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Polymorphism of seroproteins in communities of the Briançons region: comparison with European populations

N. Salis, E. Rabino Massa

Department of Animal and Human Biology, Anthropology Laboratory,
University of Turin – Via Accademia Albertina 13, 10123 Turin, Italy

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Abstract

The present study is an analysis of seroproteins conducted on blood samples of subjects living in mountain communities of the French Western Alps. In particular, the third component of complement (C3), the group specific component (Gc), properdin B factor (Bf), haptoglobin (Hp) and transferrin (Tf) were considered, these being very important markers in human genetics research.

The data for these systems are the first results of the biological study of populations of the Western Alps. They add to our otherwise scanty knowledge about the distribution of these polymorphisms in the populations under study.

The results were compared with those in the literature on European populations, in order to identify origins and microevolutionary processes, as well as biotransformations related to environmental adaptation.

Introduction

Study of the genetic polymorphisms of C3 (third component of complement), Gc (group specific component), Bf (properdin B factor), Hp (haptoglobin) and Tf (transferrin) seroproteins allowed us to define the genetic position of communities of the Briançon region compared to European populations. The study referes to Vallouise, a small valley between Briançon and Embrun, in the French department of Hautes-Alpes, formerly part of the ancient Dauphiné (Cézard, 1981).

The ancient Dauphiné acquired unity and political autonomy under the dynasty of the counts Viennais d'Albon who, in the first half of the XIIth century with George IV, chaged the title of count to that of *Dauphin*. Five administrative territorial units were created to equally divide the contributions to be paid to the *Dauphin*: Briançon, Queyras, Oulx, Valchisone and Casteldelfino (figure 1).

Fig. I - *Ancient Dauphiné*

The last three administrative territorial units passed to the dukedom of Savoy in April 1713 on the basis of the Treaty of Utrecht (Baccon-Bouvet, 1999).

The study of mountain populations is particularly interesting since the inhabitants have been rendered homogeneous by the processes of adaptation to the alpine ecosystem and the long period of endogamy caused by geographical isolation and the virtual absence of immigration.

There is an urgent need to collect data on isolated mountain populations, which risk disappearing or losing the characteristics caused by isolation that make them particularly interesting from the genetic point of view.

Materials and Methods

The sample consisted of 150 adults of both sexes, belonging to families resident in the Vallouise valley for at least two generations.

The genetic typing was carried out on serum supplemented with 0,02% *sodium azide* and preserved at −25°C.

The Gc, C3 and Bf systems were determined by cellulose acetate electrophoresis and subsequent immunofixation with specific anti-Gc, anti-C3 and anti-Bf antisera (Alper et al., 1972; Germenis et al., 1982); the Hp and Tf systems were determined by agarose electrophoresis and subsequent immunofixation with specific anti-Hp and anti-Tf antisera (Smithies, 1955; Smithies, 1957).

The genetic relationships among the mountain populations and those of the Mediterranean region were analysed by *maximum likelihood* and multivariate techniques, principal components and *cluster analysis* (Cavalli Sforza et al., 1967). Analyses based on different methods were used to verify the reproducibility of the results. Specific programs such as Statistica and Phylip v. 3.6 were used for the statistical analyses (Felsenstein, 1989).

Results and Discussion

The genotypes observed in the populations of Vallouise are in agreement with the expected values according to Hardy-Weinberg equilibrium. The Chi^2 and the G tests is not significant for each of the markers tested.

The serum polymorphism analyses revealed only one rare polymorphism for properdin, the S1F variant. The polymorphisms of the other proteins are the commonest ones, even though their allele frequencies are peculiar.

The table I reports the allele frequencies for each system.

		Vallouise N=150	Mean European values
C3	S	0,48	0,80 (Scacchi & al., 1987)
	F	0,52	0,20 (Scacchi & al., 1987)
Gc	I	0,59	0,73 (Spedini., 1966)
	2	0,41	0,27 (Spedini, 1966)
Bf	S	0,58	0,69-0,82 (Davrinche et al., 1981; Kuhn et al.. 1978) in Spedini.1966
	F	0,42	0.18 (Mauff et al. 1975) in Spedini, 1966
Hp	I	0,41	0.40 (Facchini, 1988)
	2	0,59	0,60 (Facchini et al., 1988)
Tf	C	0,98	0,90- 0,98 (Fuciarelli et al., 1997)
	B	0,02	0,02 (Fuciarelli et al., 1997;)
	D	/	0,02 (Fuciarelli et al., 1997)

Table I - *Allele frequencies.*

For example, the low frequency Gc1 (0,59 vs. the European mean of 0,73) places the Vallouise population among low-frequency European populations. Indeed, the value is much lower than the lowest values previously found in Europe: Germans 0,68 and Polish 0,66 (Spedini, 1966). The high frequency of Gc2 (0,40) is exceptional in Europe (mean 0,20), although high values have also been observed in Sweden, Finland and in an area on the eastern slope of the Pyrenees (Constans, 1978). The high values for Gc2 and C3F (0,57 vs. the European mean of 0,20; Scacchi, 1987) could represent the upper limits for European populations.

As regards properdin, the frequency of BfS (0,58) differentiates Vallouise from other French populations, with frequencies of 0,81 (Hauptman, 1977) and 0,70 (North, 1981); in fact, it is closer to Sardinian, North African and French Basque populations (from Gruppioni, 1993).

The Hp frequencies found in the Vallouise sample are in good agreement with those already known for Europe, show-ing a frequency of the Hp2 allele higher than the Hp1 allele, 0,4 with a slight tendency toward lower frequencies in the mountain communities. The geographical distribution of the Hp1 allele seems to confirm the hypothesis of an increasing east-west and north-south gradient (De Stefano et al., 1987).

Gene frequencies of TfC and TfB in the Vallouise sample are similar to values reported from different European populations, although the frequencies show slight and non-significant differences.

The results can probably be interpreted as the combined effect of drift and very low local gene flow.

Comparison with other populations

Our results were compared with literature data for populations from northern Europe and the Mediterranean area in order to identify the origin and microevolutionary processes of the Vallouise population, as well as biotransformations related to environmental adaptations.

In all the figures (2, 3 and 4), the Vallouise population is separate from the other Mediterranean and European populations (which form groups), thus confirming its genetic peculiarity.

The decision to carry out different types of analyses made it possible to compare the different trees. This showed that, although based on different principles and methods, the trees exhibit good reproducibility of the different clusters.

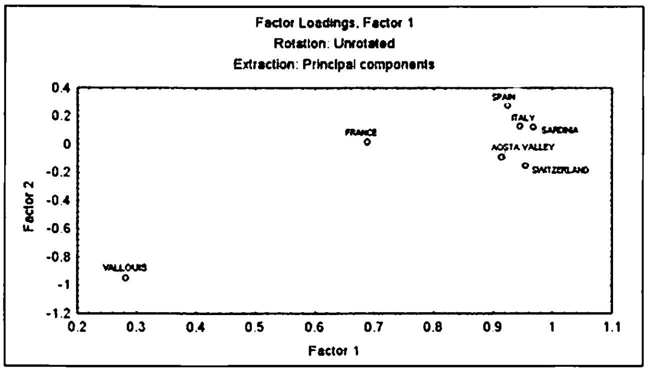

Fig. 2 - *Principal components analysis*

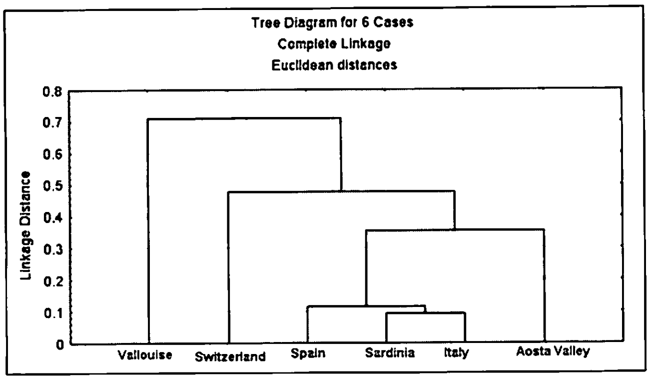

Fig. 3 - *Cluster analysis*

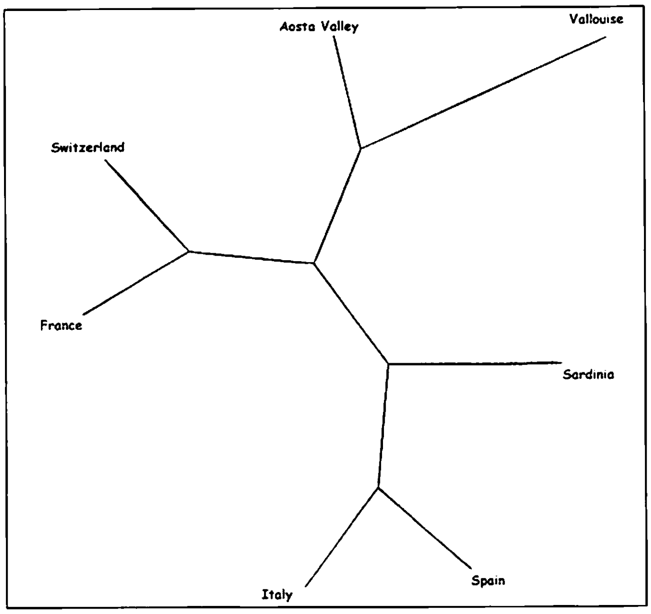

Fig. 4 - *Dendrogram obtained according to the maximum likelihood principle.*

Conclusions

The data for these systems are the first results of the biological study of populations of the Western Alps. They add to our otherwise scanty knowledge about the distribution of these polymorphisms in the populations under study.
In general, the results for these mountain communities agree with the literature data for European populations, even though there are peculiar allele frequencies. Comparison with other populations of Europe generally shows that the populations of Vallouise present mainly European characteristics. However, some peculiar aspects have emerged, probably attributable to the strong geographical isolation.
The genetic distance between Vallouise and the other populations (0,05741) was rather high, indicating that the community of this small valley can be considered a genetic isolate.
The present study demonstrated that the allele frequencies of these five polymorphisms adequately describe the genetic structure of the study population, revealing its peculiar characteristics.

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