**ONLINE MUTATION REPORT**

Ser19→Trp polymorphism within the apolipoprotein AV gene in hypertriglyceridaemic people

M Vrablík, A Hořínek, R Češka, V Adámková, R Poledne, J A Hubacek

**SUBJECTS AND METHODS**

Cardiovascular disease (CVD) is the most common cause of death in industrialised countries. Raised plasma triglycerides (TGs) have been shown to be an independent risk factor for CVD. Recently, a new gene designated *APOAV* has been identified in the *APOAI/APOCIII/APOAV* gene cluster by comparative sequencing by Pennacchio *et al.* The human *APOAV* gene consists of four exons and codes for a 369 amino acid protein, which is only expressed in the liver. Generation of transgenic and knockout mice assessed the importance of this gene for plasma TG determination. The transgenic mice show decreased and the knockout mice increased concentrations of plasma TGs, whereas the plasma cholesterol concentrations are not influenced significantly.

In the human *APOAV* gene, T-1131C (originally referred to as SNP3) and Ser19→Trp polymorphisms have been detected. Associations between these polymorphisms and TG concentrations have been found in healthy, non-smoking subjects not receiving lipid lowering medication as well as in different population samples. The C allele of the T-1131C polymorphism was found to be associated with extreme concentrations of plasma TGs.

The aim of this study was to evaluate the putative association of a common *APOAV* variation (Ser19→Trp) in those with extreme plasma TG concentrations.

**RESULTS AND DISCUSSION**

Heteroduplex analysis of the *LPL* gene did not detect any mutation in the 83 hypertriglyceridaemic patients; neither in the population nor in patient groups was *APOAV* polymorphism associated with diabetes.

The pattern of distribution of *APOAV* genotypes is summarised in table 1. The frequency of carriers of the Ser/Trp and Trp/Trp genotypes was much higher (p<0.0001) compared to the population sample. This suggested a strong association between the Ser19→Trp polymorphism in the *APOAV* gene and extreme concentrations of plasma triglycerides.

**Key points**

- A new apolipoprotein AV gene has been identified, which is expressed just in the liver. Generation of transgenic and knockout mice assessed the importance of apoAV for plasma triglyceride determination. Associations between T-1131→C and Ser19→Trp polymorphisms and plasma triglycerides have been found in population samples.

- This prompted us to study the Ser19→Trp polymorphism in 83 unrelated patients with extreme lipid indices (triglycerides of 20.4 (SD 12.8) mmol/l and total cholesterol of 10.4 (SD 3.7) mmol/l) and in a control group consisting of 2559 unrelated white people.

- In patients, the frequency of carriers of the Ser/Trp and Trp/Trp genotypes was much higher (30.1% vs 14.1%, p<0.0001) compared to the population sample. This suggested a strong association between the Ser19→Trp polymorphism in the *APOAV* gene and extreme concentrations of plasma triglycerides.

**Abbreviations:** *APOAV*, apolipoprotein AV; *CVD*, cardiovascular disease; *LPL*, lipoprotein lipase; *TGs*, triglycerides;
Pennacchio et al. have found a higher frequency (23% vs. 9.5%) of Trp19 carriers in 82 male patients with plasma TG >90% compared to 82 patients from the opposite end of the distribution curve (TG <10%). A similar association was found in the groups of 50 and 50 females selected. A similar association was found in the groups of 50 and 50 females selected according to the same criteria (22% vs. 0%).

In the same groups of 83 patients and 2559 controls, we have previously detected a strong association (p<0.0001) between T-1131C and C-1131C genotypes and extreme concentrations of plasma TGs. There is no linkage disequilibrium between rare alleles of both APOAV polymorphisms, thus the effect of both polymorphisms is independent.

Although the exact mechanism by which APOAV influences the plasma concentrations of TGs is unknown, the present results support the notion that this newly described gene is one of the most important genetic determinants of plasma triglycerides detected so far.

Our study included 83 unrelated hypertriglyceridaemic patients and 2559 representatively selected controls from the same population and suggested a strong association between the Ser19→Trp polymorphism in the APOAV gene and extreme concentrations of plasma TGs.

### Table 1

<table>
<thead>
<tr>
<th>Ser19→Trp polymorphism</th>
<th>Controls (2559)</th>
<th>Patients (83)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
</tr>
<tr>
<td>Ser/Ser</td>
<td>2198</td>
<td>85.9</td>
</tr>
<tr>
<td>Ser/Trp</td>
<td>352</td>
<td>13.8</td>
</tr>
<tr>
<td>Trp/Trp</td>
<td>9</td>
<td>0.3</td>
</tr>
</tbody>
</table>

### ACKNOWLEDGEMENTS

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### REFERENCES

Ser19→Trp polymorphism within the apolipoprotein AV gene in hypertriglyceridaemic people
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