* and *Leucocytozoon*

Plasmodium has the smallest mt genome in the form of a circular and/or tandemly repeated linear element of 6 kb [9]. Copy numbers for this element are approximately 20-fold and 150-fold of the nuclear genomes in *P. falciparum* [9] and *P. yoelii* [4], respectively. The 6-kb element encodes only three mt protein-coding genes (*cox1*, *cox3* and *cob*) in addition to the large subunit (LSU) and small subunit (SSU) ribosomal RNA (rRNA) genes [10] (Fig. 2A). The two rRNA genes are highly fragmented with 20 rRNA pieces having been identified [6,10]. Very recently, eight additional fragmented rRNA candidates have been identified in the *P. falciparum* mt genome [11] (Fig. 3A). Curiously, no transfer RNA genes have been identified. The mt-genome organization is perfectly conserved among 23 *Plasmodium* species [6], and pairwise sequence similarity of complete mt-genome sequences between these 23 species is very high at 84%–99%.

Leucocytozoon, closely related to the genus *Plasmodium*, is a bird parasite that does not form hemozoin pigment, a heme detoxification product. The complete mt-genome sequences are available for three *Leucocytozoon* species (*Leucocytozoon caulleryi*, *L. fringillinarum* and *L. majoris*) [5,12]. The mt-genome organization is highly conserved among these three *Leucocytozoon* species. In addition, the size and organization of these mt genomes are consistent with those of *Plasmodium* [11].

Recently, transcription of almost all intergenic regions of the *P. falciparum* mt genome has been demonstrated [13]. Some of these transcriptional regions have been additionally identified as LSU and SSU rRNA gene fragments [11]. Although function of the other transcriptional intergenic regions remains unknown, the size, nucleotide sequence and arrangements are almost completely conserved among the *Plasmodium* and *Leucocytozoon* genera [11]. Thus, it appears that these highly conserved sequence regions code for functional RNAs.

2.2. *Babesia* and *Theileria*

The genera of *Babesia* and *Theileria* are closely related to the genus *Plasmodium* and divided into three groups, babesids,