Correspondence

Toxoplasma Strain Nomenclature

To the Editor—I read the excellent work by Ajzenberg et al. [1] about Toxoplasma strains in patients with immunodeficiency. In the article, the denominations type I, type II, type III, and nonarchetypal strains were used. Previous work with multilocus markers showed that global Toxoplasma populations could be grouped into 4 major populations (SA1, SA2, RW, and WW) [2] and that, by analyzing intron sequences, Toxoplasma could be grouped into 11 haplogroups [3]. It is also important to point out that, for notation of results for a single-marker locus such as SAG2, all results should be specifically indicated as SAG2 type I, SAG2 type II, or SAG2 type III.

I think that the generalized use of the type I, II, and III nomenclature has been misleading. An early article that correlated the groups of parasites classified in this manner concluded that type I was found mainly in congenital toxoplasmosis, type II in reactivation forms, and type III in animals [4]. Subsequent work showed that this was a biased observation resulting from the geographical origin of the strains used in the study (Europe and North America). Multilocus analysis has been performed not only in Brazil and Guyana but also in Colombia in strains obtained from cats [5] and chickens [2]. Altogether, the results of haplotype analysis, multilocus analysis, and serogenotyping [6, 7] are concordant and point to a predominance of different parasite populations in South America, named SA1 and SA2 by multilocus markers or by the exclusive haplogroups that exist only in South America. The clinical relevance of this geographical restriction of Toxoplasma strains was recently shown by a comparison of cohorts in South America and Europe [7, 8]. The risk of ocular lesions was much higher among Colombian and Brazilian children (47% [18/38]) than among children in Europe (14% [79/550]); the crude risk of intracranial lesions was also much higher among children in South America (53% [20/38]) than among those in Europe (9% [49/550]) [8]. Additionally, a comparative prospective cohort study of congenitally infected children in Brazil and Europe found that Brazilian children had eye lesions that were larger, more numerous, and more likely to affect the part of the retina responsible for central vision, compared with their counterparts in Europe [9].

The nomenclature for parasite populations should reflect the discriminatory power of the genetic locus. Thus, the use of the type I, II, and III nomenclature for different techniques that use different genetic markers enhances confusion about what can be expected for the strain definition; instead, nomenclature that indicates geographical origin should be preferred. Of importance for clinicians is that the available genetic markers that have been studied in environmental and clinical samples, whether by single-locus marker, multilocus, or haplotype analysis, cannot predict clinical outcome. What we need now is a true and clinically relevant parasite genotype classification system, and we need to evaluate the presence of ROP16 polymorphisms and of the insertion-deletion polymorphism in the promoter region of the gene ROP18 in Toxoplasma strains from clinical samples [10].

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References


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Reply to Gómez-Marin

To the Editor—Gómez-Marin raises some interesting issues in his letter [1]. We agree...
that housecleaning in *Toxoplasma* strain nomenclature is needed, but not for strains belonging to the “big three”—that is, the archetypal lineages named type I, type II, and type III. The markedly clonal population structure of these lineages cannot be called into question and has been largely validated by correlation between independent sets of genetic markers (multilocus enzyme electrophoresis, restriction fragment–length polymorphism, and microsatellites), with the same reference strains leading to the designation of these 3 genetic types [2]. That these genotypes have been sampled from different hosts in different geographic regions is also a strong indication of clonality. Of the big three, type III seems to be the more widespread genotype, as it has been found on all continents. Type II strains are predominant in Europe and North America but are rare outside these areas. Historically, the first *Toxoplasma* strain, named RH, was isolated in 1939. This strain, which is highly virulent in mice, belongs to the type I lineage and is currently used as the reference *Toxoplasma* strain in many laboratories worldwide. Paradoxically, it has turned out that type I strains have been rarely isolated from humans or other animals in multilocus studies. The results of numerous older studies that considered only a single marker for genotyping (mainly SAG2) and that identified strains as type I are misleading because of inadequate genetic information.

Collection of strains from areas outside Europe or North America, especially Brazil and French Guiana, revealed a higher genetic diversity than expected. These strains were not genetically related to the 3 major types and were designated as atypical, exotic, or nonarchetypal. Recently, *Toxoplasma* strains were classified into 11 haplogroups on the basis of polymorphisms in introns: groups 1–3 were reserved for the big three, and groups 4–11 were reserved for 36 atypical strains [3]. This classification system has limitations, because the addition of different markers and a more extensive geographical sampling of strains could alter the classification. We should learn from recent history and be aware that previous studies of the genetic diversity of *Toxoplasma* did not reveal all its secrets. Consequently, we should not classify *Toxoplasma* strains into “groups,” especially when some of these groups are composed of only 1 or 2 individual members. We believe that all available atypical strains worldwide should be exchanged and genotyped using as many markers as possible. With such complete information, it seems reasonable to propose a nomenclature for atypical strains based on geographic origins. We initiated this concept in our article [4] with certain nonarchetypal genotypes that were repeatedly recovered from different patients who acquired toxoplasmosis in sub-Saharan Africa (genotypes Africa 1 and 2) and in the French West Indies (genotype Caribbean 1).

Gómez-Marin underscores the greater severity of toxoplasmosis in South America in comparison with Europe. This is a reality, but there is no evidence that this can be explained only by strain differences. Brazilian or Guianan strains are genetically different from European strains, but are they really more pathogenic in humans? To our knowledge, there is no clear answer to this question. The choice of *ROP16* and *ROP18* as markers of pathogenicity is interesting, but we must keep in mind that they are key virulence factors in mice, and we do not know the role that they play in different hosts, especially in humans. We recently described an outbreak of toxoplasmosis in Suriname [5]. The same strain was responsible for different clinical outcomes in each of 11 patients: 2 cases were congenital and lethal, and 9 cases occurred in immunocompetent adults (5 patients, 1 of whom died, had disseminated toxoplasmosis and needed hospitalization, and 4 had less severe disease with no life-threatening signs or need for hospitalization). This amounts to indirect evidence that factors other than strain virulence are of major importance in the natural course of toxoplasmosis in humans.

These factors include the immune status and genetic background of the host, the life-cycle stage of the pathogen (oocysts vs cysts), and diverse environmental conditions leading to more frequent exposure to *Toxoplasma* and higher inoculum size in certain areas—for example, in South America in comparison with Europe.

**References**


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