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: Imran Haque

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The paper is a case study describing a single instance of PGD/PGS applied to a double-carrier couple, with parents heterozygous for pathogenic variants in both F7 (father compound het) and CFTR. Using WGA'd material from trophectoderm biopsy, the authors perform PGD for both the F7 and CFTR loci in conjunction with PGS for aneuploidy, with followup by amniocentesis and Sanger sequencing.

In general, this seems like nice work with appropriate followup (and a good result for the couple), but is not groundbreaking: the authors apply well-understood, off-the-shelf kits for WGA, mutation detection, STR locus sizing, and aneuploidy detection, and apply them to more than one condition at a time. My main concern with the paper is whether or not it contributes novelty to the literature.

PGD was clearly valuable in this case (carrier/compound het couple for F7 and carrier/carrier couple for CFTR). I would suggest that the conclusion or message of the paper be retargeted at this point: if PGD were not performed, we would expect a 3/8 chance of a fetus unaffected by either condition (50% chance unaffected for F7 times 75% chance unaffected by CF), so in this case the use of PGD significantly improved the reproductive outcome for the couple.

However, in order for the study to actually provide generalizable information to the scientific literature beyond "we did this", at the very least more information needs to be provided about the methods. In particular, since the assay relies on PCR enrichment for a variety of loci, primer sequences used should be provided for each locus analyzed. Additionally, there are references to a variety of "standard" (L104) or "previous" (L85) methods, with very little description of methods in this paper. It would be valuable to include a brief summary of the analysis performed for aneuploidy analysis by PGM as well as the bioinformatics performed for ECS (in particular, filtering and QC criteria).
Finally, there are a number of typographical and grammatical errors in the paper that should be corrected before final acceptance/publication. A short list of examples (certainly incomplete): "challanging" L48; "who are" at L51 should be "are"; "both were carrier of another gene" L60 should be "both were carriers of pathogenic variants in another gene"; "is a carrier" L73 vs "harbors a heterozygous mutation" L74; "previos" L85; "form" L117; "crypt recessive" L158; "necesscity" L171;

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

No

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

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