Reviewer's report

Title: High Resolution Melt analysis for mutation screening in PKD1 and PKD2.

Version: 1 Date: 1 June 2011

Reviewer: Jitka Stekrova

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The manuscript High Resolution Melt analysis for mutation screening in PKD1 and PKD2 describes the detection of PKD mutations in ADPKD patients. The question posed by the authors is well defined, the used methods are appropriate.

However, the major revisions must be added before publication:

1) in „Methods“: There should be concise characteristics of the tested group – at least gender, age, family history, renal function,

2) in „Methods“: There should be addended the PKDB database in methods (paragraph- „Sequence variation analysis and classification“ (https://portal.biobase-international.com/hgmd/pro/start.php)

3) in Results - paragraph 3: The number of new detected mutations must be corrected. „Of these 28 variants, 9(7 is not correct) were already described in literature. Of the 18 (20 was not correct) sequence variants,

4) in Results - paragraph 3: Mutations have to be described according to „Nomenclature for the description of sequence variants“ (http://www.hgvs.org/mutnomen/) Example: First sentence of the paragraph: „The first in frame deletion, p.Thr2337_Phe2338del (instead of p.del2337_2338ThrPhe),….. Second sentence of the paragraph: „The second deletion, p.Leu2433del (instead of p.del2433Leu).

5) in „Results“ – paragraph 4, sentence: „Since leucine 2433 is a conserved residue (in chicken, frog and takifugu but not in mouse or rat),….“ the number of compared species should be enlarged (not only vertebral).

6) in „Results“ – paragraph 4, last sentence: „The two in frame deletions were not found in 100 control chromosomes tested.“ Control group should be enlarged- at least 100 individuals (200 chromosomes) and the description of the selection of control group should be added. The enlargement of kontrol group is necessary for the establishment of probably pathogenic mutations.

7) „Results“ - paragraph 5: the description of the mutation must be corrected according „Nomenclature for the description of sequence variants“ (http://www.hgvs.org/mutnomen/) Example: „The intronic sequence variation c.7210-5C>G (there is incorrect IVS18-5C>G) was predicted to alter splicing.“ All other splice-site mutations have to be corrected in manuscript and tables.
8) The short description of phenotype should be added to identified mutations (at least age of end stage renal disease)

The segregation of mutation in the affected family must be finished. The segregation is the most important in families with probably pathogenic mutations.

9) Table 1: The description of all mutations must be corrected according to „Nomenclature for the description of sequence variants“ (http://www.hgvs.org/mutnomen/)

10) Table 1: References should be changed in: mutation c.7108T>A - Ref. 11 (10 is incorrect); mutation c.9859_9861delCTC - Ref. 32 (30 is incorrect); mutation c.11512C>T - Ref. 43 (31 is incorrect); mutation IVS44+2T>C (correction according to nomenclature) - Ref. 20 (22 is incorrect); mutation c.2599C>T of the PKD2 gene – reference Torra et al. Am j Kidney Dis. 36(4), 2000 (32 is incorrect); References should be corrected in all manuscript and tables.

11) Table 1: Mutation c.7298_7300delTGC was already described: Xu et al. Am J Physiol Renal Physiol 292: F930-F945, 2007; Mutation c.11249G>A was already described: Ref. 30. The number of new mutations has to be corrected in all manuscript.


Minor Essential Revisions

13) in „Figures legends“ – Figure 1: you had better DNA change: „The three fragments with the red curves carry the same sequence variant p.Ala1555Ala (c.4665A>C), which is different from the fragment with the green curve p.Thr1558Thr (c.4674G>A).“