



## Review

## Geographical distribution of *Toxoplasma gondii* genotypes in Asia: A link with neighboring continents



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## ABSTRACT

Defining the pattern of genetic diversity of *Toxoplasma gondii* is important to understand its worldwide distribution. During the last decades, a large number of studies have been published on *Toxoplasma* genotypes circulating in Europe, in North and South America. Two continents are still largely unexplored, Africa and, to a less extent, Asia. In this last continent, an increasing number of publications reported genotypes circulating in diverse provinces of China, but very few data are available for other Asian countries. After a systematic database search, 47 papers related to *T. gondii* genotypes in Asia were analyzed. Genetic characterization of DNA was performed by microsatellite markers, or more usually by a multiplex PCR using 11 PCR-RFLP markers, allowing data comparison to draw a first global picture of the population structure of this parasite throughout Asia. Overall, 390 isolates or DNA extracts were completely typed by PCR-RFLP and/or microsatellite marker methods, revealing 36 different PCR-RFLP or equivalent microsatellite genotypes: 15 genotypes identified by a ToxoDB number and 21 atypical or unique genotypes. The most common genotype found in Asia is the genotype ToxoDB#9 (*Chinese 1*). The clonal types I, II and II variant, and III were also commonly found in Asia. The geographical distribution of these genotypes across Asia may reflect either a continuum with Europe for the western part of Asia (presence of Type II), or the circulation of strains through animal migration or human activities between Africa and the Southwestern part of Asia (*Africa 1* genotype in Turkey or ToxoDB#20 both I Sri-Lanka and in Ethiopia or Egypt). Although there are some indications of a genetic population structure in Southeast Asian countries different from the rest of Asia, more studies in this tropical part of Asia will be necessary for a region which represent as well as Africa one of the missing links of the *T. gondii* genetic diversity.

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## 1. Introduction

*Toxoplasma gondii* is one of the most common parasites, infecting human and other warm-blooded animals. It is estimated that *T. gondii* infects one third of the world population (Weiss and Dubey, 2009). Human infection rates vary around the world depending on several sociogeographical factors. Acquisition of *T. gondii* infection is commonly acquired by the ingestion of tissue cysts that contain bradyzoites or by the ingestion of oocysts containing sporozoites. The sources of human infection could vary greatly between different ethnic groups and different geographical locations.

*Toxoplasma gondii* strains have now been isolated and identified in a large number of hosts (humans and wild and domestic animals). Several molecular markers have been developed to evaluate *T. gondii* genetic diversity. According to the techniques used for characterizing *Toxoplasma* strains, different designations may be encountered. Correspondence between these designations is presented in Table 1. The last global population structure picture based on DNA sequence typing and whole genome sequencing of 62 representative strains identified 16 haplogroups originating from 6 ancestral populations or clades (Su et al., 2012; Lorenzi et al., 2016). They clustered genotypes defined by multilocus markers, either a set of 11 PCR-RFLP genetic markers (ToxoDB#1, #2, #3 ...) (Su et al., 2006, 2010, ToxoDB website: <http://toxodb.org/toxo/>) or a set of 15 microsatellite (MS) markers (Ajzenberg et al., 2010).

The global distribution of *T. gondii* genotypes is widely known in Europe, North and South America. The clonal lineages Type II and, to a less extent, Type III predominate in Europe (Dardé et al., 2014). They are also present in North America, but a fourth clonal lineage (haplogroup 12) and other atypical genotypes are prevalent in this part of the world (Dubey et al., 2011). A high diversity was found in South America with no predominant genotype (Shwab et al., 2014). The diversity on the African continent is less well known: apart from Type II and III, other genotypes were identified by MS markers as *Africa 1* (belonging to haplogroup 6) that circulates in large area of Western and Central Africa and *Africa 3* in Gabon (Mercier et al., 2010), or by PCR-RFLP markers such as the ToxoDB#20 genotype found in Egypt (Al-Kappany et al., 2010) and Ethiopia (Dubey et al., 2013).

In Asia, an increasing number of studies have been conducted on strains circulating in China. A largely predominant genotype, *Chinese 1* (ToxoDB#9) is found in diverse provinces of China. But little is known about strains circulating in other Asian countries. This study aims through a literature review on genetic diversity of *T. gondii* in Asia to understand the circulation and propagation of *T. gondii* strains in Asia, and to propose hypotheses about their relations with strains circulating on neighboring continents.

## 2. Materials and methods

### 2.1. Literature search

To identify published studies on genetic characterization of *T. gondii* strains in Asia, we conducted a systematic search of the literature published in English until September 2016. We used online databases MEDLINE and Google Scholar to find the information. The keywords and research equations used were: *Toxoplasma gondii* [AND] genotypes [AND] Asia, and *Toxoplasma gondii* [AND] genotypes [AND] each country in Asia (Fig. 1).

Box 1 List of Asian countries selected for literature search.

Afghanistan, Armenia, Azerbaijan, Bahrain, Bangladesh, Bhutan, Brunei, Cambodia, China, Cyprus, Georgia, India, Indonesia, Iran, Iraq, Israel, Japan, Jordan, Kazakhstan, Korea, Kuwait, Kyrgyzstan, Laos, Lebanon, Malaysia, Maldives, Mongolia, Myanmar, Nepal, Oman, Pakistan, Palestine, Philippines, Qatar, Russia, Saudi Arabia, Singapore, Sri Lanka, Syria, Taiwan, Tajikistan, Thailand, Timor Leste, Turkey, Turkmenistan, United Arab Emirates, Uzbekistan, Vietnam, Yemen.

\*Underlined countries correspond to the countries where *T. gondii* strains were genotyped.

### 2.2. Selection of studies

Articles were selected based on their titles and then their abstracts. Only those articles that met the exclusion criteria were finally included. Those retained were read in full. Exclusion criteria were: (i) publications that do not describe *T. gondii* genotypes in Asia, (ii) publications using genetic characterization methods with less than 5 typing markers, considering that they do not allow a reliable genotyping (Fig. 1). However, some papers presenting incomplete genotypes were considered for discussion, notably for countries where no other genotyping data were available (Japan, India), but they were not considered for the global picture presented in Table 2 and Fig. 2. For publications before 2010 using PCR-RFLP markers, the genotype number was not defined, and the database ToxoDB (<http://toxodb.org/toxo/>) was used to attribute a ToxoDB genotype number according to the combination of alleles. It was also used to retrieve geographical distribution of a given genotype outside Asia. The results of literature review were classified by country.

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