Reviewer's report

Title: Expanded carrier screening and preimplantation genetic diagnosis in a couple who delivered a baby affected with congenital factor VII deficiency

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Reviewer: Danya Vears

Reviewer's report:

Overall, this paper provides a valuable contribution by detailing the diagnostic pathway of a high-risk couple through an array of reproductive genetic tests. The multi-step strategy described in the manuscript has the potential to improve high-risk couples' chances of giving birth to a healthy child. However, there are a few aspects of the paper that require attention before it is suitable for publication.

As a general comment, the authors would benefit considerably by utilizing a professional language editing service. In its current form, the manuscript contains a large number of stylistic and grammatical errors, which often negatively affects the clarity of the manuscript.

Detailed comments:

Line 43: One of the references is too old, dating to 1985, when many of the currently known recessive disorders were not yet characterized. This source should not be relied upon when assessing the overall burden of recessive diseases.

Lines 50-53: Given the context, the authors use a very conservative estimate (1-2%) for the proportion of at-risk couples in the general population. The CGT Igenomix ECS test, which was utilized in this study, identifies 5% of all couples as carriers (Martin et al. 2015; Website of Igenomix).

Line 80: In general, we suggest that the authors use 'both members of the couple' or 'both reproductive parents' throughout the paper, as opposed to 'two couples', or 'both couples'. This would avoid linguistic confusion over the number of couple(s) tested.

Line 81: While the authors discuss a 'customized panel', based on the number of genes and disorders they provide, it appears that the panel they used was virtually identical to the standard
CGT Igenomix panel. Therefore, we recommend that they mention how customization was performed.

Line 85: A verb is missing at the end of the sentence

Line 103: For the reader unfamiliar with Ion PGM platform, could the authors briefly mention which chromosomal aneuploidies are tested?

Line 129: Do the authors mean that embryo number 3 was not a carrier of congenital FVII deficiency or CF, rather than not affected?

Lines 139-143: The principal added value of this manuscript is a detailed description of the diagnostic trajectory undertaken by a high-risk couple. To form a more comprehensive opinion about the merits and disadvantages of the entire pathway, many readers would probably find it helpful if the authors also briefly discussed issues such as: genetic counseling, psychological challenges (if experienced by the couple) and costs. Alternatively, these issues can be reflected upon in the Discussion.

Line 152: This should state "caused by mutations in the F7 gene".

Lines 178-180: The statement that the proposed protocol can decrease workload and costs cannot be directly inferred from the preceding discussion. We therefore invite the authors to further elaborate on how they arrived at this conclusion.

Are the methods appropriate and well described?  
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?  
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?  
If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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