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

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Background

Spinal muscular atrophy (SMA) is an autosomal recessive condition in which muscle weakness and atrophy arise from progressive degeneration and irreversible loss of the anterior horn cells in the spinal cord (i.e., lower motor neurons) and the brain stem nuclei.[1] It is caused by biallelic loss of function of the survival motor neuron 1 gene (*SMN1*).[1] SMA is routinely included in carrier screening offered to those planning or expecting a pregnancy (ACOG, ACMG).[2,3]

Objective

To evaluate whether capillary electrophoresis (CE)-based preimplantation genetic testing (PGT) can distinguish zero from *SMN1* copy number in embryos without probe development or linkage analysis, and demonstrate clinical utility in challenging SMA cases.

Design

Analytical validation study with retrospective chart review.

REFERENCES

1.Prior TW, Leach ME, Finanger EL. Spinal muscular atrophy. GeneReviews. 2024. 2.ACOG Comm Opin No. 690. Carrier screening in the age of genomic medicine. Obstet Gynecol. 2017;129:e35–40. 3.Gregg AR, et al. Screening for autosomal recessive and X-linked conditions. Genet Med. 2021;23:1793–806.

Materials and Methods

50 samples with known *SMN1* status including Coriell cell lines and embryo specimens

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DNA was diluted to picogram concentrations followed by whole genome amplification

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Amplified DNA underwent CE to assess *SMN1* copy presence

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Confirmation using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP)

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Concordance between CE, PCR-RFLP and known *SMN1* status was calculated

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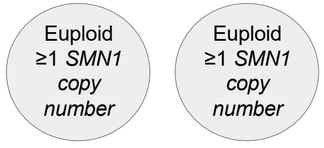
Clinical application was assessed in two at-risk couples undergoing PGT for SMA

Results

99% concordance with known *SMN1* status with PCR-RFLP confirming all concordant results.

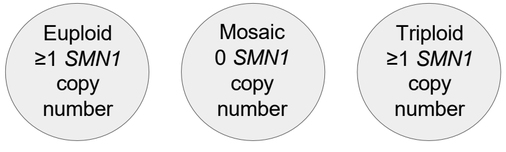
Case 1

Both partners were increased-risk SMA carriers. Conventional PGT-M was not feasible because phase determination could not be established, and no informative family members were available for linkage analysis.



Case 2

Both partners were confirmed SMA carriers.



Conclusion

Direct assessment of *SMN1* copy number using CE provides a reliable method for identification of SMA-affected embryos and expands access to PGT in cases where traditional linkage-based approaches are not feasible, including unphased or silent carrier scenarios.