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A new consensus for Trypanosoma cruzi intraspecific nomenclature: second revision meeting recommends Tcl to TcVI

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In an effort to unify the nomenclature of Trypanosoma cruzi, the causative agent of Chagas disease, an updated system was agreed upon at the Second Satellite Meeting. A consensus was reached that T. cruzi strains should be referred to by six discrete typing units (T. cruzi I-VI). The goal of a unified nomenclature is to improve communication within the scientific community involved in T. cruzi research. The justification and implications will be presented in a subsequent detailed report.

Key words: Chagas disease - Trypanosoma cruzi strains - taxonomy - discrete typing units

The biological, biochemical and genetic diversity of Trypanosoma cruzi strains has long been recognised, along with their eco-epidemiological complexity, which has been reviewed extensively elsewhere (Macedo & Pena 1998, Campbell et al. 2004, Miles et al. 2009). Over the years, numerous approaches have been used to characterise the population structure of T. cruzi, aiming at defining the number of relevant subgroups. Accordingly, these subgroups received different designations, including zymodemes (Miles et al. 1977, 1978, 1981, Romanha et al. 1979), schizodemes (Morel et al. 1980), biodemes (Andrade 1974, Andrade & Magalhães 1997), clonets (Tibayrenc & Ayala 1991), lineages (Souto et al. 1996), clades (Kawashita et al. 2001) and, more recently, discrete typing units (DTUs) (Tibayrenc 1998) and haplotypes (Freitas et al. 2006, Herrera et al. 2007).

In a Satellite Meeting held at Fiocruz in 1999, an expert committee reviewed the available knowledge that indicated a convergence toward clustering T. cruzi strains into two major groups. Recommendations were issued that can be summarised as follows (Anonymous 1999). T. cruzi strains characterised by biological and biochemical features (e.g., biodemes and zymodemes) and molecular techniques [e.g., multilocus enzyme electrophoresis (MLEE), random amplification of polymorphic DNA (RAPD), mini-exon and 24Sr ribosomal DNA sequences] should be classified into two principal groups, named T. cruzi I and T. cruzi II. The classification of apparent hybrid strains and strains equivalent to Zymodeme 3 (Miles et al. 1978, 1981) and Biodeme Type I (Andrade 1974) would be decided later after further studies.

In the 10 years that followed the meeting at Fiocruz, the scientific community has advanced in the knowledge of T. cruzi diversity. Multilocus genotyping has revealed six distinct DTUs, which partition into two major subdivisions, termed DTU I and DTU II. DTUs are defined as “sets of stocks that are genetically more related to each other than to any other stock and that are identifiable by common genetic, molecular or immunological markers” (Tibayrenc 1998). T. cruzi DTU II was further split into five DTUs, Ila-e (Brisse et al. 2000, 2001), based on congruent phylogenetic information from MLEE and RAPD markers. DTUs I and IIB correspond, respectively, to the T. cruzi I and T. cruzi II groups recommended by the original expert committee in 1999 (Table I). Current studies indicate that four subdivisions have emerged within DTU I as well (Herrera et al. 2007, Falla et al. 2009), although these have not been integrated into the nomenclature revision.

Although the major genetic variability of T. cruzi was proposed initially to have resulted from predominant clonal evolution (Tibayrenc et al. 1986), increasing evidence indicates that genetic exchange between parasites has contributed to the present popu-
The advances in the understanding of T. cruzi population structure (Sturm & Campbell 2009). This was first documented by the existence of hybrid organisms in sylvatic T. cruzi populations and sympatric clinical strains and, later, experimentally (Gaunt et al. 2003 and cited references). The prevailing view is that DTU I and DTU IIb are ancient lineages and that DTU IId and DTU IIe strains are the products of a minimum of two hybridisation events (Westenberger et al. 2005, Freitas et al. 2006, Tomazi et al. 2009). The evolution of DTU Ia and DTU Iic strains is insufficiently understood for the moment, although these DTUs may also have a hybrid origin (Sturm et al. 2003, Westenberger et al. 2005). Based on microsatellite and mitochondrial DNA analyses, DTU Iic may represent a third ancestral lineage, which was named T. cruzi III (Freitas et al. 2006).

The advances in the understanding of T. cruzi population structure indicate that it is time to revise the nomenclature of T. cruzi strains. The standardisation of nomenclature will facilitate communication among researchers working with T. cruzi aimed at characterisation of its eco-epidemiological features, pathogenicity and questions of basic biology.

A Second Satellite Meeting was held in Buzios, Brazil, on August 23, 2009, preceding the XIII International Congress of Protistology, the XXV Annual Meeting of the Brazilian Society of Protozoology and the XXXVI Annual Meeting on Basic Research in Chagas Disease. By consensus, the expert committee recognised that the nomenclature for T. cruzi strains should be classified into six DTUs, T. cruzi I-VI and issued recommendations accordingly. Detailed justification and implications of these decisions will be presented in a future publication.

**Recommendations of the Second Satellite Meeting** - (i) The known isolates and strains of T. cruzi should be assigned to one of six DTUs (T. cruzi I-VI). Additional variants may arise in the future; (ii) DTUs T. cruzi I and T. cruzi II correspond to the two groups originally defined in the First Satellite Meeting (Anonymous 1999). A notable exception is the CL Brener strain, classified at that time as T. cruzi II and now reclassified as T. cruzi VI; (iii) The designation of the six DTUs, their abbreviations and equivalence are summarised in Table I; (iv) Authors and reviewers of manuscripts describing studies on T. cruzi are encouraged to use the new nomenclature; (v) Editors of sci-

### TABLE I

2009 nomenclature for Trypanosoma cruzi divisions

<table>
<thead>
<tr>
<th>DTU designation</th>
<th>Abbreviation</th>
<th>Equivalence to former T. cruzi grouping schemes</th>
</tr>
</thead>
<tbody>
<tr>
<td>T. cruzi I</td>
<td>TcI</td>
<td>T. cruzi I etc and DTU I etc.</td>
</tr>
<tr>
<td>T. cruzi II</td>
<td>TcII</td>
<td>T. cruzi IIa and DTU IIb.</td>
</tr>
<tr>
<td>T. cruzi IV</td>
<td>TcIV</td>
<td>Z3', Z3-B' and DTU IId.</td>
</tr>
<tr>
<td>T. cruzi V</td>
<td>TcV</td>
<td>Bolivian Z2', rDNA 1/2', clonet 39' and DTU IId.</td>
</tr>
<tr>
<td>T. cruzi VI</td>
<td>TcVI</td>
<td>Paraguayan Z2', Zymodeme B' and DTU IIe.</td>
</tr>
</tbody>
</table>


### TABLE II

Representative strains and corresponding discrete typing units (DTUs)

<table>
<thead>
<tr>
<th>Strain</th>
<th>DTUs</th>
<th>Country</th>
<th>Host/vector</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 SF</td>
<td>T. cruzi II</td>
<td>Bahia, Brazil</td>
<td>Homo sapiens</td>
</tr>
<tr>
<td>21 SF</td>
<td>T. cruzi II</td>
<td>Bahia, Brazil</td>
<td>Homo sapiens</td>
</tr>
<tr>
<td>3663</td>
<td>T. cruzi III</td>
<td>Amazonas, Brazil</td>
<td>Panstrongylus geniculatus</td>
</tr>
<tr>
<td>3869</td>
<td>T. cruzi III</td>
<td>Amazonas, Brazil</td>
<td>Homo sapiens</td>
</tr>
<tr>
<td>4167</td>
<td>T. cruzi IV</td>
<td>Amazonas, Brazil</td>
<td>Rhodnius brethesi</td>
</tr>
<tr>
<td>4182</td>
<td>T. cruzi III</td>
<td>Amazonas, Brazil</td>
<td>Rhodnius brethesi</td>
</tr>
<tr>
<td>92.80 cl2</td>
<td>T. cruzi V</td>
<td>Santa Cruz, Bolivia</td>
<td>Homo sapiens</td>
</tr>
<tr>
<td>92101601P cl1</td>
<td>T. cruzi I</td>
<td>Georgia, USA</td>
<td>Didelphis marsupialis</td>
</tr>
<tr>
<td>9212102R</td>
<td>T. cruzi V</td>
<td>Georgia, USA</td>
<td>Procyon lotor</td>
</tr>
<tr>
<td>Bug2148 cl1</td>
<td>T. cruzi V</td>
<td>Rio Grande do Sul, Brazil</td>
<td>Triatoma infestans</td>
</tr>
<tr>
<td>Bug2149 cl10</td>
<td>T. cruzi V</td>
<td>Rio Grande do Sul, Brazil</td>
<td>Triatoma infestans</td>
</tr>
</tbody>
</table>
Strain\textsuperscript{a} & DTUs & Country & Host/vector \\
\hline
CA-1 & \textit{T. cruzi} I & Argentina & \textit{Homo sapiens} \\
CanIII cl1 & \textit{T. cruzi} IV & Pará, Brazil & \textit{Homo sapiens} \\
CL & \textit{T. cruzi} VI & Rio Grande do Sul, Brazil & \textit{Triatoma infestans} \\
CL Brener\textsuperscript{b} & \textit{T. cruzi} VI & Rio Grande do Sul, Brazil & \textit{Triatoma infestans} \\
CM17 & \textit{T. cruzi} III & Meta, Colombia & \textit{Dasypus sp.} \\
Colombiana & \textit{T. cruzi} I & Colombia & \textit{Homo sapiens} \\
Cuica cl1 & \textit{T. cruzi} I & São Paulo, Brazil & \textit{Philander opossum} \\
Cutia cl1 & \textit{T. cruzi} I & Espírito Santo, Brazil & \textit{Dasyprocta aguti} \\
Davis 9.90 & \textit{T. cruzi} I & Tegucicalpa, Honduras & \textit{Triatoma dimidiatia} \\
Dm28c\textsuperscript{c} & \textit{T. cruzi} I & Carabobo, Venezuela & \textit{Didelphis marsupialis} \\
Dm7 & \textit{T. cruzi} I & Casanare, Colombia & \textit{Didelphis marsupialis} \\
Dog Theis\textsuperscript{d} & \textit{T. cruzi} IV & Oklahoma, USA & \textit{Canis familiaris} \\
Esmeraldo cl3 & \textit{T. cruzi} II & Bahia, Brazil & \textit{Homo sapiens} \\
G & \textit{T. cruzi} I & Amazonas, Brazil & \textit{Opossum} \\
Gambá cl1 & \textit{T. cruzi} I & São Paulo, Brazil & \textit{Didelphis azarae} \\
IVV cl4 & \textit{T. cruzi} II & Cuncumen, Chile & \textit{Homo sapiens} \\
JEM C & \textit{T. cruzi} I & Boyacá, Colombia & \textit{Homo sapiens} \\
José & \textit{T. cruzi} I & Paraíba, Brazil & \textit{Homo sapiens} \\
K-98\textsuperscript{e} & \textit{T. cruzi} I & Argentina & \textit{Homo sapiens} \\
M5631 cl5 & \textit{T. cruzi} III & Pará, Brazil & \textit{Dasypus novemcinctus} \\
M6241 cl6 & \textit{T. cruzi} III & Pará, Brazil & \textit{Homo sapiens} \\
MAS cl1 & \textit{T. cruzi} II & Minas Gerais, Brazil & \textit{Homo sapiens} \\
MN cl2 & \textit{T. cruzi} V & Region IV, Chile & \textit{Homo sapiens} \\
NR cl3 & \textit{T. cruzi} V & Salvador, Chile & \textit{Homo sapiens} \\
P63 cl1 & \textit{T. cruzi} VI & Makthlawaiya, Paraguay & \textit{Triatoma infestans} \\
PALC & \textit{T. cruzi} I & Casanare, Colombia & \textit{Rhodnius prolixus} \\
Peruvian & \textit{T. cruzi} II & Peru & \textit{Homo sapiens} \\
RA & \textit{T. cruzi} VI & Argentina & \textit{Homo sapiens} \\
Sc43 cl1 & \textit{T. cruzi} V & Santa Cruz, Bolivia & \textit{Triatoma infestans} \\
SO3 cl5 & \textit{T. cruzi} V & Potosí, Bolivia & \textit{Triatoma infestans} \\
Sylvio\textsuperscript{f}/X10 cl1 & \textit{T. cruzi} I & Pará, Brazil & \textit{Homo sapiens} \\
Tdl1C & \textit{T. cruzi} I & Boyacá Colombia & \textit{Triatoma dimidiatia} \\
Tu18 cl1 & \textit{T. cruzi} II & Tupiza, Bolivia & \textit{Triatoma infestans} \\
Tulahuen & \textit{T. cruzi} VI & Tulahuen, Chile & \textit{Homo sapiens} \\
Tulahuen cl2 & \textit{T. cruzi} VI & Tulahuen, Chile & \textit{Homo sapiens} \\
X10/1\textsuperscript{g} & \textit{T. cruzi} I & Pará, Brazil & \textit{Homo sapiens} \\
X109/2 & \textit{T. cruzi} III & Makthlawaiya, Paraguay & \textit{Canis familiaris} \\
Y & \textit{T. cruzi} II & São Paulo, Brazil & \textit{Homo sapiens} \\
YuYu & \textit{T. cruzi} I & Minas Gerais, Brazil & \textit{Triatoma infestans} \\
\hline
\textsuperscript{a} the term cl following the name of the strain indicates it is a clone derived from the original isolate; \textsuperscript{b} CL Brener is a clone derived from the CL strain; \textsuperscript{c} Dm28c is a clone derived from the Dm28 strain; \textsuperscript{d} Dog Theis sometimes shortened to DogT or DogTh; \textsuperscript{e} K-98 is a clone derived from the CA-1 strain; \textsuperscript{f} Sylvio referred to as Silvio; \textsuperscript{g} same as Sylvio (Silvio) X10 cl1.

To obtain the greatest effectiveness, the new recommendations for the naming of \textit{T. cruzi} will require a simple and reproducible schema for typing isolates into their respective DTUs. Lewis et al. (2009) described such a schema using currently available markers in the form of a triple assay that employed rDNA PCR (Souto et al. 1996) and PCR-RFLP of the HSP60 and GPI loci (Westenberger et al. 2005). The expert committee is exploring the possibility of a multicentric study to standardise and validate different protocols for genotyping reference and laboratory strains, as well as field isolates. Any multicentric study will make a call for comparative typing protocols that are under development currently in other laboratories.
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