Direct Detection of SMN1 Copy Number by Capillary Electrophoresis for Preimplantation Genetic Testing in Challenging Spinal Muscular Atrophy Cases

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PURPOSE & OBJECTIVES

To evaluate whether capillary electrophoresis (CE)-based preimplantation genetic testing (PGT) can accurately distinguish between zero and non-zero SMN1 copy number in embryos without the need for probe development or linkage analysis.

MATERIAL & METHODS

Fifty samples with known SMN1 status, including Coriell cell lines and embryos, were analyzed. DNA was diluted to picogram levels to simulate embryo biopsy conditions, followed by whole genome amplification (WGA). Amplified DNA underwent CE to assess SMN1 copy presence. Results were confirmed using polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP). The WGA method was validated to minimize allele dropout. Concordance rates between CE and PCR-RFLP were calculated.

RESULTS

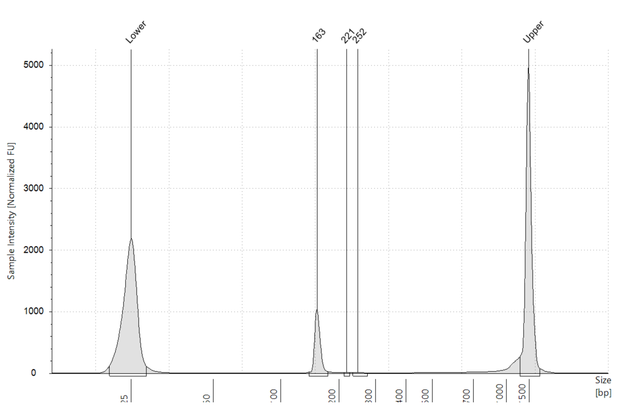


Figure 1: ***SMN1* exon 7 not detected by capillary electrophoresis.** Fragment size (bp) versus normalized fluorescence intensity. No peak is present at the *SMN1* bin, consistent with homozygous absence of *SMN1* exon 7.

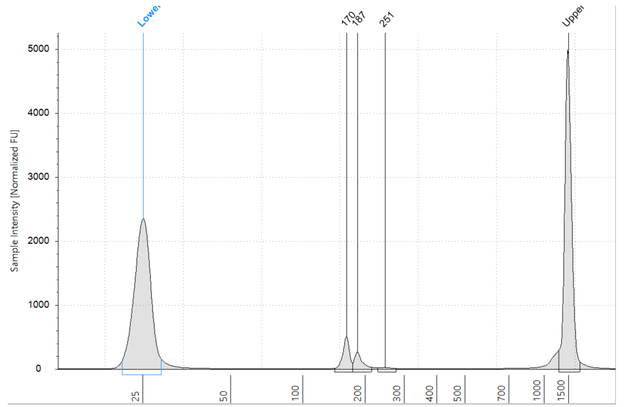


Figure 2: ***SMN1* exon 7 detected (≥1 copy).** Fragment size (bp) versus normalized fluorescence intensity. A peak is present at the SMN1 bin. *SMN1* exon 7 is present; this assay does not resolve copy number.

This method expands PGT options for patients at risk of SMA, including silent carriers, by enabling accurate embryo selection without complex assay customization, thereby improving clinical accessibility and reducing residual disease risk.

RESULTS

CE-based PGT achieved >99% concordance with known SMN1 status. PCR-RFLP results matches CE calls in all 50 samples. The assay reliably distinguished between zero (figure 1) and non-zero (figure 2) SMN1 copy numbers, enabling identification of embryos affected by spinal muscular atrophy (SMA). This approach eliminates the need for probe development or linkage analysis, including in cases involving silent carriers.

CONCLUSIONS

Direct assessment of SMN1 copy number using CE provides a reliable method for detecting SMA-affected embryos. This approach overcomes limitations of traditional preimplantation genetic testing for monogenic condition (PGT-M) strategies that rely on linkage analysis and may be ineffective in certain carrier scenarios.

CONTACT INFORMATION

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