Scientific Summary of 22nd International Conference on Preimplantation Genetics, Leuven, Belgium, April 7-9, 2025

The 22nd International Conference on Preimplantation Genetics took place in Leuven, Belgium, coinciding with the Hosting University's 600th anniversary celebrations. Held at the historic Irish College, the event brought together 250 leading scientists and key opinion leaders from over 40 countries to discuss the progress and future of preimplantation genetic testing (PGT), with the conference theme, *"Insights from and for PGT"*. The meeting showcased the latest discoveries in embryo and oocyte biology—many of which have emerged directly from PGT—and presented cutting-edge technological advances driven by these biological insights. Overall, this high-level scientific meeting underscored a dynamic exchange: insights gained from PGT are deepening our understanding of reproductive biology, while those insights continue to fuel innovation in embryo selection and genetic testing technologies.

With its keynote speakers, the congress returned to its *raison d'être*: genetics. The meeting opened with a presentation by Professor Han Brunner, who shared his research on the consequences of being cariers of recessive disorders. His work demonstrated that, at the population level, carriers of recessive conditions experience a slight selective disadvantage. Dr. Charlier presented a study on *de novo* mutation rates in cattle breeds. Her findings suggest that mutation rates are higher in IVF/IVM-derived cattle embryos compared to those conceived via *in vivo* fertilization. She also revealed that the mutational signatures differ between these two modes of conception. Dr. Vermeesch explored the mechanisms underlying the origins of haploidy and polyploidy, providing fresh insights into these fundamental genomic processes.

The use of PGT-A is rapidly expanding—not only in its widespread implementation to improve IVF live birth rates, but also in its scope. Several groups presented data showing how integrating genotypic information enhances the detection of chromosomal anomalies, thereby improving IVF outcomes. The growing trend toward incorporating genotyping is clear, with both commercial and academic teams demonstrating their added clinical value. Another notable trend is the rise of non-invasive preimplantation genetic testing. Comprehensive PGT programs that include genotyping and haplotyping are generating vast genomic datasets from both euploid and aneuploid embryos. Analyzing this data is yielding important new biological insights. For example, Drs. McCoy, Gruhn, and Tsuiko identified genetic variants that influence the risk of maternal meiotic aneuploidies. Furthermore, extracting information about ploidy variation has provided new understanding of the frequency of ploidy abnormalities and the mechanisms underlying genome-wide segregation errors.

The origins of PGT lie in its primary goal: preventing the transmission of life-threatening genetic variants from parents to their offspring. Today, identifying couples at risk of carrying such disorders is increasingly population-based, aided by the growing power and accessibility of genome sequencing technologies—now expanding toward whole-genome analysis. Expanded carrier screening, a key focus in this domain, was addressed by Dr. Goldberg. Its impact is already evident in PGT laboratories, with a sharp rise in PGT-M cycles, as presented by Dr. Rechitsky. Beyond detecting inherited conditions, population screening is also shedding light on broader reproductive issues, including the causes of infertility (Dr. Sako) and the role of mitochondrial variation (Dr. Spits). While embryo screening has

traditionally relied on arrays or targeted sequencing, the field is now moving toward whole-genome sequencing (WGS) of embryos. Drs. Munné and Zamani presented data on embryonic WGS programs, which may represent a turning point in PGT. WGS not only allows for the detection of inherited variants but also holds the potential to identify *de novo* mutations. If proven sufficiently accurate and specific, this approach could eventually enable PGT to prevent the transmission of *de novo* pathogenic mutations. Looking further ahead, the prevention of pathogenic variants may extend beyond embryo selection. Genome editing of embryos—presented by Drs. Wells and Fogarty—offers a glimpse into future possibilities. They demonstrated how genome editing cannot only correct mutations but also serve as a tool to study lineage specification and early developmental processes in embryos.

Lineage tracing and understanding the pathways and mechanisms leading to cell differentiation is also of importance to improve on embryo selection in the future, addressed by fascinating talks on blastoid/ embryoid models to decode early threatening or life embryogenesis. Dr. Pasque showed how embryoids can be generated and how they unmask the secrets of the first phases of differentiation. Dr. Cantas has developed models which recapitulate development after 10 days and demonstrated how different tissues are developing. Magic movies of the first day of life!

While the field has improved IVF success rates, a substantial number of transferred embryos does not implant or make healthy live births. Understanding why this is the case and further improving the success rates will require novel technologies. Different novel methodologies enabling improved genetic analysis were presented: Dr. Voet demonstrated how single-cell multi-omics analysis, combining genomic, transcriptomic and epigenomic analysis of single embryonic cells provides extra information on the cellular and molecular status of the embryo. Dr. Choy showed how haplotyping provides extra information on ploidy and Dr. Madjunkova showed how transcriptome data provides addition information about competent embryos.

Combining those different data types, especially the development and implementation of polygenic risk scoring in embryo selection, both technical, clinical and socio-ethical aspects were debated by Dr. Marin and Dr. Siermann. The expanding scope and increased importance of PGT will keep on raising ethical, societal and clinical challenges.

Thus, the field is progressing with new sequencing technologies and novel insights propelling the industry towards ever better selection and success rates.