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Fetal aneuploidy with dual-probe fluorescence in situ hybridization analysis in circulating trophoblasts after enrichment using a high-sensitivity microfluidic platform

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Objective

To evaluate a microfluidics-based positive selection technology for isolating circulating trophoblasts (CTs) from peripheral blood of women whose pregnancies are affected by aneuploidy and to evaluate fetal karyotype using fluorescence in situ hybridization (FISH).

Methods

Thirteen 18-ml samples of peripheral blood were collected consecutively from pregnant women whose fetus was affected by aneuploidy. A preservation buffer was added to the collected blood and the specimens were shipped overnight to the testing laboratory at ambient temperature. The whole blood specimen was applied to microfluidic chips coated with either anti-huEpCAM or a proprietary antibody mixture specific to CT surface epitopes. Sample processing was fully automated using the BioFluidica LiquidScan™ system. No pre-processing was necessary. FISH analysis was performed on the isolated cells.

Results

Fetal aneuploidy evaluated included trisomy 21 (n = 5), trisomy 18 (n = 2), trisomy 13 (n = 1), monosomy X (n = 3), 47 XXY (n=1), and triploidy (n = 1). CTs for analysis by FISH were identified in all samples. The average number of mononucleate cells per 1 ml of whole blood was 2.46 (range 0.38–4.63) overall and was 2.98 (range 0.63–5.50) using the proprietary combination of antibodies. FISH results were concordant with the aneuploidy based on other testing in all cases. Multinucleate cells were searched for in the last nine samples and were found in eight (average number: 0.70/ml). The average number of all fetal cells (mononucleated plus multinucleated) was 3.72/ml. The average number of all cells (fetal plus maternal) was 140.23/ml.

Conclusion

Our study demonstrates that the LiquidScan™, a high-sensitivity microfluidic platform, can enrich circulating trophoblasts (mononucleate and multinucleate). FISH can then be used to detect fetal aneuploidy.