Beyond Segmental Aneuploidy: Unique Challenges In Evaluating And Testing Microdeletions And Microduplications Via PGT-M

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INTRODUCTION

- PGT-M can be used to test for both single-gene disorders and small chromosomal deletions/duplications (microdeletions and microduplications).
- These microdeletions/duplications are typically <5 Mb and involve gains or losses of chromosome segments with well-defined clinical impacts.
- PGT-M is usually performed using linkage analysis that compares genetic markers between the egg and sperm providers and embryo biopsies.
- Direct mutation analysis for microdeletions or microduplications is often limited, making linkage analysis essential for accurate testing.
- PGT-M for microdeletions/microduplications typically requires a second generation for linkage analysis

OBJECTIVES

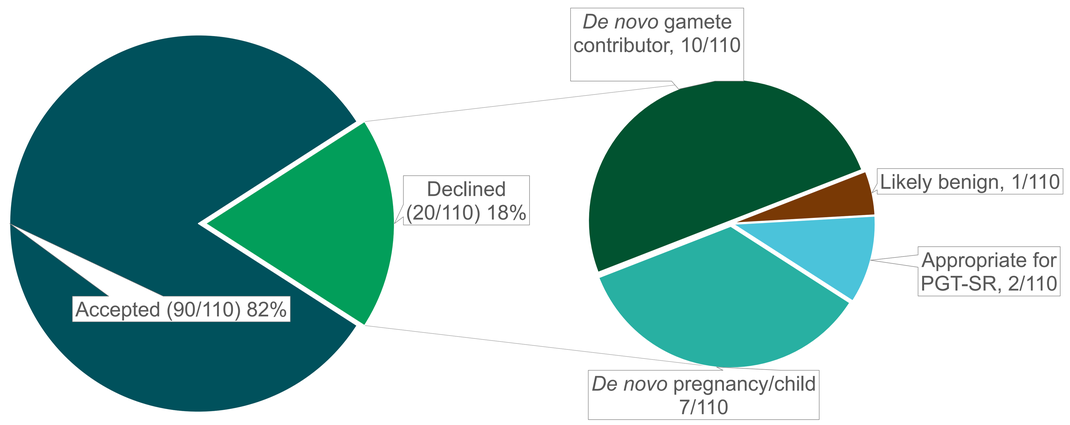
To describe the experience of one PGT-M laboratory with microdeletion and microduplication cases referred for PGT-M

METHODOLOGY

- Retrospective chart review
- PGT-M January 2023 - August 2025
- Conducted at CooperGenomics laboratory, Livingston, NJ

RESULTS

Microdeletion And Microduplication Cases Referred For PGT-M



Over this 2.5-year period, 110 cases involving microdeletions or microduplications were referred for PGT-M testing.

Key Findings

90 patients completed PGT-M for microdeletions or microduplications (Table 1)

All accepted cases involved a gain or loss ≤5 Mb in size, with 14 between 2-5 Mb, and 75 variants smaller than 2 Mb (Table 1)

77 of these variants were identified in a pregnancy, termination of pregnancy (TOP), or in a child

Losses or gains of chromosome 22q were the most common reason for referral (Table 2)

Table 1. Microduplication/Microduplication Cases Tested by PGT-M

	Microdeletions	Microduplications
Cases tested	48	42
Average size (Mb)	0.985	1.368

Table 2. Characteristics of PGT-M cases involving 22q11.2

	# of cases	Maternal inheritance	Paternal inheritance	Average size (Mb)
22q11.2 microdeletion	5	3	2	0.92
22q11.2 microduplication	8	4	4	2.35

CONCLUSIONS

- Chromosomal microdeletions and microduplications often cannot undergo direct mutation analysis, making PGT-M infeasible for many *de novo* cases.
- Most cases require a second-generation relative to establish linkage, limiting PGT-M case acceptance.
- These variants are smaller than the resolution of standard PGT-A, so standard PGT-A is not typically a viable alternative for detection.
- Microdeletions/microduplications differ from PGT-A–detected segmental aneuploidies due to their small size and inherited nature, complicating detection.
- In 22q11.2 cases, duplications aligned with expected sizes, but inherited microdeletions were even smaller than typical, both falling well below PGT-A resolution.

IMPLICATIONS

These findings highlight the need for enhanced PGT-A detection capabilities and refined PGT-M workflows to better address small, inherited copy-number variants.