



Contents lists available at ScienceDirect

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Short Communication

Class II HLA in Georgia Caucasus Tbilisi Georgians and their Mediterranean ancestry: *The Usko Mediterranean languages*

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ARTICLE INFO

Keywords:

HLA
Georgia
Usko-Mediterranean
Dene-Caucasian
Caucasus
Svan
Iberian
Tartessian
Etruscan
Basque
Berber
Iberia
Kartli
Sakartvelo
Tbilisi
Kura
Ebro

ABSTRACT

Georgia (or Sakartvelo in its own language) is a South Caucasus Mts. country with its easternmost part is enigmatically named Iberia, like the Iberian Peninsula, which may refer to rivers “Kura” and “Ebro” or their valleys respectively. Most of their inhabitants speak Georgian which is included within Dene-Caucasian group and Usko-Mediterranean subgroup of languages. The latter includes Basque, Berber, ancient Iberian-Tartessian, Etruscan, Hittite, Minoan Lineal A and others. In the present paper, HLA class II -DRB1 and -DQB1 alleles has been studied and extended haplotypes calculated. Most frequent haplotypes are also of Mediterranean origin (i. e.: (A*02-B*51)-DRB1*11:01-DQB1*03:01, (A*02-B*51)-DRB1*13:01-DQB1*06:03, or (A*24-B*35)-DRB1*01:01-DQB1*05:01) and DA genetic distances show that closest world populations to Georgians are Mediterraneans. Georgians also show common extended haplotypes ((A*02-B*51)-DRB1*11:01-DQB1*03:01, (A*02-B*13)-DRB1*07:01-DQB1*02:01 and (A*03-B*35)-DRB1*11:01-DQB1*03:01) with Svan people, a secluded population in North Georgia mountains. We can conclude that Georgians belong to a very old Mediterranean substratum according to both linguistics (Usko Mediterranean languages) and HLA genetics.

Georgia is a country placed in the South Caucasus Mts. between South Russia and North Anatolian Peninsula. It is believed that by 1200 BCE an admixture of Mesopotamian Anatolians (Hittites and Assyrians) took place with people inhabiting Georgian mountains: this should be the main basis of people stock of nowadays Georgia. Alexander the Great did not invade Georgia, but later Romans did: an orthodox Christianity religion has remained despite Arab invasion [1,2]. Golden Fleece and Medea classic histories occurred in Georgian Black Sea [3]. In addition, different parts of this relatively small size country there exist today (Fig. 1, [Supplementary Material](#)): Abkhazia and Adjara western autonomous regions, South Ossetia (Iranian language) which includes Central Caucasus main pass through Caucasus Mts., and eastern part of Kartli or Iberia, with an intriguing same name like Iberian Peninsula (Spain and Portugal). The name of Iberia may mean “river” or “river valley” according to a related Basque (or old Iberian

Peninsula language) cognate: “ibar”. Iberian Peninsula probably refers to “Ebro” and “Ibero” River and Georgian Iberia to Kura River valley. Georgia is called Sakartvelo by Georgians and the main language they speak is Georgian (spoken by 88 % of Georgia population), which is a Dene-Caucasian one related to Basque language [4–7].

In the present work we aim to study HLA-DRB1 and -DQB1 alleles and extended haplotypes in order to ascertain a possible Mediterranean and/or other origin for Georgians.

One hundred and nineteen unrelated Georgians volunteered to donate blood after signed consent; they were living at Tbilisi and at least their three generations were also living there (Fig. 1, [Supplementary Material](#)). They were studied for HLA-DRB1 and -DQB1, and typings were carried out by PCR-SSOP-Luminex technique [8]. HLA-DRB1 and HLA- DQB1 typing was confirmed when necessary by DNA sequencing in a Perkin Elmer 310 automated DNA sequencer (Foster

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<https://doi.org/10.1016/j.humimm.2022.08.005>

Received 29 July 2022; Revised 3 August 2022; Accepted 4 August 2022

Available online xxx

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City, CA, USA). Statistical analysis was performed with Arlequin v3.0 [9]. IMG2 3.1.20 (December 14th 2018) version was used to analyze data.

Thirty-two different HLA-DRB1 alleles and fourteen HLA-DQB1 alleles have been found in Georgian population sample studied in present work. Their frequencies are shown at Table 1 (Supplementary Material). The most frequent Georgian HLA extended haplotype also using low resolution HLA class I data [10] was HLA-(A*02-B*51)-DRB1*11:01-DQB1*03:01 (12.61 %, Mediterranean and Caucasus); the second most frequent haplotype was HLA-(A*02-B*51)-DRB1*13:01-DQB1*06:03 (9.66%,Mediterranean) and the third most frequent class II haplotype was HLA-DRB1*01:01-DQB1*05:01 (8.82 %) (Table 2, Supplementary Material). This semi-haplotype is frequently found in other Mediterranean populations but some combinations in which this haplotype appears in combination with class I alleles are specific of Georgian population i.e.: (A*68-B*15)-DRB1*01:01-DQB1*05:01 and HLA-(A*68-B*35)-DRB1*01:01-DQB1*05:01, see Table 2, Supplementary Material [10–12]. It is remarkable that some of the highest frequency Georgian HLA extended haplotypes obtained in this study are also found in Svan population (a strongly isolated population in the North of Georgia): (A*02-B*51)-DRB1*11:01-DQB1*03:01, (A*02-B*13)-DRB1*07:01-DQB1*02:01 and (A*03-B*35)-DRB1*11:01-DQB1*03:01 [10,12].

Nei's genetic distances (DA) were also calculated among Georgians and 26 other worldwide populations (detailed in Fig. 2 footnote, Supplementary Material); results show that Mediterranean populations like Macedonians, French, Italians and Cretans are the genetically closest populations to Georgians [10]. Neighbour-Joining dendrogram and correspondence analyses further support the Mediterranean relatedness of Georgians as previously shown by DA calculations [10].

Caucasus languages were included within the ancient Dene-Caucasian group of languages (Basques, Caucasians, Athabaskans, Apache Navajo, etc.) [7]. However, we included Caucasus languages in the very old Mediterranean languages substratum (the Usko-Mediterranean languages) talked by the “Usko-Mediterranean peoples” [13–17]. Extant languages of this group are Basque (related or very similar to old Iberian-Tartessian), North African Berber and Caucasus languages; dead Usko-Mediterranean languages are for example ancient Iberian-Tartessian, Etruscan, Minoan Lineal A, Hittite and other Mediterranean ones (Fig. 2, Supplementary Material). They all may have a common origin coming from Sahara/Canary Islands/Iberia Cultural Prehistoric Circle (Fig. 2, Supplementary Material) [15,16].

All genotype data included in this paper are held in <https://www.allelefrequencies.net> and identifier number is 3775. Population is named “Georgia Caucasus Tbilisi” [11].

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We thank Georgian population that participated in this study. This work was supported by grants from the Spanish Ministry of Science and Universities (PI18/00626, PI18/00721) and European FEDER funds.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.humimm.2022.08.005>.

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