

Review Report

Review on the genetic history of Algerians within North African populations from the HLA point of view

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Abstract - This article aims to take stock of knowledge on the history of the human settlement of North Africa and the genetic history of Algerians within North African populations by gathering the most important published results related to HLA allele analysis. These results revealed a strong genetic relationship between studied North African populations (Algeria, Morocco and Tunisia). Such evident genetic affinity between North African populations, also proved by the use of other powerful autosomal markers, agrees with historic data considering North African populations as having similar origins. HLA allele analysis also indicated a genetic link between North African populations (Algeria, Tunisia and Morocco) and the populations of the South-Western Europe particularly the Basques and Spaniards. This would reflect a Neolithic relationship between Iberians and the natives of North Africa (the Berbers). However, other results showed a genetic distinction between samples from North African populations and Middle Eastern populations (Arab-Palestinians, Lebanese's and Jordanians). Beside these results related to Mediterranean populations, the HLA allele variation was analyzed at the world scale showing low genetic differentiations among the three broad continental areas, with no special divergence of Africa.

Keywords: Genetic diversity; Molecular Anthropology; Genetic History; HLA genes; North Africa; Algeria.

History of the human settlement of North Africa

Due to its geographical location, bordered by the Mediterranean Sea in the North and by the Sahara Desert in the South, North Africa has behaved like an anthropological island on the African continent. Thus the exploration of the genetic history of its populations would be interesting.

Although the ancient human occupation of North Africa is widely documented by archaeological and paleo-anthropological sources, the settlement and evolution of human groups in this area remains poorly understood. This is mainly due to the succession of a large number of prehistoric and historical events that have occurred, notably through two intercontinental migration routes; the Suez Isthmus Canal to the East and the Gibraltar Strait to the West connecting, respectively, this region of the Near East and Europe.

Since Paleolithic times, North Africa has been inhabited by different human groups thought to be linked to early modern humans. In this area in particular, Berbers - a term for those people speaking a Berber language (Camps 1980) - is well described since the Capsian (10000 to 4700 BP). They remained in a vast territory extending from the West to Egypt (oasis of Siouah) and the Sahara Desert to the mountainous regions of the Moroccan Atlas (Coudray *et al.* 2009). Currently speaking Berber populations live in a dozen African countries, from the Mediterranean to southern Niger, and the Atlantic Near the Nile (Camps 1981).

In historical times, North Africa was an area of turbulence with many ongoing invasions from the East and West, conquests, and attempts at assimilation. Since the end of the ninth century the North African coastline has been occupied respectively by the Phoenicians, Romans, Vandals and Byzantines, their contribution to Berbers, the natives of North Africa, seems to have been limited (Brett and Fentress 1996). This small demographic contribution of these foreigners would be due to the fact that (1) intermarriages would have been rare because Berbers belonged to a tribal endogamous system and often they were in continuous rejection of the domination of these arrivals, who themselves avoided inter-marriage because of their feeling of superiority as invaders and (2) the majority of foreign arrivals generally left the country after their defeat due to the arrival of a new power (Ben Halima *et al.* 2014).

Moreover, one of the most important facts in the history of this region is the Arab conquest that, occurred during the 7th century, had led to profound cultural, linguistic and religious changes on North African natives, including islamization and arabization have durably determined the fate of Berbers. The last occupations of North Africa, at the time of colonialism, were those of the Europeans: the Portuguese and the Spanish in Morocco; the French in Morocco, Algeria and Tunisia; Italians in Libya and Ottoman Turks, particularly in Egypt. Thus, North Africa is characterized by an extraordinarily complex history of demographic events, which could have some genetic impact on current genetic profile of North African populations.

The status of the overall ethnic structure of contemporary North African populations (Moroccan, Algerian, Tunisian and Libyan), is relatively similar. According to [Ben Halima et al. 2014, 2015](#), each of these populations is composed of a general (Arab-Berber) Arabic-speaking group (a mixture mainly between Berber and Arab) and some Berber groups who often speak both Berber and Arabic languages. Although these Berber groups are respectively important in Morocco and Algeria and moderate in Libya, they are few and small in Tunisia. Today in Algeria, the Berbers represent 15 to 33% whose Berber language (Tamazight) is composed of several different dialects, the most important of which are: Kabyle, Chaoui, Mozabite and Touareg, the most indisputable criterion for identifying these people as their Language ([Danver 2015](#); [Abdeli and Benhassine 2019](#)).

In recent years, several studies using classical markers (blood types, serum proteins, etc.) were conducted to explore the genetic history of North African populations (e.g., [Chaabani and Cox 1988](#), [Bosch et al. 1997](#); [Lefevre-Witier et al. 2006](#); [Coudray et al. 2006](#); [Aouar et al. 2012](#); [Ben Halima et al. 2015](#)). Many other studies were carried out using different molecular markers STR, SNP, mtDNA, Chromosome Y, Chromosome X, etc.) (e.g., [Chaabani et al. 1989](#); [Arnaiz-Villena et al. 1995](#); [Côte -Real et al. 1996](#) ; [Ivanova et al. 1999](#); [Macaulay et al. 1999](#); [Bosch et al. 2000](#) ; [Comas et al. 2000](#) ; [Plaza et al. 2003](#); [Arredi et al. 2004](#); [Bahri et al. 2008, 2014](#); [Robino et al. 2008](#); [Vermeulen et al. 2009](#); [Bekada et al. 2010, 2013, 2015](#) ; [El Moncer et al. 2010](#); [González-Pérez et al. 2010](#) ; [Pereira et al. 2010](#); [Henn et al. 2012](#); [Ben Halima et al. 2014](#); [Triki-Fendri et al. 2013, 2015](#); [Amir et al. 2015](#) ; [Solé-Morata et al. 2017](#); [Badache et al. 2019](#)).

In addition, several works were done on the genetic characterization of North African populations using the analysis of the HLA gene frequencies. In fact, this highly polymorphic HLA system is very informative for anthropological studies thanks to the patterns of its variation, which could reveal spatial and demographic expansions of the human population that would have occurred in the past. It is also known for its discriminatory force between individuals and populations (due to the high number of alleles for each locus). Moreover, positions between estimated populations based on frequency data for all HLA loci are strongly correlated with geographic distances (Sanchez-Mazas *et al.* 2011). However, recent studies confirm the natural selection acting on the evolution of HLA polymorphism and show that this selection extends beyond the heterozygous advantage model and has operated from ancient to very recent time scales and has resulted in recent changes in allele frequencies (Lindo *et al.* 2016; Meyer *et al.* 2018).

The major purpose of this article is to review the results of the analyses of HLA genes in the different North African populations, to summarize the genetic diversity between the different geographical regions and linguistic groups in North Africa, and to deduce some conclusions on the genetic history of Algerians within the other North African and neighboring populations. Owing to the high number of published works, it is not possible to present all published results and/or conclusions. Therefore, only the more informative ones deduced from the exploration of quite large samples were cited and considered in the discussion. The ambition here was to draw up a provisional state of what is known, in order to serve as a basis for subsequent researchers.

Current status of the genetic differentiation of Algerian population according to HLA system

In order to present and discuss results and conclusions of selected works on the distribution of HLA genes in Algerians within North Africans and neighboring Mediterranean populations, I have followed three levels of the hierarchy: - genetic characterization of the Algerian population and its affinity with the other North African populations, - genetic relationship between North Africans and Southern Europeans, and - genetic relationship between North African and Middle East populations.

Genetic affinity between North African populations

The genetic profile of Algerian population and its relationship with those of the other North African populations were determined by the HLA allele variation in several works (El Sawy *et al.* 1984; Izaabel *et al.* 1998; Oumhani *et al.* 2002; Brick *et al.* 2006; Galgani *et al.* 2013; Mahfoudh *et al.* 2013; Hajjej *et al.* 2015, 2016, 2017). The kinship analysis, based on phylogenetic tree genetic distances and multidimensional analyses, revealed a strong genetic relationship between different North African groups (the Algerians, the Moroccans of the region of Jadida, the Moroccans Berber, and Tunisians).

This strong genetic relationship between North African populations revealed by analysis of HLA allele variation was also revealed using other powerful classic markers (GM and RH markers) or molecular markers (Alu and Alu/STR compound systems) the analysis of which showed that when wide areas are considered, no significant differences were obtained among North African populations (Coudray *et al.* 2006; Bahri *et al.* 2008; El Moncer *et al.* 2010, Ben Halima *et al.* 2015). Such genetic homogeneity between North African populations agrees with historic data considering North African populations as having similar origins.

Genetic relationships between North Africans and Southern Europeans

Extensive scientific research on the genetic diversity of HLA Class I and II alleles has been carried out in populations of Northern Africa and certain populations of the Iberian Peninsula in order to determine the genetic relationships between the ethnic groups of the Iberian Peninsula (Spain) and Berbers, the natives of North Africa (the Paleo-North Africans).

Results of serological and molecular polymorphism studies of the HLA-A, -B, -DRB1, -DQA1 and DQB1 alleles in the Algerian and Iberian populations (Bouali *et al.* 1981; Djoulah *et al.* 1994; Arnaiz-Villena *et al.* 1995, 1997, 2002) indicate a genetic link between the populations of the South-Western Europe and that of Algeria. This confirms the evidence that the latter, mainly its Berber component, has a common descent with the Basques and Spaniards, probably reflecting a Neolithic relationship between Iberians and Paleo-North Africans. Similarly, the genetic distance analysis of the HLA DRB1, DQA1 and DQB1 polymorphisms in the population of Morocco

(Izaabel *et al.* 1998) showed that the Moroccan population is close to those of the Spain and Algeria.

In addition, the results of the molecular diversity of Class II genes of the HLA system in three populations in Southern Tunisia compared to the entire population Mediterranean region demonstrate a close genetic relationship between populations of Africa and the North-western and South Western Europe, while the populations of the Eastern Mediterranean region are much more differentiated (Abdennaji Guenounou *et al.* 2006).

Other studies, conducted on Spanish populations (Martinez-Laso *et al.* 1995, Comas *et al.* 1998; Sanchez-Velasco *et al.* 2003), show that allelic frequencies between the Spanish and the Basques do not differ significantly. Comparison with other Mediterranean populations places the Basques and Spaniards closer to the paleo-North African populations than other Europeans. This goes in favor of the Basques being a relative genetic isolate from primitive Iberian/paleo-North African populations.

Genetic relationships between North Africans and Eastern populations

However, with regard to genetic relations between the North African and Eastern populations (especially the Arab populations of the Middle East), the analysis of haplotypes of the HLA system of the various works (Hajje *et al.* 2016, 2015, 2017; Buhler and Sanchez-Mazas 2006), shows a distinction between North Africans (Arabic-speaking and Berber-speaking) and Middle East populations (Arab-Palestinians, Lebanese and Jordanians) despite the depth of Arab incursions and arabization.

Beside these results related particularly to North African and Mediterranean populations, the HLA allele variation was analyzed at the world scale showing high levels of genetic diversity within sub-Saharan Africa and East Asia, and low within Europe, and low genetic differentiations among the three broad continental areas, with no special divergence of Africa (Sanchez-Mazas 2001).

Conclusion

In this report, after a general overview on the history of the human settlement of North Africa and the ethnic composition of North African populations, I have reviewed published anthropogenic data of HLA allele variation in these populations. The comparison of these data with those found in other world populations, particularly the

Mediterranean and Middle-Eastern ones, has recapitulated the genetic position of the populations of North Africa (the Maghreb) among the world populations.

The analysis of the HLA genotyping results and the phylogenetic data of the various studies carried out indicate first, a close genetic link between samples from the Algerian population and those from the neighboring North African populations, including Morocco and Tunisia. The North African ancestral genetic structure clearly observed also in each population sample reflects almost the same migratory flow, in other words, they followed the general evolution of Maghreb demographic movements. This homogeneous genetic pattern due to the fact that North Africa was inhabited by Berber groups (the natives of North Africa) shows that North Africa would be considered a separate geographical and ethnic entity in Africa.

Published results also show a genetic relationship between these populations and populations of South-West Europe in particular those of the Basques and Spaniards. This could be proof that the North Africans, mainly its Paleo-North African population (the Berber component), has a common descent with the Basques and the Spaniards, probably reflecting a prehistoric (Epi-paleolithic) relationship between Iberians and Paleo-North African and supporting the theories of flow during the late Neolithic of trans-Gibraltar genes.

However, North African populations are not genetically close to the Arab populations of the Near East. This confirms that despite the expansion of Arabs in the East and arabization, gene flow from the Arab Peninsula and its impact on North African populations was not really significant.

Moreover, the analysis of the genetic diversity of the HLA system in the populations of North West Africa seems to be rather complex and cannot be studied in isolation without referring to the polymorphism of this system among the European populations, Near Eastern populations and Sub-Saharan populations. In this way beside these results related particularly to North African and Mediterranean populations, the HLA allele variation was analyzed at the world scale showing high levels of genetic diversity within sub-Saharan Africa and East Asia, and low within Europe, and low genetic differentiations among the three broad continental areas, with no special divergence of Africa.

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