Use of low pass whole genome sequencing in clinical cytogenetics, pathogenic cnv detection

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Objective
Low-coverage whole-genome sequencing appears to be a feasible alternative to chromosomal microarray analyses when searching for clinically relevant copy number variations.

Methods
Genome-wide CNV analysis (>50 kb) was performed on a multicenter group of 570 patients using a low-coverage whole-genome sequencing pipeline. These samples were referred for chromosomal analysis; CNVs (i.e., pathogenic CNVs, pCNVs) were classified according to the American College of Medical Genetics and Genomics guidelines.

Results
Overall, a total of 198 abortions, 37 stillbirths, 149 prenatal, and 186 postnatal samples were tested. Our approach yielded results in 549 samples (96.3%). In addition to 119 subjects with aneuploidies, 103 pCNVs (74 losses and 29 gains) were identified in 82 samples, giving diagnostic yields of 53.2%, 14.7%, 28.5%, and 30.1% in each group, respectively. Mosaicism was observed at a level as low as 25%.

Conclusion
The study highlights the potential for using next-generation sequencing to facilitate genetic diagnoses in the prenatal and postnatal samples that have not been detected by conventional karyotyping and/or chromosomal microarray analysis.