CELL-BASED NON-INVASIVE PRENATAL TESTING (CBNIPT) CONFIRMS PREGNANCY WITH AN UNAFFECTED FETUS FOLLOWING PREIMPLANTATION GENETIC TESTING (PGT)

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Abstract Body

Introduction:
The risk of pregnancy with an affected embryo following preimplantation genetic testing (PGT) is small, but the associated consequences severe. Hence, prenatal testing is recommended, but currently the only available option is invasive chorionic villus sampling (CVS), which entails a risk of provoked miscarriage. Here we describe the first case of a couple receiving cell-based non-invasive prenatal testing (cbNIPT) following PGT, as an alternative to CVS.

Materials and methods:
The couple (maternal age 29 and paternal age 32) received PGT due to a maternal pathogenic deletion in *NF1* (c.7907+4_7del) (Figure 1A). Informative short tandem repeats (STRs) for the parents combined with direct mutation analysis were used for embryo diagnosis (Figure 1A). Maternal blood was sampled on the day of CVS. Fetal cells were isolated by ARCEDI Biotech using an in-house developed protocol and classifier. Fetal cells were analyzed using the same STRs used for embryo diagnostics combined with direct mutation detection. CVS and fetal cells were analyzed at separate laboratories.

Results:
Two STRs located 1.7 and 1.3 Mb upstream and downstream, respectively, of NF1 were used (recombination risk of 0.022 percent). Maternal blood sampling and CVS were performed at gestational week 10+5. Two fetal cells were isolated from maternal blood (Figure 1A). One cell showed maternal STR markers only and absence of the deletion, indicating an unaffected fetal cell with allele drop out (ADO) of one or two paternal STR markers (most likely) or a maternal cell with ADO for both STRs and the mutated allele (unlikely) (Figure 1A and B). The second cell proved to be an unaffected fetal cell showing the same profile as the transferred embryo (Figure 1A and B). CVS diagnosed the fetus as unaffected (Figure 1A).

Conclusion:
CbNIPT successfully confirm the genetic non-carrier status of the fetus verified by CVS.

Abstract image

Figure 1

Cell-based non-invasive prenatal testing following preimplantation genetic testing for a maternal pathogenic deletion in *NF1* (c.7907+4_7del). A) flowchart describing the case. B) Short tandem repeat and and direct mutation analysis of isolated and parental cells.