Cardiovascular disease is a general term defining not only ischemic heart disease and stroke, but also venous thrombosis.1

In this complex disease multiple genes with varying effects are involved. Among them, the factor V Leiden (FVL) and the PTG20210A mutations predispose individuals to a substantial increase risk of venous and arterial thrombosis. In addition, the C677T in the MTHFR gene has a direct effect on the level of homocysteine, which in turn is a well-established cause of vascular disease.4

As genes that predispose people to common diseases are more readily identified in isolated rather than diverse continental populations,5 we compared the allelic frequencies of these three mutations, genotyped as previously described,6,8 between 283 unrelated individuals from the Basque country in the north of Spain (all with at least four generations of family names of Basque origin) and 204 unrelated Spanish blood donors. Only 9 out of 283 Basques were heterozygous for the PTG20210A mutation, which corresponds to a prevalence of 3.2% (95% CI: 0.46-5.59). We did not find FVL mutation carriers in this sample. The prevalence of the C677T mutation was 50.6% (95% CI: 44.2-57.0) heterozygotes and 14.9% (95% CI: 10.3-19.4) homozygotes. The allelic frequencies of the PTG20210A and the C677T mutations were both in Hardy-Weinberg equilibrium.

We calculated that the prevalence of FVL in the Basque sample presents a difference of 2.9% (95% CI: 0.6-5.3) with our Spanish population, corresponding to a p=0.0057. For the PTG20210A the difference was 3.3% (95% CI: 0.0-6.73), and although this was not statistically significant it was lower. The difference in the PTG20210A mutation in this isolated population strongly supports the hypothesis that this mutation originated before the isolation of the Basques from other populations.6,9

Table 1. Comparison of the different prevalences (%) of the analyzed mutations between Basque and Spanish populations by a Fisher’s exact test and Chi-squared test.

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Spanish (%)</th>
<th>Basque (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVL</td>
<td>2.9 (6/204)</td>
<td>0.0 (0/283)</td>
<td>p=0.0057</td>
</tr>
<tr>
<td>PTG20210A</td>
<td>6.5 (13/201)</td>
<td>3.2 (9/283)</td>
<td>N.S.</td>
</tr>
<tr>
<td>C677T heterozygous</td>
<td>47.2 (97/204)</td>
<td>50.7 (119/235)</td>
<td>N.S.</td>
</tr>
<tr>
<td>C677T homozygous</td>
<td>17.5 (36/204)</td>
<td>14.9 (35/235)</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

N.S.: not significant.

In conclusion, given the many difficulties that can hamper genetic dissection of complex traits such as thrombosis, it is advantageous to restrict the patient population to a specific ethnic group, such as the Basques. This approach has been successfully applied to other isolated populations for a variety of complex diseases.1

José Manuel Soria, M ontserrat Baiget, Luis Cañas,o María Isabel Tejada, Guimer P erez-Nanclares, Jordi Fontcuberta

*Hemostasis and Thrombosis Unit. Department of Hematology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; †Genetic Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; ‡Endocrinology and Diabetes Research Group, Hospital de Cruces, Barakaldo, Spain; § Genetic Unit, Hospital de Basurto, Bilbao, Spain

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Correspondence: José Manuel Soria Fernández, Ph.D., Unitat d’Hemostasi i Trombosi. Departament d’Hematologia, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain.
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