

Genome and epigenome approaches in human assisted reproduction

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Propositions

1. Compositionally different *in vitro* fertilisation (IVF) culture media are associated with similar DNA methylation signatures in both cord blood and saliva (this thesis).
2. The demonstrated differential methylation at growth-related sites between assisted reproductive technology (ART) and naturally conceived neonates is not replicated in culture medium cohorts despite reported birth weight differences (this thesis).
3. Genome sequencing, alongside combined direct and indirect mutation detection, offers a simple, scalable, and universal option for preimplantation genetic testing of IVF embryos (this thesis).
4. Methylome-based non-invasive prenatal testing (NIPT) has several potential applications in evaluating maternal-fetal health, including identifying the fetal fraction for genetic testing and as a biomarker for pregnancy pathologies such as pre-eclampsia (this thesis).
5. Standardised outcome measures, assessable during pre-implantation embryo development and pregnancy, are needed to evaluate the safety and efficacy of assisted reproductive technology (ART) innovations, as prospective long-term follow-up studies are not feasible in this context.
6. Single-cell (low-input) multi-omics methods are critical to understanding molecular interplay in scarce, heterogeneous, or rapidly evolving specimens.
7. The recent finding that human naïve pluripotent stem cells can spontaneously form blastoids suggests that models for early embryonic development will become available soon.
8. The current trend towards increasing parental age at conception is driving a strong demand for more effective IVF procedures.
9. Given that artificial intelligence can be used to integrate data from disparate sources, it has many potential applications in (reproductive) healthcare; for instance, combining morphological and genetic data from embryos for quality assessment.