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ISOZYMIC VARIABILITY OF *TRYPANOSOMA CRUZI*: BIOLOGICAL AND EPIDEMIOLOGICAL SIGNIFICANCE

by

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Summary — Genetic interpretation of *T. cruzi* zymograms has led to various hypotheses which are reviewed.

KEYWORDS : *Trypanosoma cruzi*; Zymograms; Genetic Interpretation.

Isozymic studies on *Trypanosoma cruzi* were initiated by Toyé (1974) and largely developed by Miles *et al.* (1977, 1980). These authors, by means of a phenetic interpretation of *T. cruzi* zymograms, distinguished in Brazil 3 main isozymic strains (« zymodemes ») which were classified by numerical taxonomy using isozymic banding (Ready and Miles, 1980).

Genetic interpretation of *T. cruzi* zymograms was performed by comparison with better known organisms and led us to the following hypotheses.

Diploidy

T. cruzi zymograms exhibit some typical heterozygous patterns for a diploid organism (Tibayrenc *et al.*, 1981a). By DNA measurement, we verified that the ploidy is constant among all the isozymic strains (Lemesre and Tibayrenc, 1983). This fact was also verified with isozymic patterns (Tibayrenc *et al.*, 1985). Diploid structure was inferred by Tait (1980) for *T. brucei* with similar arguments. Lanar, Levy and Manning (1981), by a DNA study, proposed also the hypothesis of diploidy for *T. cruzi.*

Enzyme quaternary structure

Heterozygous patterns reveal a monomeric structure for phosphoglucomutase, a dimeric structure for isocitrate deshydrogenase, glucose phosphate isomerase, 6-phosphogluconate deshydrogenase, the two loci of malic enzyme, and a pentameric structure for glutamate deshydrogenase Nadp+ (Tibayrenc *et al.*, 1981a and 1985).

Lack of Mendelian sexuality at present

T. cruzi zymograms show: a) a lack of segretation (« fixed heterozygosity » for some isozymic strains); b) a lack of recombination : each

isozymic strain has its own isozymic patterns without recombination with other strains; one can observe very often the sympatric presence (even in the same Triatomine bug) of alternative alleles without recombination between them (Tibayrenc *et al.*, 1981b and 1985). Tait (1980) inferred the existence of Mendelian sexuality for *T. brucei.*

Classification by genetic distance

Calculation of genetic distance according to Nei (1972) and Tibayrenc (1980) shows : a) the existence of 3 main groups, which correspond roughly to Miles' zymodemes (1980), but with much higher intragroup variability; b) the presence of high genetic distance values (up to 2.6), which indicates a huge level of proteic divergence (Tibayrenc and Miles, 1983; Tibayrenc and Le Ray, 1984).

Evolutive origin and biological status of T. cruzi *isozymic strains*

Isozymic data are consistent with 2 alternative hypotheses : a) Genetic distances between isozymic strains do represent an ancient divergence time, either by mitotic evolution or by real biological speciation; b) isozymic strains or at least part of them have a very recent origin by random sampling of clones within a sexuate ancestral population, and they are the genetic equivalent of individual variants without any taxonomical significance. In the case (a), other characters of the parasite are expected to be roughly correlated to genetic distances. In the case (b), they are expected to be randomly distributed among the isozymic strains. Epidemiological data (Tibayrenc *et al.*, 1985), pharmacological experiments (Barnabé, Tibayrenc and Dujardin, 1983) and pathogenicity studies (Brénière, in preparation), show a lack of correlation between genetic distances and other characters, and so seem to be more consistent with hypothesis (b) (Tibayrenc *et al.*, 1985b).

Bolivian isozymic strains in domestic transmission cycles

One can observe two main isozymic strains with some lesser ones. Heterozygous strains seem more frequent at low altitude (Tibayrenc *et al.*, 1985a). It is easy to sample several different isozymic strains in the same house (Tibayrenc *et al.*, 1985) and two different ones in the same Triatomine bug (Tibayrenc *et al.*, 1985). All isozymic strains are sympatrically transmitted by the same species, *Triatoma infestans.*

Genetic interpretation of *T. cruzi* zymograms yielded some interesting data on the biology of the parasite. Nevertheless, this theoretical approach did not yield a general theory to explain the huge biological and medical variability of Chagas' disease's causative agent.

Variabilité isoenzymatique de *T. cruzi* : portée biologique et épidémiologique.

Résumé — L'auteur passe en revue les diverses hypothèses soulevées par l'interprétation génétique de l'analyse enzymatique de *T. cruzi.*

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