Reviewer's report

Title: Clinical Outcome of Preimplantation Genetic Diagnosis and Screening with the Use of Massively Parallel Sequencing

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Reviewer: Montserrat Barragan

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The authors report a clinical outcomes evaluation and accuracy of Massive Parallel Sequencing (MPS)-based Preimplantation genetic diagnosis/screening (PGD/PGS) comparing with SNP array-based PGD/PGS. This study provides an evaluation of 1,531 blastocysts, among 394 couples presenting high risk of chromosomal abnormalities, either carriers of translocations or patients with advanced maternal age (AMA) and/or repeated miscarriage (RM). The clinical outcomes analysed are implantation, clinical pregnancy and miscarriage rates. Given the fact that this technique is already offered by several Fertility clinics and that it has been recently reported the first birth after MPS-PGD, this work is useful to notice that the technique seems to be at least safer than the already used PGD/PGS techniques.

The manuscript is well-written.

- Major Compulsory Revisions

1. As authors point out, “MPS is entering human medicine as a precise and comprehensive genetic analysis technique”. Moreover, it is clearly described as a powerful technique to address mitochondrial DNA sequencing, as well as genomic DNA sequencing.

On page 4, “Analysis” section, first paragraph, authors describe the coverage of 98.1% of mitochondrial DNA. However, there is no mention about results regarding this.

Is there any information about mitochondrial abnormalities in these samples?

2. On page 5, 2nd and 3rd paragraphs of “Analysis” section describe table 1 and 2. However, I did not find how to understand if there is some relationship between genomic alterations and couples that could not enter to transfer cycles. I think this is an important issue to address in the mean text and discussion, as it would be useful to set some expectations around this for the readers.

3. In the first paragraph of the “Discussion” section, authors say that “It illustrates that MPS based PGD/PGS is applicable not only for the genetically high risk populations but also for the genetically low risk populations”. In my opinion, it could be necessary to show some extra correlations between carriers and alteration results, for instance, from the couples transferred, how many present chromosomally abnormal phenotype, AMA and/or RM?
Discretionary Revisions
1. Changing MPS (Massively Parallel Sequencing) by NGS (Next Generation Sequencing) may increase the chance of increase the number of readers/citations. In Pubmed, there are more than 9000 papers about NGS and around 150 for MPS. In addition, MPS can be confused with Mucopolyssacharid, for instance.

2. I think it is important to refer to the first birth reported to increase the relevance of the work. (Successful Live Birth following Preimplantation Genetic Diagnosis for Phenylketonuria in Day 3 Embryos by Specific Mutation Analysis and Elective Single Embryo Transfer. Lavery S, Abdo D, Kotrotsou M, Trew G, Konstantinidis M, Wells D. JIMD Rep. 2013;7:49-54. doi: 10.1007/8904)

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.