Reviewer's report

Title: Familial hypercholesterolemia in St.-Petersburg: the known and novel mutations found in the LDL receptor gene.

Version: 1 Date: 1 November 2004

Reviewer: Kimmo Kontula

Reviewer's report:

General
This report describes the LDL receptor mutation spectrum underlying familial hypercholesterolemia (FH) in St. Petersburg region, Russia. While the study does not provide fundamentally new ideas on molecular pathogenesis of FH, it represents an interesting contribution to population genetics of FH, as previous data on molecular genetics of FHG in Russia were scanty and fragmentary. The data of Zakharova et al. support the molecular heterogeneity in FH and tend to exclude occurrence of any founder-like "Slavic FH mutation".

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Introduction: add a couple of sentences to remind that, in addition to FH and familial defective apoB, some other forms of monogenic hypercholesterolemia have recently been described.

2. Please give some phenotypic details on the group of the 45 FH probands selected (lipid levels, coronary artery disease etc.). Criteria: "Highly elevated plasma total cholesterol and LDL-cholesterol" may also require some sharpening.

3. The authors should more clearly state that a formal proof of the pathogenic role of the two novel point mutations require functional studies to be carried out.

4. Mutations previously found in Denmark, Finland and other nearby countries: Did the authors try to find out the ethnic origin of their families?

5. Some of the Figures are rather trivial and (e.g. Fig. 2 or 3) and could be deleted.

6. Discussion: The reader may have some difficulties in trying to figure out how many and what type of FH mutations were previously identified in Russia and which were the new ones. A summary paragraph collecting the present and previous data (from the same and other groups) and taking into account geographical information in Russia would be of value.

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Discretionary Revisions (which the author can choose to ignore)
What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:

None