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Short population report

HLA in Las Alpujarras Mts., South-East Spain: A *Renaissance* process of population artificial substitution

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ABSTRACT

Spain was invaded in 711 CE by mostly Berber North Africans carrying Muslim religion to a mostly Christian/Catholic Kingdom. A fight to expel Muslims soon started and were apparently driven out of Iberia (Spain) starting in 1492 CE. However, many of these expelled people were of Iberian old ancestry that had become Muslims at Las Alpujarras Mts. (South-East Spain). Also, Muslim North Africans converted to Christianity either remained there or came back after they more definetively were expelled by 1609 CE. Las Alpujarras region was also repopulated by northern Spaniards mostly from Galicia. Our HLA study of present day Alpujarrans shows that typical North Spain and European Atlantic façade HLA extended haplotypes are very frequent in nowadays Las Alpujarras region, i. e.: HLA-(A*29-B*44)-DRB1*07:01-DQA1*02:01-DQB1*02:01 and (A*02-B*27)-DRB1*15:01-DQA1*01:02-DQB1*06:02. It is concluded that repopulation had a noticeable success even in today Alpujarran population.

1. Introduction

By year 711 CE Muslims entered Iberian Peninsula across Gibraltar Strait towards North: they were mostly North African Berbers recently converted by Muslims or just recruited by them [1]. Whether or not "invasion" was provoked by a call for help by one Iberian fraction of rival leaders in conflict is a matter of debate although it is admitted now that Muslim entrance to Iberia was facilitated by nowadays Spaniards (Iberians) and even that was not massive compared with already extant population number [2]. On the other hand, North Africans and Iberians are genetically and culturally related since prehistoric times [3]: Tartessos at West and Los Millares/ El Argar at eastern Iberia and their precursor Megalithic culture at least 5000 years BC [4] were common to both sides of Gibraltar Strait [5,6]. Thus, North African Berbers and Iberians are nowadays difficult to genetically be distinguished [5,6,7]. The Catholic Kings expelled or forced to convert to Catholicism Muslims in Spain, who were both of Iberian and North African ancestry since generations before Muslim "invasion" took place (711 CE). In this context, Las Alpujarras is a secluded mountainous South-East Spanish region bordered by Mediterranean Sea with valleys of difficult access (Fig. 1, Supplementary Material). In a second stage, Muslims were officially and practically expelled from Spain in 3 different stages by 1609, when Royal Decrees were issued by king Phillip III. Another Royal Decree forced to repopulate Las Alpujarras region (Fig. 1, Supplementary Material) by northern Spaniards, mainly from North-West Galicia and neighbouring areas. The success of this repopulation is uncertain, in part due to that many Muslims converted to Christianity and either did not leave or came back from neighbouring North Africa [8,9]. In the present paper we aim to test whether HLA markers typical from North Spain are now frequently found in Las Alpujarras region and test the degree of repopulation and expulsion processes success.

Eighty-five healthy and non-related individuals from main villages of Las Alpujarras region (see Figure 1,Supplemetary Material

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) donated blood for this study after signed consent. Individuals had both grandparents belonging to the same area and spoke Spanish language. They were studied for HLA-A, -B and -C loci by low resolution SSOP method (results not shown), and for HLA-DRB1, -DQA1 and - -DQB1 loci by high resolution SSOP method (Amplicor, Hoffmann La Roche, Basel, Switzerland). HLA-DRB1 and HLA-DQB1 typing was confirmed when necessary by DNA sequencing in a Perkin Elmer 310 automated DNA sequencer (Foster City, CA, USA). Statistical analyses were performed with Arlequin v3.0 software [10] to obtain HLA-DRB1, -DQA1 and -DQB1 allele and haplotypes frequencies and for the population comparison analyses (Tables 1 and 2, Supplementary Material). IMGT 3.1.20 (December 14th, 2018) version was used to analyze data.

Analyzing class II data together with low-resolution class I typing [11], the most frequent Alpujarran extended HLA haplotype was HLA-(A*29-B*44)-DRB1*07:01-DQA1*02:01-DQB1*02:01 (13.52%) (Table 2, Supplementary Material), which is a marker for older West Europeans, including Portuguese [12], Basques [13] and Spaniards from Madridthat is an immigration centre [14]; however, it is absent in North Africans (Algerians) [12]. In summary, it is also frequent in West Atlantic Europe including Irish, southern British and western French, and excluding Scandinavians [11]. This area is mostly coincidental with the Rh-negative blood group highest frequencies area [11]. The second most frequent haplotype (A*02-B*27)-DRB1*15:01-DQA1*01:02-DQB1*06:02 (Table 2, Supplementary Material) was also found in Algerians, Iberians, Basques, British and Cornish (i. e.: European-Atlantic façade) [7,12,15]. Semi-haplotype DRB1*15:01-DQA1*01:02-DQB1*06:02 is the third most frequent in Alpujarran population (Table 2, Supplementary Material). North Africans and Iberians bidirectional prehistoric gene flow may explain that this is a common haplotype to both groups [3,5,6,7,16]. HLA-(A*25-B*18)-DRB1*15:01-DQA1*01:02-DQB1*06:02 (7.65%) and HLA-(A*26-B*38)-DRB1*13:01-DQA1*01:03-DQB1*06:03 (6.47%) haplotypes (Table 2, Supplementary Material) are both probably of ancient Iberian origin. Thus, HLA haplotypes and comparisons with other Mediterranean and European populations by using Neighbour-Joining and Vista analyses [11,17,18] show that Alpujarran relatively secluded population shows frequent North-West Iberian and West European HLA markers in addition to typical Iberian/North African ones. It is concluded that Muslim Alpujarran repopulation by North-West Iberians was probably successful as reflected in present HLA data.

All genotype data included in this paper are held in https://www.allelefrequencies.net and identifier number is 3769. Population is named "Spain Las Alpujarras" [19].

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.humimm.2022.03.009.

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