# Non-invasive preimplantation genetic diagnostics

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**Statement of the Problem**: The number of assisted reproductive techniques is increasing due to rising infertility rates in highly industrialized countries. Advanced maternal age increases the risk of fetal aneuploidy, reducing implantation and successful pregnancy chances. Non-invasive pre-implantation genetic testing for aneuploidy has potential, but its practical implementation in routine IVF centers is yet to begin. Our work group developed a clinically applicable NIPGT strategy using Spent Culture Media (SCM) for testing embryos, based on Next-Generation Sequencing (NGS) technology.

**Methodology and Theoretical Orientation**: For our proof-of concept study we sequenced cell-free embryonic DNA from SCM of Day 3 and Day 5 embryos fertilized with Intra Cytoplasmic Sperm Injection (ICSI) and the corresponding blank culture media as a background control. The MALBAC WGA method was used to amplify DNA from the culture media samples and the blank control media as well. Sequencing was performed on Illumina 6000 platform and embryonic chromosomal abnormalities were identified by an optimized bioinformatics pipeline applying a Copy Number Variation (CNV) detecting algorithm Figure 1.

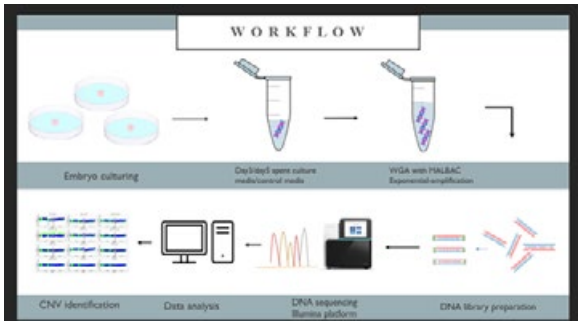


**Figure 1**. Our workflow from sample collection to copy number variation identification. 1. Collection of day 3/day 5 embryonal culture media after embryo implantation. 2. Amplification of gDNA in the sample. 3. New Generation Sequencing. 4. Data analysis by bioinformatical methods. 5. Copy number variation identification and statistical analysis.

**Findings**: Analysis of DNA profiles of embryonic SCM demonstrated that higher gDNA copy number is associated with impaired intrauterine development and indicated miscarriage outcomes. We found some chromosomal abnormalities that occur only in a specific region of chromosome 18, where two important genes are located which are associated with congenital abnormalities and involved in various cellular processes

and can be related to Edwards syndrome. In some cases, the chromosomal ploidy aberration was found to be multiple, which can be irreconcilable with healthy embryonic development and embryonic viability.

**Conclusions**: In the recent presentation we aim to demonstrate the comprehensive workflow covering both wet and dry-lab procedures supporting a clinically applicable strategy for NIPGT-A. The described integrated approach of non-invasive evaluation of embryonic DNA content of the culture media can potentially supplement existing pre-implantation genetic screening methods.

## Biography

Henrietta Orsolya Gellen in a clinical laboratory researcher graduated in 2021. She is a second year PhD student at Pecs University, Faculty of Medicine Doctorate School of Medical Sciences; in addition, she is also involved in education by teaching the Modern Methods in Molecular Genetics course in the MSc program. She's a member of the National Laboratory on Human Reproduction since 2021. Her research focuses on developing non-invasive molecular diagnostic techniques on embryonic culture media to improve implantation procedures and increase success rates.

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