Targeted Sequencing of Maternal Plasma for Haplotype-based Noninvasive Prenatal Testing of Spinal Muscular Atrophy

Min C, Sen L, Dunjin C
Department of Fetal Medicine and Prenatal Diagnosis, The Third Affiliated Hospital of Guangzhou Medical University, Guangzhou, China, GuangDong, China

Objective
To investigate the feasibility study of haplotype-based noninvasive prenatal testing (NIPT) of Spinal Muscular Atrophy (SMA).

Methods
Five families with proband children affected by SMA were recruited from November 2014 to March 2015. Deletions of exon 7 and 8 in SMN1 gene were identified by multiplex ligation-dependent probe amplification (MLPA). A 221.43K NimbleGen EZ array containing 28Kb coding region of SMN1 gene and 2,011 linkage SNPs in the flanking regions was designed for this study. Parental and fetal haplotypes was obtained. Results from the haplotype based testing were compared to MLPA on fetal cells from amniotic fluid or chorionic villi, the current standard diagnostic method.

Results
Parental haplotypes along SMN1 gene and the flanking region were successfully constructed in the five families in this study. Assisted by parental haplotypes information, 1 case to be homozygous deletion of exon7 and exon8, 2 cases to be heterozygous deletion of exon7 and exon8 and 2 normal cases were identified. All these results were consistent with the prenatal diagnosis by MLPA.

Conclusion
Targeted sequencing and haplotype-based noninvasive prenatal testing for SMA are accurate and have potential in clinical applications.