

Frequency of the C282Y Mutation of Hemochromatosis in Five French Populations

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ABSTRACT: Hereditary hemochromatosis mutation 845A (C282Y) in the HFE gene was recently described, and the C282Y frequencies were reported for various world populations. The aim of this study was to determine the Y allele frequencies of the C282Y mutation for five French populations. The most elevated value (= 5.6%) was obtained for Bretons, in accordance to the hypothesis indicating a Celtic origin of the hereditary hemochromatosis mutation. © 1998 Academic Press

Keywords: hereditary hemochromatosis, C282Y mutation, French populations

INTRODUCTION

Hereditary hemochromatosis is an autosomal recessive disorder characterized by iron overload and a variety of clinical manifestations such as liver cirrhosis, diabetes mellitus, arthropathy, cardiomyopathy and endocrine dysfunctions. Hereditary hemochromatosis is considered to be the most common genetic disease of northern European origin. Simon et al. (1) observed an association between hereditary hemochromatosis and the HLA-A3 and B14 antigens. More recently Feder et al (2) reported a candidate gene for hereditary hemochromatosis called HLA-H [designated now as HFE, according to Mercier et al. (3)]. Homozygosity for a single point mutation 845A (C282Y) was found in 83% of 178 hereditary hemochromatosis patients collected from different clinical centers across USA(4): in 155 healthy American controls the Y allele was found in only 3.2%, corresponding to a carrier frequency of 6.4%. In a recent publication (5), C282Y allelic frequencies were reported in a world wide study, but where France was not represented. We report the results of a study of the HFE codon 282 (C/Y) in five geographic regions in France.

MATERIALS AND METHODS

Samples concerned healthy adults of both sexes, originating from these five regions. Extraction of DNA and PCR amplification was performed as previously described in (6). The PCR product has a constant *RsaI* site producing two fragments of 247 and 140 bp in the normal C allele, and another *RsaI* site in the mutant Y allele generates two fragments at 111 and 29 bp by cleavage of the 140 bp fragment.

RESULTS AND DISCUSSION

Table 1 shows the HFE genotypes and Y allele frequencies in the five French populations, with some variations between them. The population samples were in good agreement with the Hardy-Weinberg equilibrium. In the whole, allelic Y frequency = 3% for France. The most elevated value (= 5.6%) is obtained for Breton peoples, in accordance to the theory of Simon et al. (7) postulating that the geographical distribution of hemochromatosis is similar to the migration pattern of Celtic peoples. In our Breton population percentage of heterozygotes = 11.3%, almost twice the value recently reported (8) in

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another Breton population from Rennes. That percentage of 11.3% corresponds to a theoretical frequency for the disease of about 1 per 314, comparable to previously estimated values reported by Beaumont et al. (9).

The Basques, who are known to differ from neighboring populations in most genetic markers tested (10,11) had the lowest allelic Y frequency

(= 1.6%) compared to other French populations tested. Low Y allelic values are also obtained from French Catalans (= 1.9%), a slightly lower value than that previously reported for Spanish Catalans (5), and from peoples of Grasse (a region near Italy in France) = 2.2%, comparable also to that reported in North Italy (12).

Table 1. *HFE* Genotypes and Y Allele Frequencies in some French Populations

Populations	Towns	Number	<i>HFE</i> genotypes			Y frequencies
			CC	CY	YY	
Bretons	Brest	62	55	7	0	0.0564
	Paris	126	116	10	0	0.0396
Basques	Biarritz	92	89	3	0	0.0163
Catalans	Perpignan	76	73	3	0	0.0197
	Grasse	90	86	4	0	0.0222
Total		446	419	27	0	0.0302

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