Popularised Summary

Preimplantation genetic testing for aneuploidies (PGT-A) is a procedure that can be performed as part of a normal IVF cycle and involves testing embryos to confirm if they have the correct number of chromosomes. During this process, highly trained scientists microscopically remove a few cells from the outer layer of the embryo, which can then be analysed. The results generally allow embryos to be classified as either normal or abnormal, and subsequently an embryo free of abnormalities is selected for transfer or frozen for future use.

Over the past years the technology used for PGT-A has undergone several improvements. Recently, these have also allowed the reliable detection of so-called “mosaic” embryos. These are embryos that contain both normal and abnormal cells. At present, fertility experts remain torn on whether these embryos should be considered for transfer. Current studies suggest that mosaic embryos are less likely to implant and more likely to miscarry compared to normal embryos. However, several healthy babies have also been born from mosaic embryos. In such cases it has been speculated that abnormal cells may be eliminated while the embryo develops. As the biopsy only represents a small portion of the embryo, the challenge is estimating the extent of abnormal cells and what this means for pregnancy.

As part of this thesis we examined a substantial number of normal, abnormal and mosaic embryos donated to research. We used improved testing strategies to compare four portions of the same embryo and determined that up to 38% of embryos contained some abnormal cells. In certain cases, the abnormal cells were not contained in the part of the embryo that forms the baby, but rather the portion that contributes to the placenta. This suggests that some mosaic embryos may in fact be viable and able to progress normally.

We then used a model of implantation to examine the chromosomes and outcomes of normal, abnormal and mosaic embryos. This model allowed for embryos to be maintained in the lab for up to 12 days. While a portion of mosaic embryos failed to develop, over half progressed normally, with no abnormal cells found at later stages. To ensure that our model was reliable, in a separate study, we evaluated numerous day 12 embryos in detail. We were able to identify precursor cells of various tissue types within the embryo outgrowths, demonstrating that they mimicked normal human development. We also focused on identifying founder cells of eggs and sperm, the origin of which is currently unknown. Ultimately, our
results confirmed that our model was valuable for studying early human development, holding
great promise for future research.

For patients struggling with infertility and limited embryos, mosaic embryos may offer new hope. However, it is important to realise that the potential of mosaic embryos is not as high as that of normal ones. Normal embryos should always be prioritised for transfer. However, mosaic embryos may be recognised as a third category of embryos alongside normal embryos, yet not equivalent to abnormal ones. It is likely that embryos with some abnormal cells have been transferred unknowingly for many years as part of routine IVF cycles. As some mosaic embryos may lead to healthy babies, excluding all such embryos for transfer may compromise treatment outcomes, especially for patients with a low number of embryos. Appropriate counselling is recommended for all couples undergoing PGT-A, especially those considering the transfer of a mosaic embryo.