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Triatominae–*Trypanosoma cruzi*/*T. rangeli*: Vector–parasite interactions

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ABSTRACT

Of the currently known 140 species in the family Reduviidae, subfamily Triatominae, those which are most important as vectors of the aetiologic agent of Chagas disease, *Trypanosoma cruzi*, belong to the tribes Triatomini and Rhodniini. The latter not only transmit *T. cruzi* but also *Trypanosoma rangeli*, which is considered apathogenic for the mammalian host but can be pathogenic for the vectors. Using different molecular methods, two main lineages of *T. cruzi* have been classified, *T. cruzi* I and *T. cruzi* II. Within *T. cruzi* II, five subdivisions are recognized, *T. cruzi* IIa–IIe, according to the variability of the ribosomal subunits 24Sα rRNA and 18S rRNA. In *T. rangeli*, differences in the organization of the kinetoplast DNA separate two forms denoted *T. rangeli* KP1+ and KP1−, although differences in the intergenic mini-exon gene and of the small subunit rRNA (SSU rRNA) suggest four subpopulations denoted *T. rangeli* A, B, C and D. The interactions of these subpopulations of the trypanosomes with different species and populations of Triatominae determine the epidemiology of the human-infecting trypanosomes in Latin America. Often, specific subpopulations of the trypanosomes are transmitted by specific vectors in a particular geographic area. Studies centered on trypanosome–triatomine interaction may allow identification of co-evolutionary processes, which, in turn, could consolidate hypotheses of the evolution and the distribution of *T. cruzi*/*T. rangeli*-vectors in America, and they may help to identify the mechanisms that either facilitate or impede the transmission of the parasites in different vector species. Such mechanisms seem to involve intestinal bacteria, especially the symbionts which are needed by the triatomines to complete nymphal development and to produce eggs. Development of the symbionts is regulated by the vector. *T. cruzi* and *T. rangeli* interfere with this system and induce the production of antibacterial substances. Whereas *T. cruzi* is only subpathogenic for the insect host, *T. rangeli* strongly affects species of the genus *Rhodnius* and this pathogenicity seems based on a reduction of the number of symbionts.

1. Introduction

The current classification of the Triatominae recognizes 140 species grouped within six tribes and 18 genera (see Schofield and Galvão, this issue). Of these, two tribes – Rhodniini and Triatomini – have greatest epidemiological importance as vectors of trypanosomes. Although it is often assumed that all species of Triatominae have the capacity to transmit *Trypanosoma cruzi*, and that several – especially of the genus Rhodnius – can also transmit the closely related *T. rangeli*, current research is indicating rather more specific associations between particular species of Triatominae and defined genotypes of these parasites. The aim of this review is to therefore to summarize the geographic distribution of the different genotypes of *T. cruzi* and *T. rangeli*, and their association with the domestic and silvatic transmission cycles of the different Triatominae species. There is evidence for specific mechanisms within the vectors that either allow or impede the transmission of these parasite populations. In addition, the intestinal immune factors of the insects not only regulate the development of air-borne bacteria and symbionts in the intestinal tract of the vector, but can also be also induced by infections with *T. cruzi* or *T. rangeli*. It appears that *T. cruzi* only affects the vector under starvation conditions and is thereby subpathogenic for the vector, whereas *T. rangeli* is pathogenic for *Rhodnius* due to the reduction of the number of symbionts.

2. Vectors of *Trypanosoma cruzi*

For *T. cruzi*, the vectorial capacity of a given species of Triatominae depends largely on its degree of association with humans, so that vector populations are often described as domestic, perido-

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Table 1
Association between subpopulations of *T. cruzi*, Triatominae, reservoir hosts, and domestic and silvatic ecotypes.

T. cruzi subpopulations	Triatomine	Associated hosts	Ecotype
T. cruzi I (Z1)	*Rhodnius*	*Didelphis*	Palms
T. cruzi I (Z1)	*Rhodnius*	Man, domestic reservoirs	Anthropic environments
T. cruzi I (Z1)	*Panstrongylus*	*Didelphis*	Trees (not palms)
T. cruzi III (Z3)	*Panstrongylus*	*Dasypus*, *Monodelphis*	Terrestrial burrows
T. cruzi II (Z2)	*Triatoma*	*Cavia*, *Leontocebus*	Rocky grounds
T. cruzi II (Z2)	*Triatoma*	Man, domestic reservoirs	Anthropic environments
T. cruzi IIa, IIc	Silvatic species	Silvatic reservoirs	Silvatic environments
T. cruzi IIb, IId, IIe	Domestic species	Man, domestic reservoirs	Anthropic environments

Adapted from Gaunt and Miles (2000), Yeo et al. (2005), Telleria et al. (2006) and Cardinal et al. (2008).

mestic, or silvatic. The majority of triatomine species are silvatic, transmitting *T. cruzi* to mammalian hosts associated with that silvatic habitat. However, at least 10 species of Triatominae appear to have strictly domestic populations in specific Latin American regions, while over 20 species are described as secondary vectors because they often invade the houses from the peridomestic habitats. To consider the interaction between subpopulations of *T. cruzi* and their different vectors, we here consider the four regions currently subject of the multinational control initiatives:

Mexico and Central America: In this region of eight countries (Belize, Costa Rica, El Salvador, Guatemala, Honduras, Mexico, Nicaragua and Panama), the main domestic vectors are *Rhodnius prolixus* and *Triatoma dimidiata*. Other species that may have an epidemiological impact are *R. pallescens*, *T. nitida*, *T. ryckmani*, and various species and subspecies of the *T. phyllosoma* complex (Ponce, 2007; Zeledón et al., 2007).
Andean countries: In the four countries, Venezuela, Colombia, Ecuador and Peru, the domestic vectors are *R. prolixus*, *R. ecuadoriensis*, *T. dimidiata*, *T. maculata* and *T. infestans*. Also present are secondary vectors such as *R. pallescens*, *T. venosa*, *T. carrioni*, *P. herreri*, *P. chinai*, *P. geniculatus* and *P. rufotuberculatus* (Guhl, 2007).
Amazonian countries: This region involves parts of nine countries, Brazil, Peru, Colombia, Bolivia, Venezuela, Ecuador, Guyana, Surinam and French Guayana. Although the Amazonian region has been greatly affected by changes in agriculture and farming over the past few decades, there is no evidence for a permanent colonization of human domiciles by a species of Triatominae associated with *T. cruzi* transmission patterns. Of the 25 registered species in the Amazonian region, only a few have been reported in domestic habitats in some countries: *T. maculata*, *P. geniculatus*, *R. neglectus* and *R. stali*. In other areas of the Amazon, human populations come into contact with some of the silvatic species such as *R. robustus*, *R. pictipes* and *R. brethesi*; thus increasing the risk of *T. cruzi* transmission (Aguilar et al., 2007).

In the Southern Cone countries – Argentina, Bolivia, Brazil, Chile, Paraguay and Uruguay – *T. infestans* is the principal vector. Other vectors that often invade and colonize human dwelling places include: *Panstrongylus megistus*, *T. brasiliensis*, *T. sordida*, *T. pseudomaculata* and *R. nasutus* (Dias, 2007).

3. Variability of *Trypanosoma cruzi* isolates

The genetic structure of *T. cruzi* is predominantly clonal, with restricted recombination, i.e. various cellular strains persist as stable genotypes that can spread through large geographic regions (Tibayrenc and Ayala, 1988; Tibayrenc et al., 1986). The clonal model does not totally exclude recombination, but is compatible with occasional genetic recombination (Tibayrenc et al., 1990; Machado and Ayala, 2001; Brisse et al., 2003). Rare genetic interchanges, on the evolutionary scale, have a profound impact on the adaptation of *T. cruzi* to new environments, new vectors, and new hosts, including humans.

The genetic polymorphism of *T. cruzi* was originally demonstrated using isoenzyme electrophoresis, leading to categorization of three main groupings: zymodeme 1 (Z1) that appeared widespread in silvatic habitats, zymodeme 2 (Z2) that seemed more closely associated with human infections in the southern cone region, and zymodeme 3 (Z3) that seemed confined to the Amazon region (Miles et al., 1978; Ebert and Schaub, 1983; Tibayrenc et al., 1986). Analysis using other molecular markers tended to endorse these groupings, including analysis by kinetoplast DNA (kDNA), Restriction Fragment Length Polymorphism (RFLP) (Morel et al., 1980), pulse field gel electrophoresis (Henriksson et al., 1990), DNA fingerprinting (Macedo et al., 1992), Randomly Amplified Polymorphic DNA (RAPD) (Steindel et al., 1993; Tibayrenc et al., 1993), and sequences of 24Sα rRNA and mini-exon genes (Souto et al., 1996; Fernandes et al., 1998). However, these analyses indicated two main lineages, now denoted *T. cruzi* I (=Z1) and *T. cruzi* II (=Z2) with the previous third group, Z3, included within *T. cruzi* II (Anonymous, 1999) (Table 1).

Classification of a fresh isolate to *T. cruzi* I, *T. cruzi* II, *T. cruzi* Z3 or *T. rangeli*, is now often done by a PCR of the non-transcribed spacer of the mini-exon gene sequence (Fernandes et al., 2001). Also RFLP-ITS rDNA analysis is a useful tool for the detection of intraspecific variability in *T. cruzi* (Fernandes et al., 1999; Cuervo et al., 2002; Mendonça et al., 2002). Analysis of the microsatellites of the *T. cruzi* strains has allowed a phylogenetic construction, and the clonal definition of various strains (Oliveira et al., 1998; Macedo et al., 2001). The microsatellites have shown that *T. cruzi* is diploid and that the majority of the strains isolated from chronic chagasic patients have a clonal phylogenetic structure, while the strains isolated from non-human hosts possess multiclonal structures (Oliveira et al., 1998, 1999; Rozas et al., 2007a). Polymorphisms of different *T. cruzi* genes have recently been used for the genotyping of isolates, e.g. the calmodulin-3'UTR (Brandão and Fernandes, 2006; Brandão et al., 2008); the trypanothione reductase and cruzipain (Rojas et al., 2007) and PCR-RFLP multilocus analysis (Rozas et al., 2007b). According to RAPD analysis and isoenzyme electrophoresis, *T. cruzi* II is made up of five phylogenetically separate groups (IIa–IIe) (Fig. 1), whereas the *T. cruzi* I group seems to be more homogeneous (Brisse et al., 2000). Similar results were obtained by analysing the 24Sα rRNA region, the mini-exon and 18S rRNA (Brisse et al., 2001). Most recently however, subpopulations of *T. cruzi* I have been classified based on the variability of the intergenic mini-exon gene sequences (O'Connor et al., 2007). Upon sequencing the intergenic mini-exon gene region of 12 Colombian *T. cruzi* I isolates, four haplotypes were identified through single nucleotide polymorphisms (SNP) (Fig. 2), and insertions/deletions were associated with the parasites' cycles of transmission in different geographic regions (Herrera et al., 2007). Haplotype 1 was associated with infections in humans and domestic vectors (*T. venosa* and *R. prolixus*), haplo-