

PGDIS Newsletter

21st INTERNATIONAL CONFERENCE ON PREIMPLANTATION GENETICS

Kuala Lumpur, 6-8 May 2024

August, 2023

The recent PGDIS Paris Conference reviewed the dramatic progress and outlined directions for future development of PGT technology, presented by leading members of PGDIS, who went beyond the beaten path. First, it was evident that PGT-M demand is growing throughout the world. Society is becoming aware of the risks for genetic disorders and the potential to avoid the transmission of rare diseases to offspring. Expanding carrier screening (ECS) is swiftly becoming a part of pre-conceptual IVF counseling programs in many countries. Consequently, more and more couples are discovered to be at risk of passing on a genetic disease and can now opt for PGT-M, with a resultant steep increase in requests. Interestingly, not only severe developmental disorders are on the top of the list, but also couples wish to select against cancer predisposition mutations with these becoming a major driver of the field. One could say: fasten your seatbelts: with population-based carrier screening on the horizon, PGT-M is bound to grow. In addition, it is obvious that the PGT-M and PGT-A worlds are merging. When performing PGT-M it seems logical to select the embryo with the best implantation potential. Thus, comprehensive screening enables exactly this and logically will improve PGT transfer success rates.

The discussion about the value of PGT-A and how to deal with mosaicism during PGT-A is slowly coming to a consensus. Mosaicism is real at all stages during embryonic development. Although technical differences amongst laboratories may cause variation in the reported aneuploidy rates, some basic research studies measuring the variation in all cells of embryos leave no doubt that mosaic aneuploidies are relatively common. The dated concept of avoiding transfer of all mosaic embryos has evolved and we now need to use this information in a sensible way to progress. Whether or not to transfer mosaic embryos has been openly discussed and debated and now a more rational approach has been proposed (see also the PGDIS guidelines on this topic on the website).

And of course, new approaches for embryo selection have also been proposed. First and foremost, a consensus is arising that non-invasive preimplantation genetic testing (NIPGT) for aneuploidy may be an alternative to invasive testing. However, it has been suggested that samples should be taken a little later during development (day 6) and a series of technical measures implemented to avoid contamination- both of which need to be considered when considering process logistics. Nevertheless, the method has been gathering a lot of experimental investigation and is likely to stay. Second, different hypotheses are put forward on why 30-50% of all embryos still fail to implant.

We saw pilot studies exploring trophoblast transcriptome and epigenome analyses to improve outcome. Finally, we saw future directions for gene therapy. On the one hand, CRISPR/Cas9 germline gene editing is still in its infancy but is likely to become a clinical/societal reality in the next decades. On the other – preventing severe *de novo* mutations still must start and the first seeds to enable this were planted.

The theme of the next conference will be technological developments with emphasis on 'PGT – Beyond PGT-A', reflecting several important aspects of our future efforts. Firstly, there is a strong desire of the PGDIS to encourage young scientists to attend and contribute to the meeting. Early-career basic and clinical scientists are urged to submit their experience, for presentation. Secondly, there is a sense that PGT is entering a new phase, as some strategies, formerly considered experimental or niche, reach

maturity and enter mainstream use, and innovative technologies begin to open entirely new avenues for understanding and interacting with gametes and preimplantation embryos. Finally, recognition of the appropriate level of information and counseling between patient and clinic regarding PGT application and outcomes relies on appropriate involvement and understanding by all specialized clinicians and counselors throughout the process. Clearly, the scope, the toolbox, the caretakers, and the population using PGT is growing and maturing.

Looking forward to welcoming you to 21th International Conference of Preimplantation Genetics, which will be held in One World Hotel, Petaling Jaya, Kuala Lumpur, Malaysia, May 6-8, 2024. The progress in the organization of the Conference may be followed in the Conference website (under development), or PGDIS websites (www.pgdis.org).

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