Clinical-grade whole genome sequencing-based haplarithmisis enables all forms of preimplantation genetic testing

Anouk E. J. Janssen, *et al. Nature Communications* 15:7164, 2024

Presenter: Rangsinee Songphim (宋麗芬) **Date/Time:** 2026/01/08 16:20-17:10

Commentator: Dr. H. Sunny Sun **Location:** Room 601, Med Collage Building

Background

Preimplantation genetic testing (PGT) has played an important role in detecting embryonic defects before *in vitro fertilization* (IVF) implantation. Nevertheless, traditional PGT offered with each different purpose of PGT-A for aneuploidy screening, PGT-M for monogenic disease, and PGT-SR for structural aberrations is commonly provided in isolation. These tests are still labor-intensive and limited by partial genome representation, inability to discriminate complex genomic loci, and incomplete accuracy in consanguineous couples.

Objective

This study aims to establish and validate whole genome sequencing-based method for PGT (WGS-PGT) as a universal PGT approach, all in one single assay with improved resolution, throughput, and diagnostic accuracy compared to what is currently possible.

Results

Clinical validation demonstrated that WGS-PGT provides a single, comprehensive platform applicable to all PGT indications while substantially reducing key technical limitations of conventional workflows. WGS-PGT decreased whole-genome amplification-related artifacts, expanded genome-wide coverage by more than fourfold, and shortened wet-lab processing time by approximately 2.5-fold. At 10X coverage, WGS-PGT enabled high-resolution haplarithmisis and direct single nucleotide variant (SNV) detection, resolving incomplete haplarithmisis in complex or de novo PGT-M cases. In addition, haplarithmisis-based analysis accurately determined the segregation origin of aneuploidies and quantified mosaicism levels above 10% (PGT-AO). For PGT-SR, WGS-PGT distinguished normal from balanced embryos and mapped breakpoints at near base-pair resolution, while for PGT-MT it achieved high mitochondrial coverage (>100X) and accurate heteroplasmy quantification, showing close concordance with PCR-based restriction fragment length polymorphism (PCR-RFLP) as the reference method.

Conclusions

WGS-PGT is a universal, configurable, and clinically applicable test encompassing all types of PGT in a single assay. It is superior to conventional methods in sensitivity, genome coverage, and diagnostic potential, and represents a transformative advance in reproductive genetic testing.