Distribution of HLA-DRB1 alleles in countries with high tuberculosis burden (Brazil, Russia, India, China and South Africa): a systematic review and meta-analysis

Cleidiane B Daltro[1]; Alice S Martins-dos-Santos[2]; Carlos MC Mendes[1]; Theolis Barbosa[1,2]

[1]Instituto de Ciências da Saúde (ICS) Universidade Federal da Bahia. 40110-100, Brasil; [2]Centro de Pesquisa Gonçalo Moniz, Fundação Oswaldo Cruz (FIOCRUZ), Salvador, 40296-710 Brasil.

HLA-DRB1 is a polymorphic gene with approximately 500 allelic variants that is crucial for antigen presentation. This allelic diversity must be considered for the development of epitope-based vaccines. Brazil, Russian Federation, India, China and South Africa (BRICS) account for almost 50% of global TB cases and 40% of all TB-associated mortality. We describe the distribution of HLA-DRB1 alleles in these countries. Articles in Portuguese, English and Spanish, with free access or with access provided by Fundacao Oswaldo Cruz or the CAPES Consortium, reporting the allele frequency for HLA class II in humans present in the PubMed platform (June 2014 to March 2016) were included. Articles that only reported the HLA-DQ or/and DP frequencies, or that reported allele frequencies in restricted groups, or where the allelic frequencies could not be deduced accurately, studies limited to abstracts and those that did not report the full results for the alleles studied were excluded. Duplicate reports as well as preliminary data if a further report extended the sample size or provided additional data were also excluded. The methodological quality of the articles was assessed using an adapted "Newcastle-Ottawa Scale". The fixed effects model was considered if $I^2 \leq 50\%$ and the random effects model was considered if $I^2 > 50\%$. We included 15 articles from Brazil, 8 from Russia, 9 from India, 19 from China and 6 from South Africa. HLA-DRB1 *01; *03; *04; *07; *11; *13; *15 alleles were the most frequent among the populations studied. HLA-DRB1*15 (in all countries), DRB1*13 (in all countries except for China) and DRB1*07 (in all countries except for South Africa) were ≥ 10%. HLA-DRB1*09 and *12 were the most frequent in China in spite of being rare in other populations. Epitope-based vaccines with high affinity for these alleles would be capable of stimulating at least 80% of the population of the countries studied.

Key-words: Vaccines; peptide; tuberculosis.

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