

# Seroproteins in alpine populations

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KEY WORDS: mountain communities, seroproteins, electrophoresis

## Abstract

**The present study is part of a research project on the genetic structure of mountain communities in the Italian-French Alps and the Madonie Mountains of Sicily. Here we analyse several seroproteins that have proved to be important markers in human genetics research: third component of complement (C3), group specific component (Gc) and properdin B factor (Bf). The results were compared with literature data on European populations, particularly of the Mediterranean area, in order to identify origins, microevolutionary processes and biotransformations related to environmental adaptation.**

## Introduction

Rural mountain populations have attracted the interest of anthropologists, who try to identify specific characteristics of the populations related to processes of adaptation to the mountain ecosystem.

The aim of this study is to investigate the genetic characteristics of rural populations in order to determine their peculiarities and their position with respect to other European populations. In this way, we can attempt to reconstruct their origins and migration routes.

The mountain communities are Valgrisenche and La Thuile (Valle d'Aosta, Italy) and Vallouise (Briançonnais, France) in the Italian-French Alps, and Valledolmo in the Madonie Mountains, north-western Sicily.

Valgrisenche and La Thuile are two communities situated in the homonymous valleys formed by the Dora Baltea River in Valle d'Aosta (a small Italian region).

Vallouise is a small French valley between Briançon and Embrun (in the Hautes-Alpes department) which extends to the Italian border in a mountainous region crossed by

the Durance and Drach rivers. Geographically, it belongs to the Briançonnais and has the typical topographical and climatic characteristics of that region.

Valledolmo is a small rural town on the western side of the Madonie Mountains, one of the most important geographical barriers in Sicily. In the past, this high-altitude community had limited communication and exchange with lowland populations, which led to isolation.

These mountain communities are particularly interesting from a genetic point of view, since they have been rendered homogeneous by the high degree of endogamy caused by geographical isolation and virtual absence of immigration; at present, they risk losing their most peculiar genetic characteristics because of progressive abandonment of the mountain.

We performed a genetic characterization of these communities using three plasma polymorphisms that are very important markers in human genetics research: third factor of complement (C3), group specific component (Gc) and properdin B factor (Bf). Previous studies have demonstrated the usefulness of seroprotein markers in reconstructing the biological history of these populations, including historically confirmed contacts with other peoples.

## Sample, materials and methods

The sample consisted of 349 adults of both sexes, native to the communities for at least two generations: 85 from Vallouise, 140 from Valle d'Aosta and 124 from Valledolmo. The genetic typing was carried out on serum supplemented with 0.02% sodium azide (N<sub>3</sub>Na) and preserved at -20°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 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 Systat and Phylip v. 3.6 were used for the statistical analyses (Felsenstein, 1989).

**Results and discussion**

The observed phenotype frequencies for Vallouise and Valledolmo agree well with the expected frequencies based on the Hardy-Weinberg law, indicating that the samples are in genetic equilibrium for all the markers.

For Valle d'Aosta, the allele frequencies of C3 and Bf agree with the expected values, while those of Gc differ significantly from HW equilibrium, probably due to an excess of homozygosis.

Only one rare polymorphism was found, the S1F variant of properdin (Vallouise). The polymorphisms of the other proteins are the commonest ones, even though their allele frequencies are peculiar and in some cases differ significantly from the European mean.

Table 1 reports the allele frequencies of the mountain populations for each seroprotein system.

		Vallouise	Valle d'Aosta	Valledolmo	Media Europea
C3	S	0,43	0,66	0,45	0,80
	F	0,57	0,34	0,55	0,20
Gc	1	0,59	0,71	0,55	0,73
	2	0,41	0,29	0,45	0,27
Bf	S	0,58	0,56	0,39	0,69-0,82
	F	0,42	0,44	0,61	0,18

Table 1 - Allele frequencies

The values of C3 in Vallouise and Valledolmo do not agree with the European mean; the frequency of C3S is 80% in most European populations while that of C3F is 20% (Seth et al., 1976).

The frequencies of Gc1 in Vallouise and Valledolmo are similar to the values in low-frequency European populations, even with respect to the lowest European frequencies, found in some populations in Poland and Germany (Kobiela et al., 1964; Spedini, 1966).

The frequency of Gc2 in Vallouise and Valledolmo is higher than the European mean, which ranges between 20 and 30% (Mourant et al., 1976); high values are exceptional in Europe, being found only in Sweden, Finland and an area on the eastern side of the Pyrenees (Constans, 1978).

In Vallouise and Valle d'Aosta, the frequency of BfS is significantly lower than the mean value for Europe, where the range is 0.69-0.82 except for the Basques (around 0.56) (Davrinche et al., 1981; Kuhn et al., 1978).

All the mountain communities have a very high frequency of BfF, whose mean value in Europe is around 0.18.

In Valledolmo, the allele frequencies of properdin are close to those of African populations, whose mean values are 0.28 for BfS and 0.65 for BfF (Mauff et al., 1976).

**Comparison with other populations**

The genetic relationships among the mountain communities and other populations of Europe and the Mediterranean region were analysed by means of multivariate analyses and other statistical procedures. Figure 1 shows the results of principal components analysis. Vallouise and Valledolmo are differentiated from the other populations, especially in comparison with France and Italy; more specifically, the two communities form a group that is separated from the other populations of Europe and the Mediterranean area.

The dendrogram in figure 2 was created to visualize the affinities and genetic divergences of the populations. Four main groupings are evident: one with Vallouise and Valledolmo; two groupings including European populations of the Mediterranean area, respectively Spain, Italy, Sardinia, and Corsica, Alia, Greece; one with Valle d'Aosta and France.

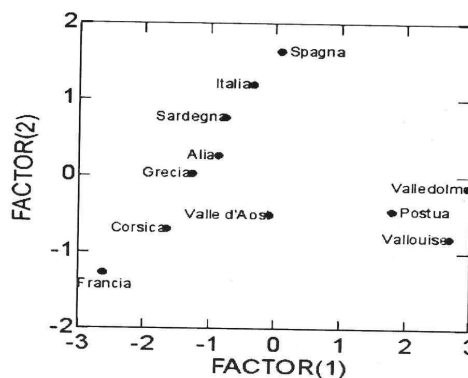


Fig. 1 - Principal components analysis

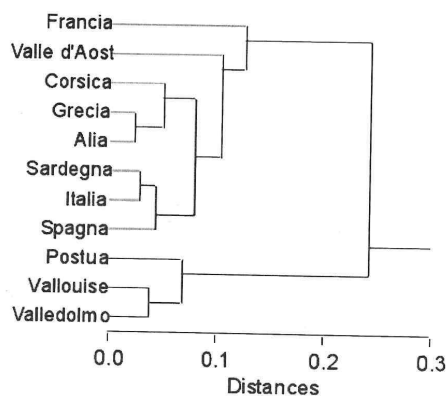


Fig. 2 - Cluster analysis

We also constructed a tree diagram according to the maximum likelihood (maximum similarity) principle (Fig. 3).

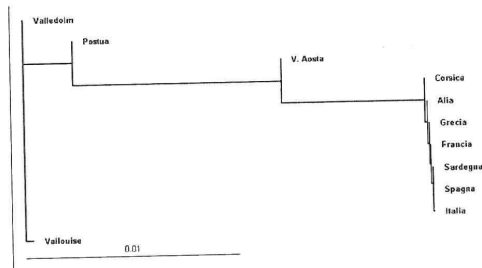


Fig. 3 - Dendrogram based on the maximum similarity principle

The groupings are substantially the same as before. Analysis of the genetic distances among the mountain communities and the other populations showed that the difference between the two Valle d'Aosta communities is negligible (0.01642), underlining the fact that the valleys of this region are not genetically isolated. However, Vallouise presents a rather high genetic distance from the other populations (0.05741), indicating that this small valley can be considered a genetic isolate. 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.

### Conclusions

The seroprotein analyses revealed a single rare polymorphism for properdin (the SIF variant) in the Vallouise sample, while the polymorphisms of the other proteins are the commonest ones, even though their allele frequencies are peculiar. The results can probably be attributed to the combined effects of drift and very limited local gene flow. The mountain communities exhibit mainly European seroprotein characteristics, albeit with some peculiar aspects referable to strong geographical isolation.

The study of plasma polymorphisms, such as C3, Gc and Bf, can provide important information about the genetic structure of populations; indeed, these polymorphisms are good markers to calculate genetic distances and to evaluate relationships among populations. The present study has shown that the distribution of the allele frequencies of these three polymorphisms can satisfactorily discriminate Alpine populations from Mediterranean ones and can identify small communities with peculiar characteristics, like Vallouise.

On the basis of these preliminary results, we will extend our research to other isolated Alpine populations to evaluate microevolutionary processes related to adaptation to the mountain ecosystem.

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